



**IHS Division of Diabetes
Advancements in Diabetes Seminar**

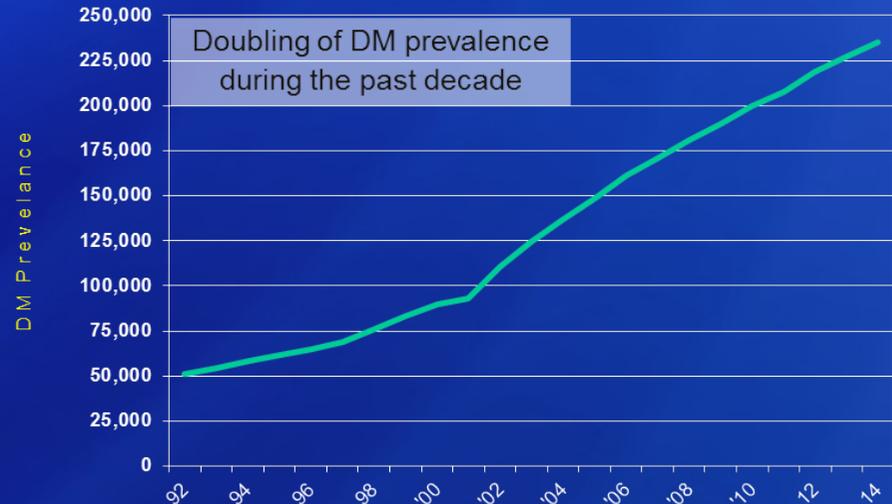
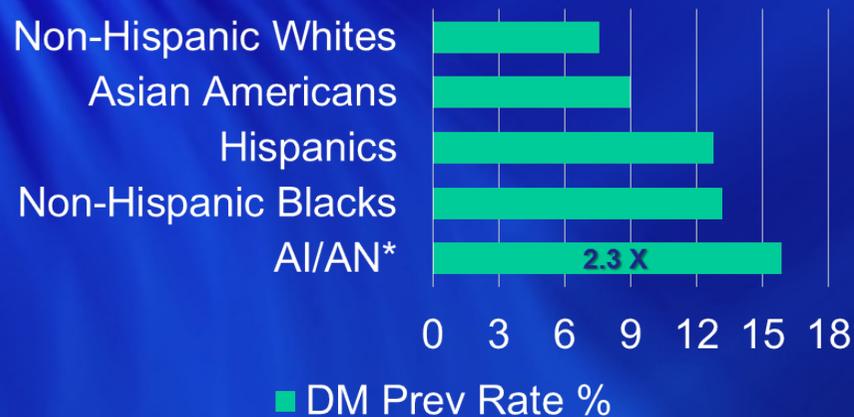
**Clinical Advancements in
Diabetes Eye Care**

Mark B. Horton, OD, MD

**Director, IHS/JVN Teleophthalmology
Program**

Diabetes Mellitus in Indian Country

Rapidly Increasing Prevalence



235,000 AI/AN with DM, 2014

*6%-24% by region

CDC National Diabetes Statistics Report 2014

<http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf>

Epidemic nature of DM paralleled by DR

Ocular Complications of DM

| Ocular Tissue | Conditions |
|----------------|---|
| Lids | Xanthelasma, Blepharitis |
| Orbit | Cellulitis |
| Cornea | Keratitis, Epithelial erosions, Keratitis |
| Iris | Poor dilation, Rubeosis |
| Lens | Transient refraction changes Cataract (and ↓surgical outcomes) |
| Retina | Retinopathy/Maculopathy Retinal vein occlusions Retinal artery occlusions Ischemic syndromes |
| Optic Nerve | Papillopathy, Ant Isch Optic Neuropathy Glaucoma |
| Cranial Nerves | 3 rd , 4 th , 5 th , 7 th CN palsies |
| CNS | CVA associated vision loss |

Ocular Complications of DM (cont.)

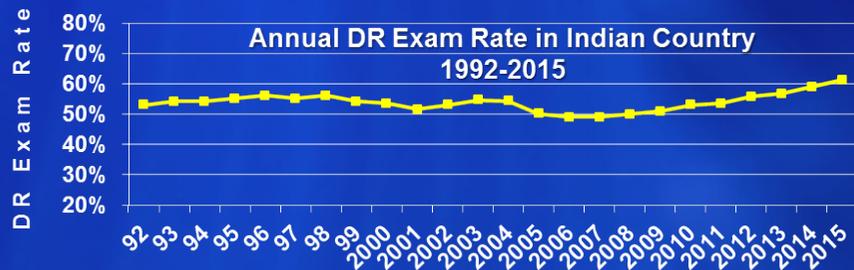
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Ocular Complications of DM (more)

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Diabetic Retinopathy

- Virtually all diabetics eventually have DR
- Diabetic Retinopathy is the leading cause of new blindness in adults
- Blindness due to diabetes can be eliminated by timely Dx and Tx



- Half of AI/AN population with DM
- do not get timely Dx and Tx

Diabetic Retinopathy

Epidemiology

- ~40% prevalence of DR among all DM pts
- 10-20 % of pts with DM have DR at Dx
- Eventually, all diabetics develop DR
 - Type I DM
 - 15 yrs duration -80% with DR, 25% with PDR
 - Type II DM
 - >20yrs duration- >60% prevalence of DR
 - » 30% prevalence of DME
 - >25 yrs duration- 25% with PDR

Diabetic Retinopathy Epidemiology

- Leading cause of new blindness in adults (20-74 y/o); 12,000-24,000 new cases/yr
- Leading cause of moderate vision loss (DME)
- ~4-5% prevalence of high risk DR in AI/AN's



Diabetic Retinopathy

- **DR blindness is nearly preventable by adhering to accepted standards of care and established best practices**
 - **Identify all patients with DM**
 - **Control confounding factors and co-morbidities**
 - **Diagnose level of DR yearly**
 - **Apply timely treatment**

Diabetic Retinopathy Standard of Care

- **Minimum standard- annual eye examination**
- **ADA- American Diabetes Association**
- **AAO- American Academy of Ophthalmology**
- **AOA- American Optometric Association**
- **VHA*- Veteran's Health Administration**
- **DoD- Department of Defense**
- **HEDIS- Health Plan Employer Data and Information Set**

Diabetic Retinopathy Clinical Management

Primary Care Diabetes Team

+

Ophthalmologist / Optometrist

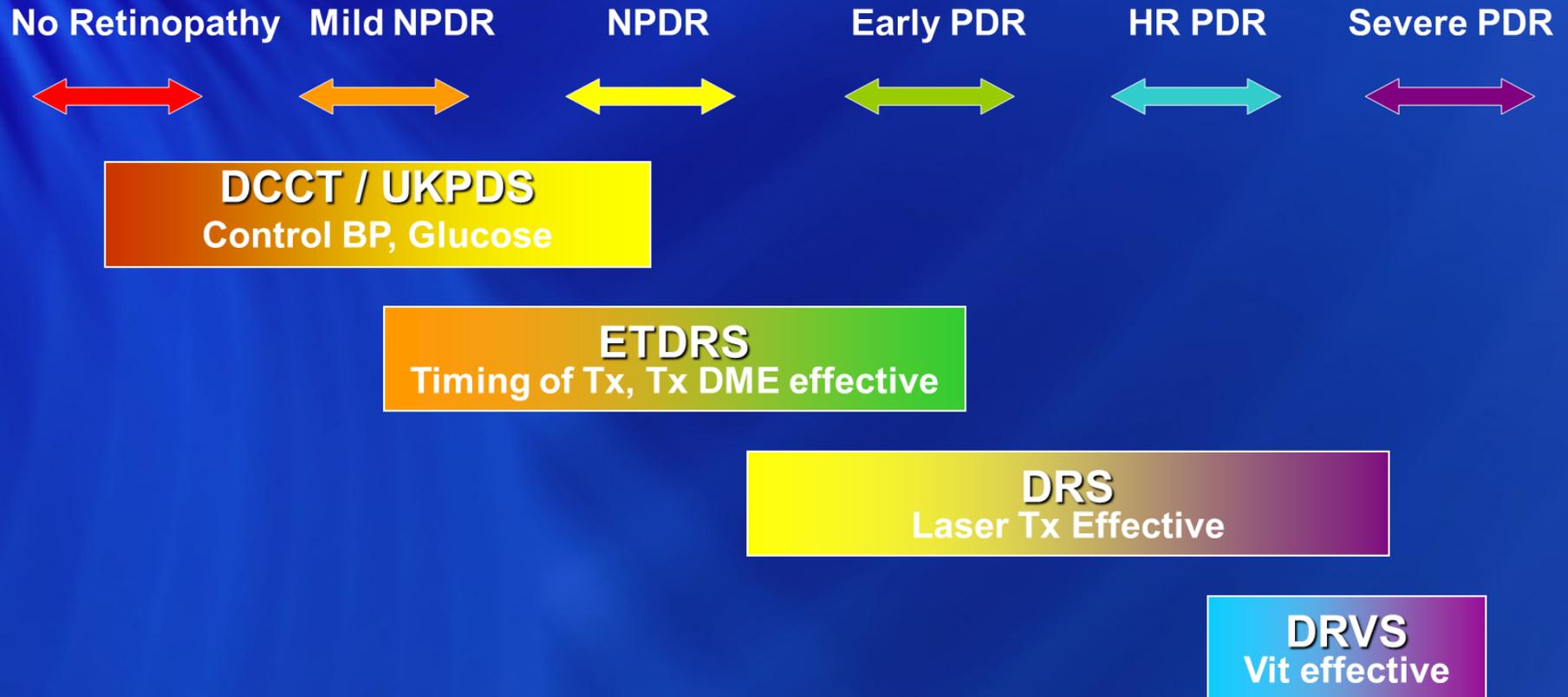


Systemic control

Timely (Early?) diagnosis

Timely (Early?) treatment

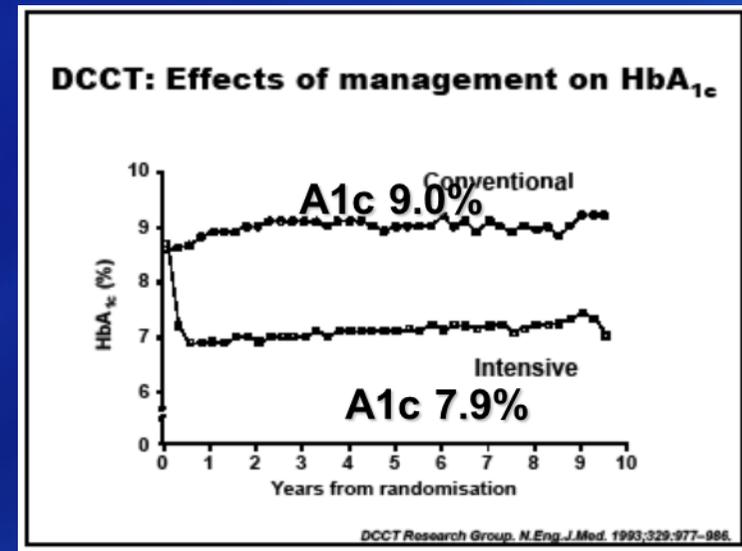
Diabetic Eye Exam and Tx Standards of Care



Diabetic Retinopathy

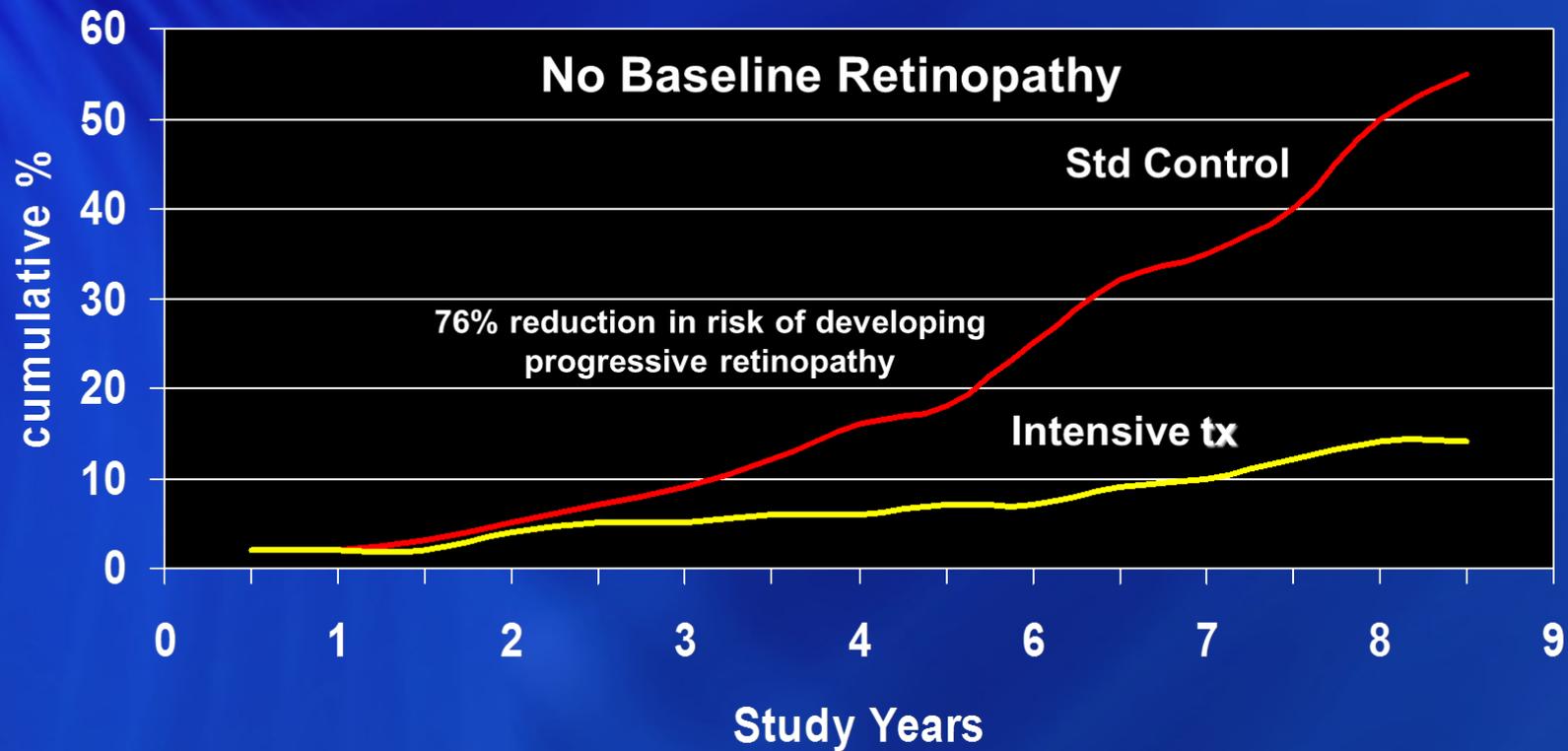
Diabetes Control and Complication Trial (DCCT) 1983-1993

- DM I
- Standard control vs Intensive control
- A1c 9.0 vs 7.9
 - Glucose levels qid
 - Insulin qid or pump
 - Diet and exercise
 - Monthly f/u



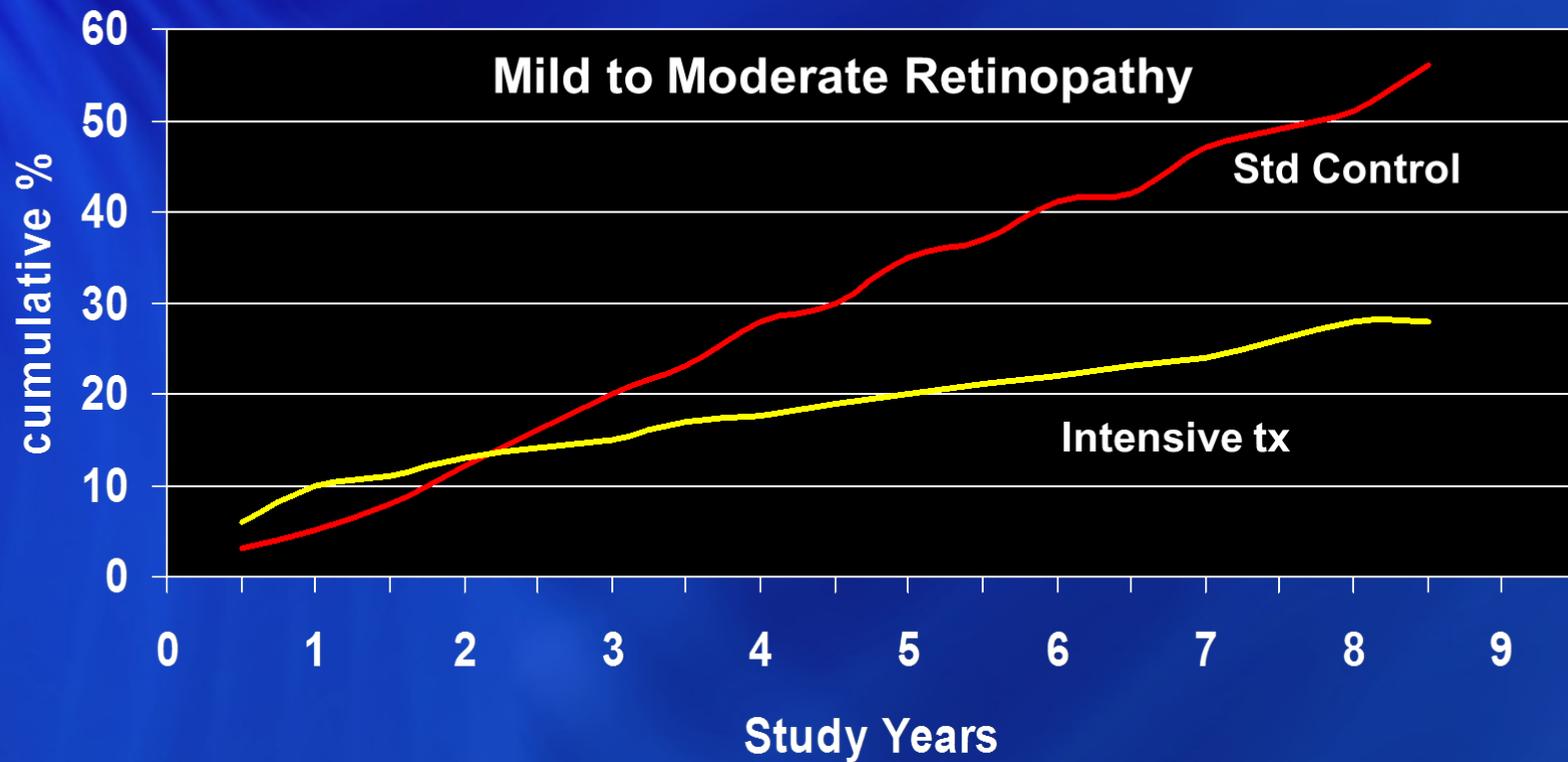
Diabetic Retinopathy

Impact of intensive DM control



Diabetic Retinopathy

Impact of intensive DM control



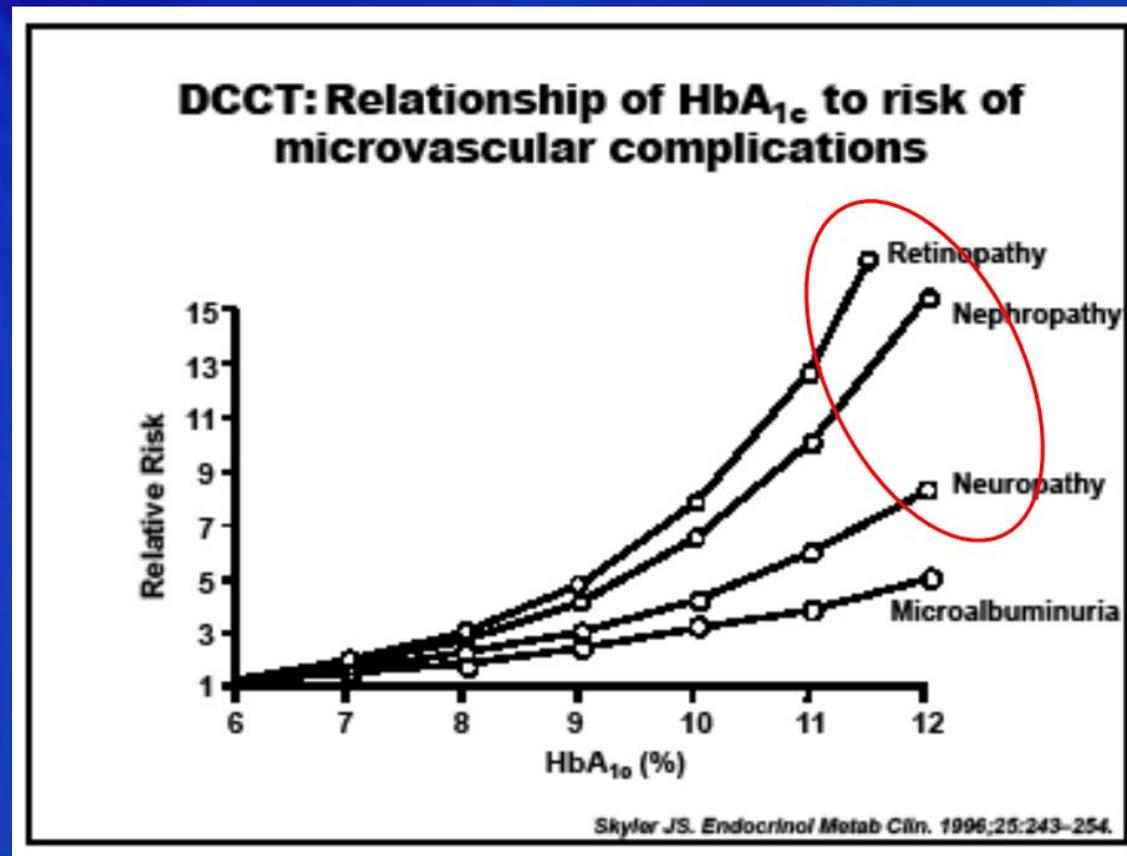
Diabetic Retinopathy

Intensive glucose control- mild-mod DR

- **54% reduction in progression of DR**
- **47% reduction in development of severe NPDR or PDR**
- **59% reduction in need for laser surgery**

Microvascular Complications

Intensive glucose control and end organ Dz



Diabetic Retinopathy

Epidemiology of Diabetes Interventions and Complications (EDIC) 1994-2003

- **DCCT Cohort**
- **Long term effects of conventional vs intensive DM treatment**
- **Nephropathy, microvascular, and cardiovascular complications**

Diabetic Retinopathy

Epidemiology of Diabetes Interventions and Complications (EDIC) 1994-2003

- **Long term benefits of improved control**
- **Metabolic memory**
 - **Effects of control are sustained even after some slippage in the degree of control**
 - **Once the processes leading to MV complications are initiated they are self-perpetuating**

Diabetic Retinopathy

UK Prospective Diabetes Study
(1977-1997)

- **DM II**
- **Standard glucose control (A_{1c} 7.9%)**
VS
Intensive glucose control (A_{1c} 7.0%)
- **Standard BP control (154/87)**
VS
Tight BP control (144/82)

Diabetic Retinopathy

UKPDS

- 34% reduction in DR progression
- 25% reduction in need for laser surgery
- BP control as important as glucose control for lowering risk for DR (<130/85)

Diabetic Retinopathy

UK Prospective Diabetes Study
(1977-1997/2007)

- **Legacy effect of glucose control**
 - Differences in A1c levels disappeared w/l one year of trial completion
 - intense tx group continued to experience significant reductions in MV disease, MI, and all-cause mortality as compared to conventional tx group
- **No legacy effect for intensive BP control**

Diabetic Retinopathy

Confounding Factors for DR

- **Control**
 - **Blood Pressure- 130/85**
 - **Blood Glucose- A1c 6.5%-7.0% (↑ risk of compl)**
 - **Blood lipids**
- **Decrease risk of DR development**
- **Decrease risk of DR progression**
- **Decrease need for laser surgery**

Diabetic Retinopathy

Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) 2005

- 9,765 DM II pts with good glycemic and BP control tx'd with fenofibrate
- 5 year f/u of 1,012 substudy for DR
- *78% reduction* of progression among pts with pre-existing retinopathy
- *31% reduction* in need for treatment (progression to sight threatening DR)

Diabetic Retinopathy

Action to Control Cardiovascular Risk in Diabetes (ACCORD-Eye) 2010

- **10,251 pts with DMII at high risk for CVD**
 - Intensive glycemc Tx (A1C <6.0% vs 7.0%-7.9%)
 - Intensive BP Tx (Systolic <120 mmHg vs <140 mmHg)
 - Intensive lipid Tx (Statin+fenofibrate vs Statin+placebo)
 - 4 year f/u of 3,472 substudy for DR
- **CV endpoint (nonfatal MI, CVA, CV death)**
- **Retinopathy endpoint (DR progression, DR Tx)**

Diabetic Retinopathy

Action to Control Cardiovascular Risk in Diabetes (ACCORD-Eye)

- **CV endpoint**
 - No fenofibrate benefit as compared to statin alone
- **Retinopathy endpoint**
 - Intensive glycemia Tx benefit
 - No intensive BP Tx benefit
 - Fenofibrate Tx
 - No benefit for pts without clinical evidence of DR
 - 38% reduction (9.8%→6.1%) with fenofibrate Tx- strongest effect in mild NPDR (78% reduction, 14.1%→3.1%)

Fenofibrate

Mechanism of Action

- *Not related to lipid effects*
(Field and ACCORD)
- **Non-lipid related mechanisms**
 - Improved endothelial function
 - Anti-apoptotic effects
 - Antioxidant (ROS)
 - Protection of blood retinal barrier (BRB)
 - Neuroprotective effects
 - Anti-angiogenic

Fenofibrate

Patient Safety

- Long hx of fenofibrate use for dyslipidemia with good safety record
- Theoretical risk of interaction with statins not a realized risk with fenofibrate (0.12% incidence) in contrast to gemfibrozil (5%)
- Well tolerated in both FIELD and ACCORD, with and without stains
 - .5% vs .8% serious ADE (placebo : fenofibrate)

Diabetic Retinopathy

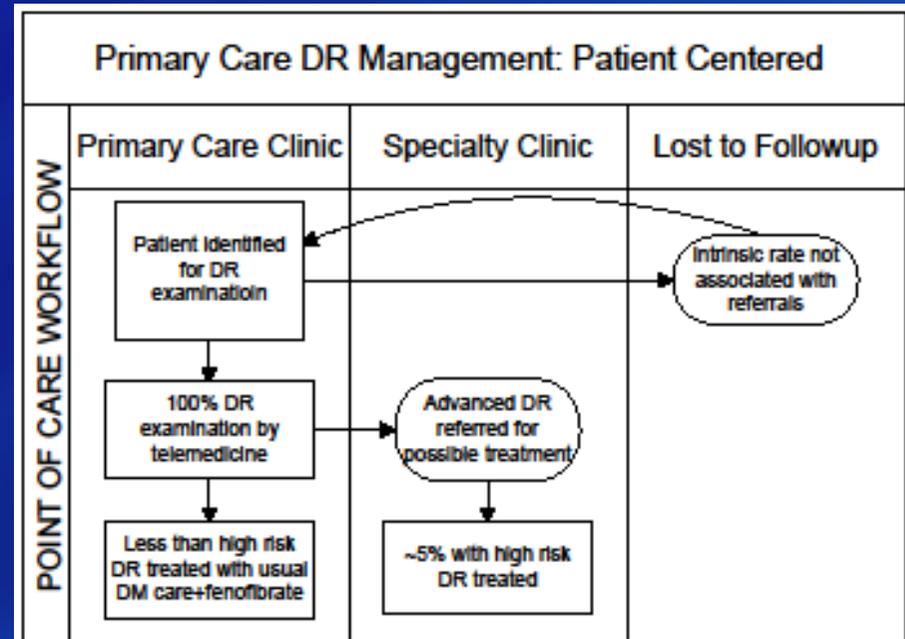
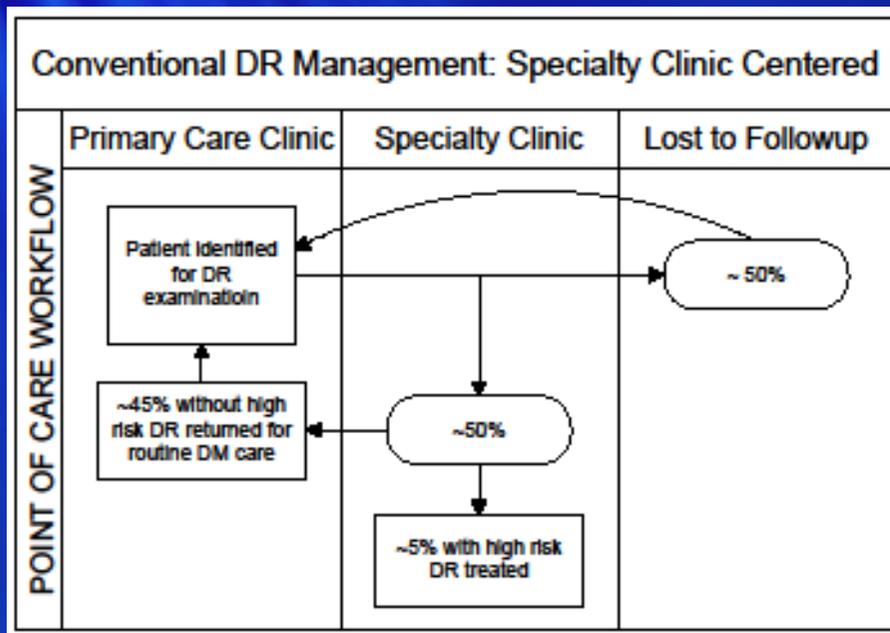
Possible Early Fenofibrate DR Tx Best
Practice in IHS

Proposed Study

Fenofibrate as an **A**gent for **R**educing
Severity and **I**nvasive **T**reatment **E**vents in
Diabetic Retinopathy (**FARSITED**)

Diabetic Retinopathy

Possible Early Fenofibrate DR Tx Best Practice in IHS



Diabetic Retinopathy

Primary Care Treatment with Fenofibrate

- **Treat early in the course of DR**
- **Treat by PCP without a referral**
- **No need for difficult and costly travel to subspecialty eye care**
- **Naturally incorporated in to a primary care based Teleophthalmology-DR program for combined benefits of pt recruitment and treatment**

Diabetic Retinopathy

Primary Care Treatment with Fenofibrate

- **Possible collateral benefits to other microvasculopathic end organ processes**
 - Renal
 - Peripheral neuropathy
- **Far less costly (patient and HC system) to avoid complications than treat complications**

Diabetic Retinopathy

- ***Non-proliferative DR*** **NPDR**
 - Intraretinal hemorrhages **H**
 - Microaneurysms **MA**
 - Venous beading **VB**
- ***Proliferative DR*** **PDR**
 - Neovascularization **NVD/NVE**
 - Hemorrhage
 - Preretinal **PRH**
 - Vitreous **VH**
 - Retinal detachment **RD**
- ***Diabetic macular Edema*** **DME**
 - Fluid accumulation
 - Hard exudates **HE**

Diabetic Retinopathy

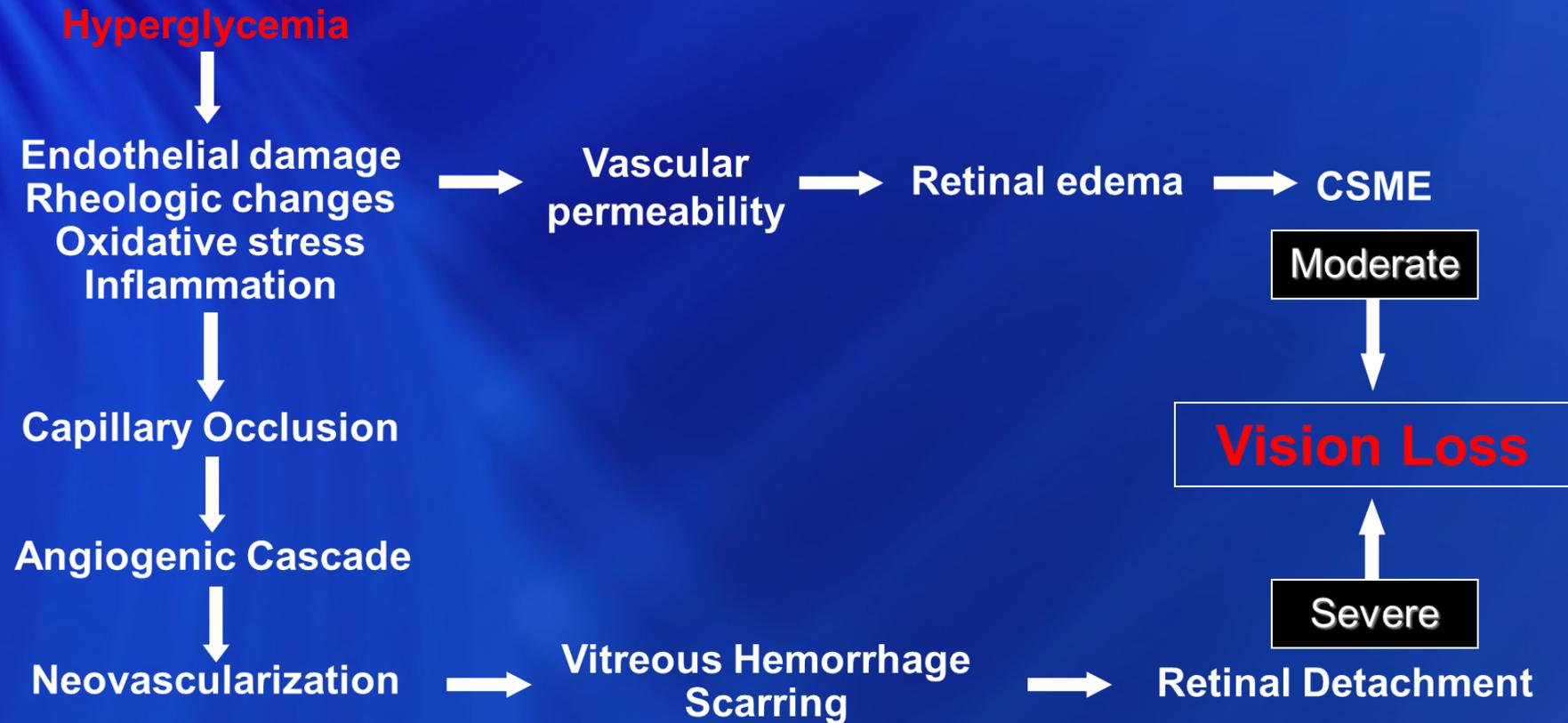
Pathophysiology of Vision Loss

Hyperglycemia



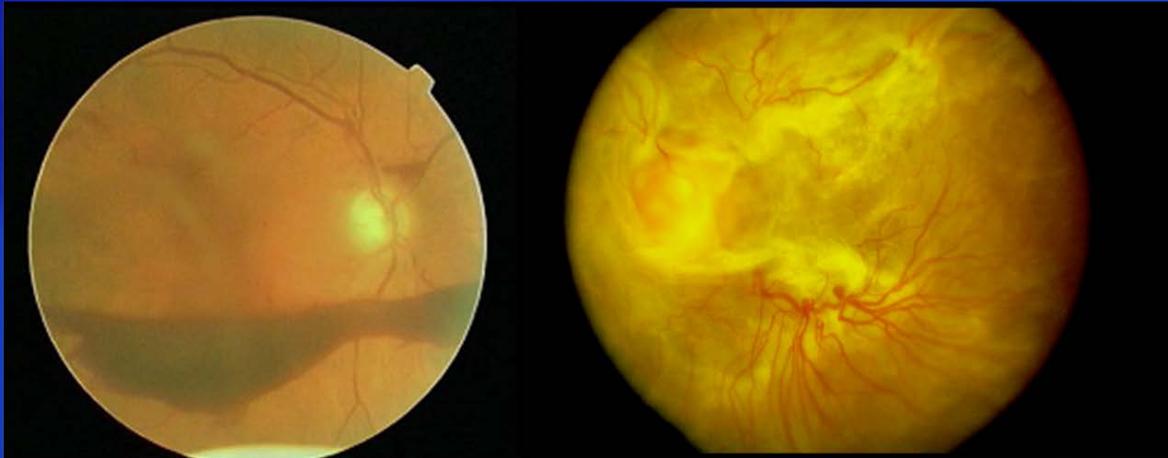
Diabetic Retinopathy

Pathophysiology of Vision Loss



Vision Loss From Diabetes

Vitreous
Hemorrhage



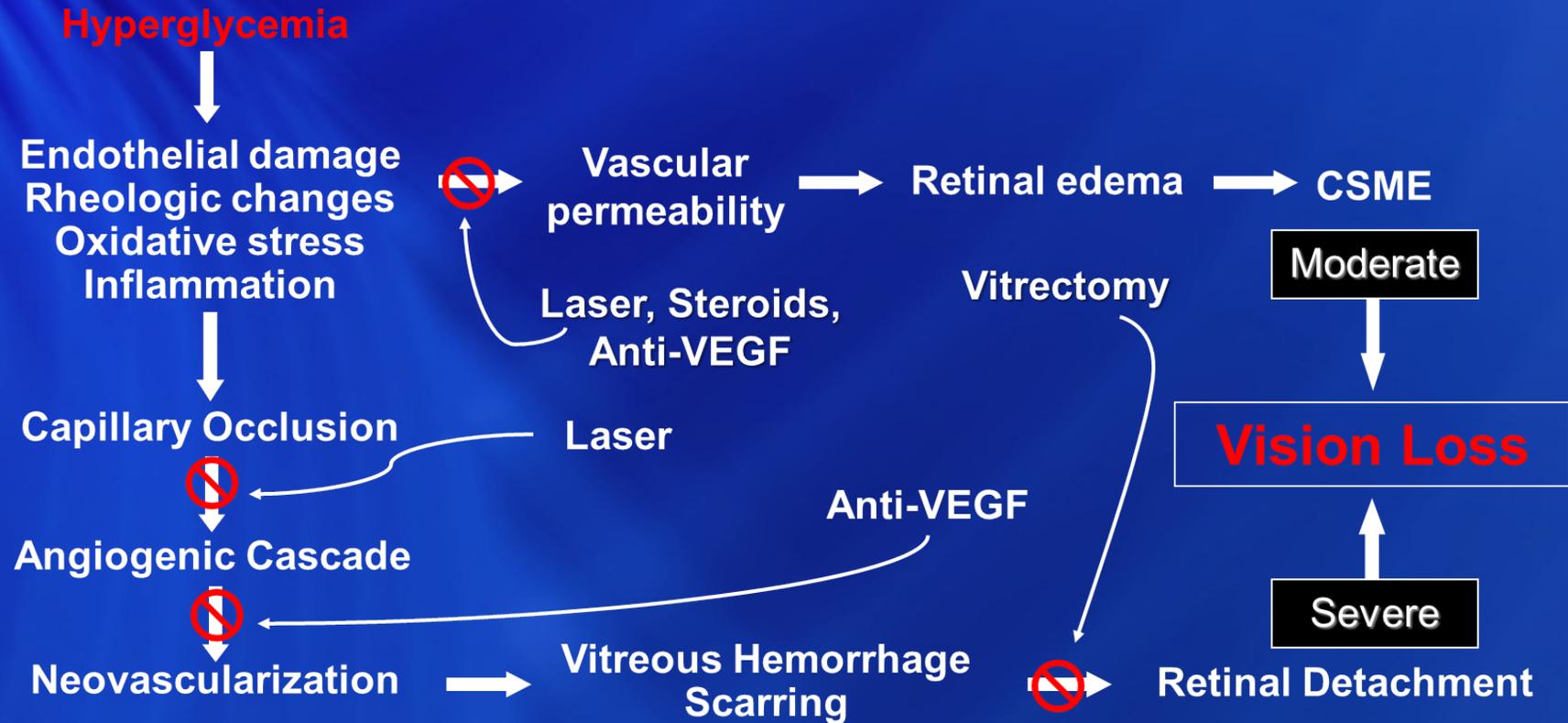
Macular
Edema



Traction Retinal
Detachment

Diabetic Retinopathy

Pathophysiology and Treatment of Vision Loss



Diabetic Retinopathy

International DR Disease Severity Scale

| DR Severity Level | Retinal Characteristics |
|-------------------|--|
| No DR | No abnormalities |
| Mild NPDR | Micro aneurysms only |
| Moderate NPDR | > Just MA, but < severe NPDR |
| Severe NPDR | > 20 intra-retinal hemorrhages in 4 quad Venous beading in 2 or more quad Prominent IRMA in 1 or more quad No PDR |
| PDR | Neovascularization Vitreous Hemorrhage |

Diabetic Retinopathy

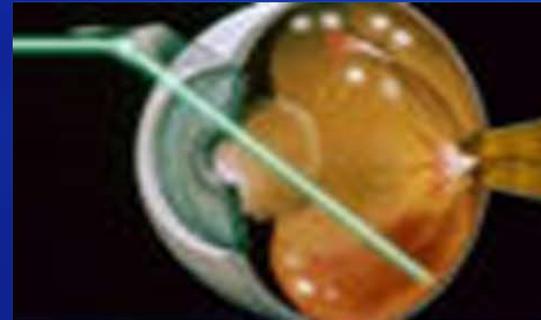
International DR Disease Severity Scale

| DR Severity Level | Retinal Characteristics |
|---|---|
| Macular Edema- not clinically significant | Retinal edema or lipids not threatening the macula |
| Macular Edema- clinically significant (CSME) | Retinal edema or lipids threatening the macula |

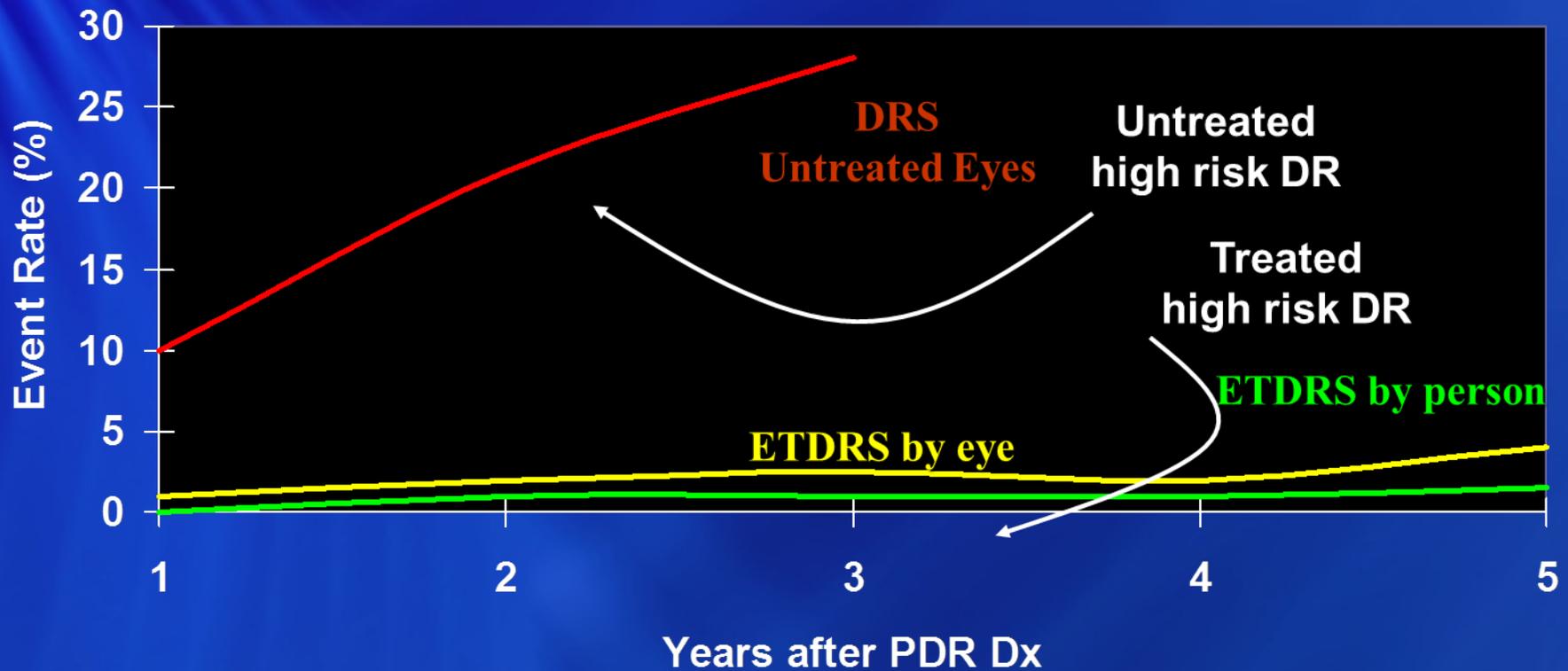
Diabetic Retinopathy Standard of Care AAO Preferred Practice Guidelines

| DR severity | CSME | f/u (mths) | Laser Tx | Focal |
|--------------------|------|------------|----------|---------|
| Minimal NPDR | No | 12 | No | No |
| Mild-Moderate NPDR | No | 6-12 | No | No |
| | Yes | 2-4 | No | Usually |
| Severe NPDR | No | 2-4 | Maybe | No |
| | Yes | 2-4 | Maybe | Usually |
| Low Risk PDR | No | 2-4 | Maybe | No |
| | Yes | 2-4 | Maybe | Usually |
| High Risk PDR | No | 3-4 | Usually | No |
| | Yes | 3-4 | Usually | Usually |

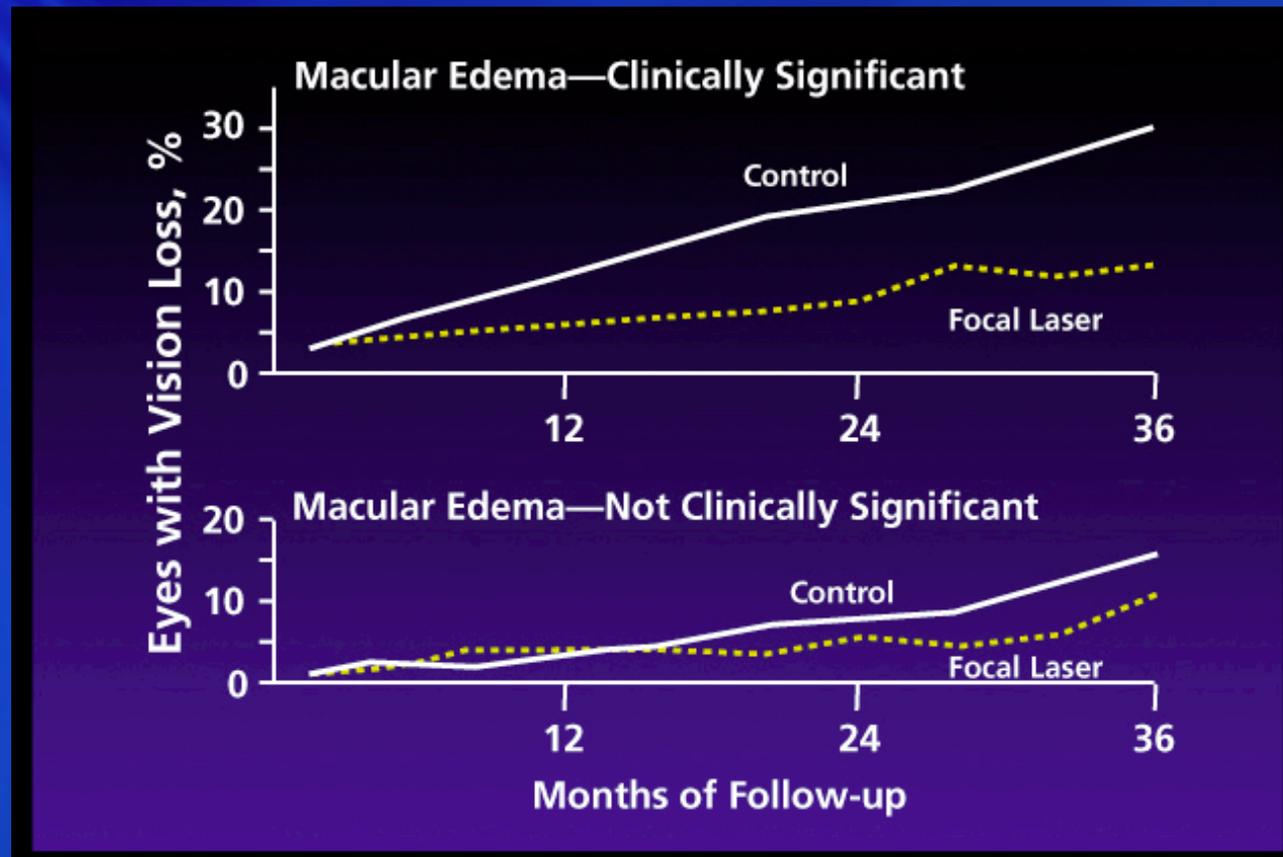
Diabetic Retinopathy- PDR Laser Treatment



Visual Acuity Less than 20/800 Proliferative Diabetic Retinopathy

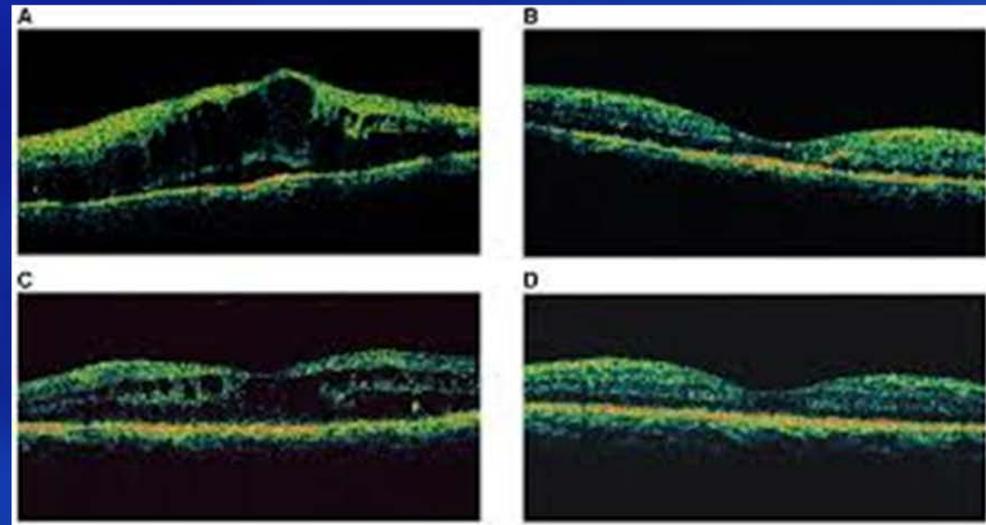


Diabetic Retinopathy- DME Focal Photocoagulation



Diabetic Retinopathy- DME

Anti-VEGF; Steroids



Diabetic Retinopathy

Anti-VEGF for DR

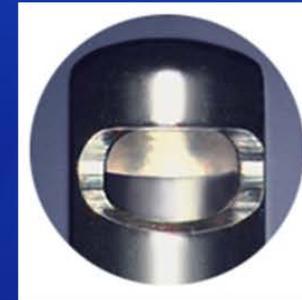
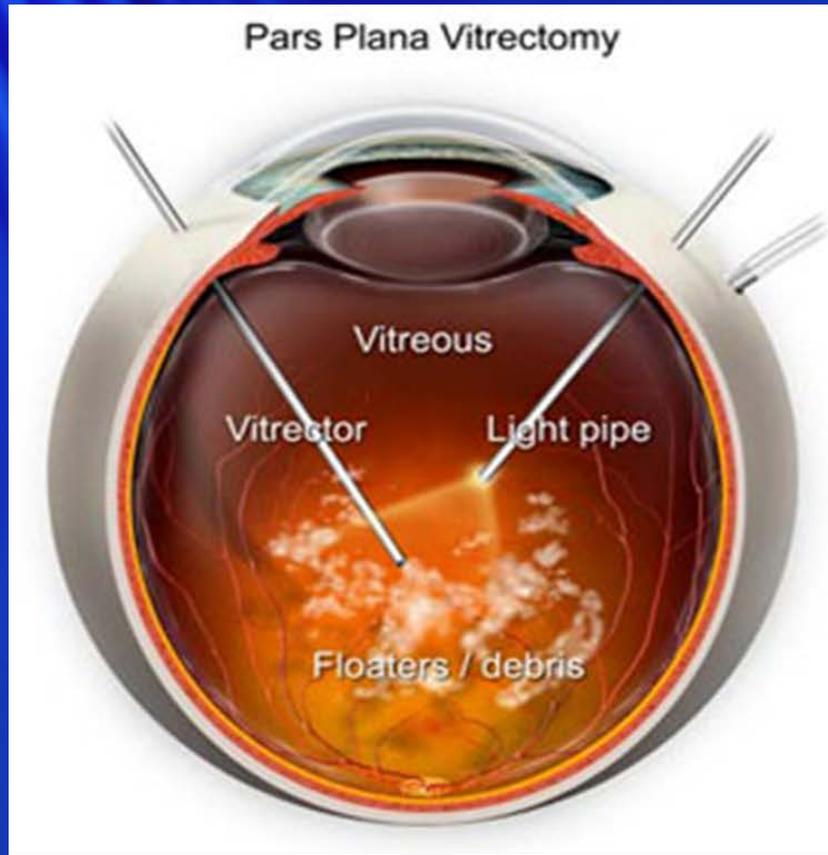
- **Lucentis- (Genetech) \$1,200/dose**
- **Eylea- (Regeneron) \$1,850/dose**
- **Avastin- (Genetech) \$60/dose**
- **Ozurdex- (Allergan) \$1,300/dose**
3-4 months
- **Iluvien- (Alimera Sciences) \$8,800/dose**
36 months

Diabetic Retinopathy- PDR / VH / RD

Vitrectomy

- **Remove vitreous hemorrhage**
- **Allow laser treatment**
- **Repair retinal detachment**

Diabetic Retinopathy- PDR / VH / RD Vitrectomy

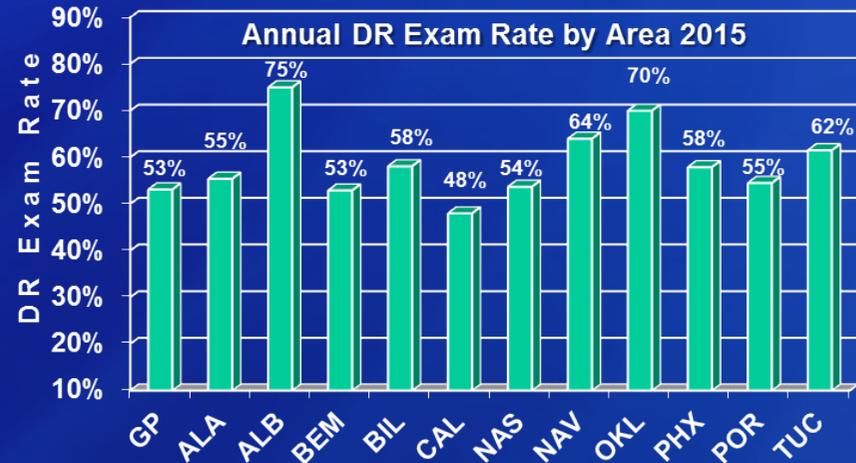
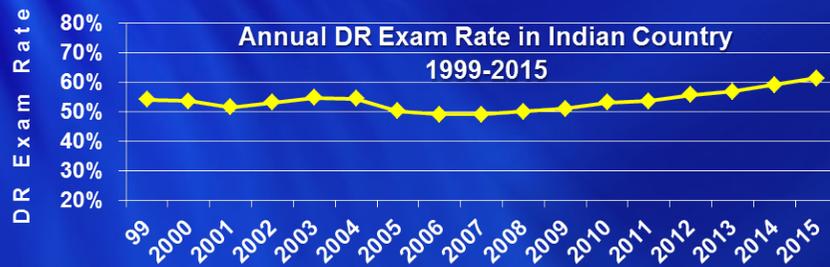


Diabetic Retinopathy

Failure to meet Standard of Care

- **40%-60% fail to receive needed treatment to prevent vision loss due to diabetic retinopathy**

Half of AI/AN population with DM do not get timely Dx and Tx



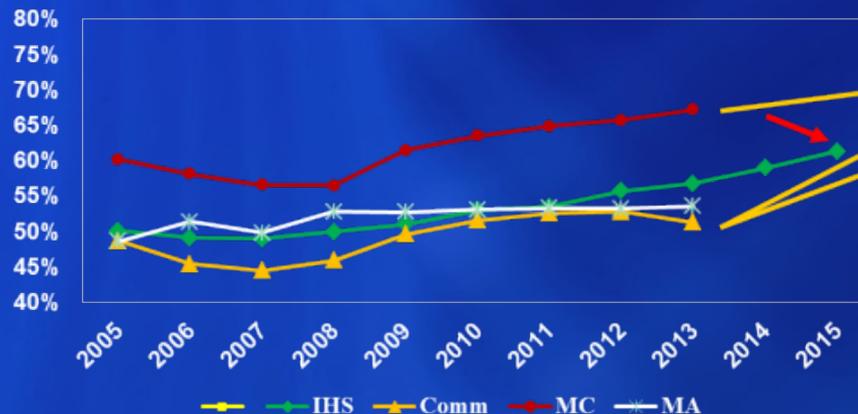
“Every system is perfectly designed to achieve the results it gets.”

Donald Berwick
Director CMS
CEO, IHI

Half of general US population with DM do not get timely Dx and Tx

A DR surveillance program limited to conventional eye exams by eye doctors has not been an effective public health approach for this problem in Indian Country or elsewhere

NCQA 2014 Report
 State of Health Care Quality
<http://www.ncqa.org/Directories/HealthPlans/StateofHealthCareQuality.aspx>



| EYE EXAMS | | | | | |
|-----------|------------|------|----------|------|----------|
| YEAR | COMMERCIAL | | MEDICAID | | MEDICARE |
| | HMO | PPO | HMO | HMO | PPO |
| 2013 | 55.7 | 46.9 | 53.6 | 68.5 | 66.0 |
| 2012 | 56.8 | 49.2 | 53.2 | 66.8 | 64.6 |
| 2011 | 56.9 | 48.4 | 53.3 | 66.0 | 63.8 |
| 2010 | 57.7 | 45.5 | 53.1 | 64.6 | 62.3 |
| 2009 | 56.5 | 42.6 | 52.7 | 63.5 | 59.4 |
| 2008 | 56.5 | 35.8 | 52.8 | 60.8 | 52.2 |
| 2007 | 55.0 | 34.0 | 49.8 | 62.7 | 50.4 |
| 2006 | 54.6 | 36.1 | 51.4 | 62.3 | 53.8 |
| 2005 | 54.8 | 42.7 | 48.6 | 66.5 | 53.8 |
| 2004 | 50.9 | - | 44.9 | 67.2 | - |
| 2003 | 48.8 | - | 45.0 | 64.9 | - |
| 2002 | 51.7 | - | 46.8 | 68.4 | - |
| 2001 | 52.1 | - | 46.4 | 66.0 | - |
| 2000 | 48.1 | - | - | - | - |
| 1999 | 45.3 | - | - | - | - |

**Half of general US population with DM
do not get timely Dx and Tx (cont.)**

**This is not a problem with eye doctors, or even an
eye doctor problem**

**About half of patient with DM chose not to get an
annual eye exam by appointment to the eye Clinic**

DR Surveillance Reporting

GPRA Performance Measure

Treatment Measures

Diabetes Group

| Performance Measure | 2015 Target | 2016 Target | 2017 Target | Headquarters Lead |
|--|---|--|--|-------------------|
| 6. Diabetic Retinopathy: Address the proportion of patients with diagnosed diabetes who receive an annual diabetic retinal examination. [outcome] | During GY 2015, maintain the proportion of patients with diagnosed diabetes at all sites who receive a qualifying annual retinal examination of 60.2% at all sites. | During GY 2016, maintain the proportion of patients with diagnosed diabetes at all sites who receive a qualifying annual retinal examination of 61.6% at all sites. | During GY 2017, maintain the proportion of patients with diagnosed diabetes at all sites who receive a qualifying annual retinal examination of ~63.0% at all sites. | Mark Horton |

DR Surveillance Methods

- **GPRA element #6- annual DR exam**
- **Qualifying examinations**
 - Dilated Exam by optometrist or ophthalmologist
 - 7 standard field stereoscopic 35mm slides using ETDRS methodology
 - Photographic method validated to EDTRS

DR Surveillance Methods

- **GPRA element #6- annual DR exam**
- **Qualifying examinations**
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IHS-JVN

Teleophthalmology Program

- Reduce vision loss through timely Dx and Tx using telemedicine in the primary care setting
- Centrally funded
- Clinical operation since 2001

Joslin Vision Network (JVN)

- **Quick and painless**
 - Low level illumination
 - No pupil dilation
- **Non-invasive**
- **Interleaved with other patient encounter events**
- **Validated**

JVN Physical Components

JVN Image Acquisition Station



- Retinal Image Acquisition by certified imager in primary care clinic
- Demographics harvested from RPMS
- Hx supplemented
- Patient Education
- Data transmission
 - Images
 - Health Summary

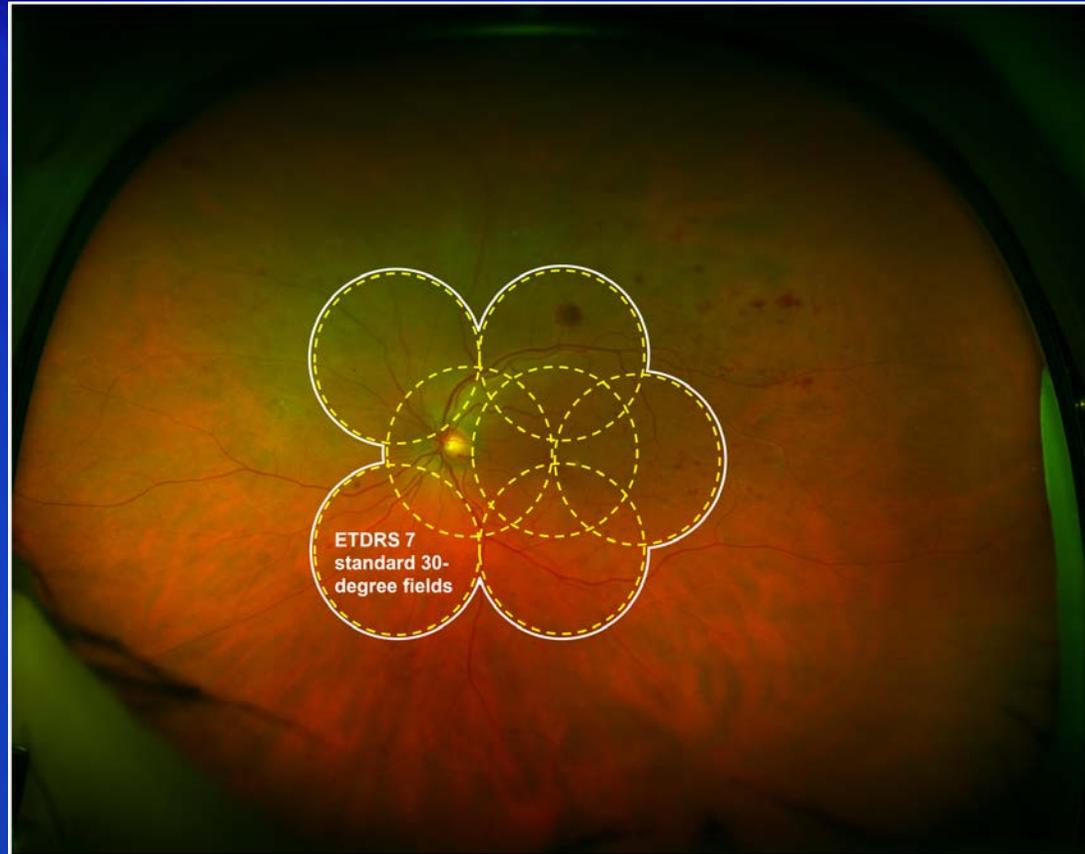
Physical Components

JVN Diagnostic Workstation

- Image analysis
- Automated diagnosis with reader validation
- Automated documentation



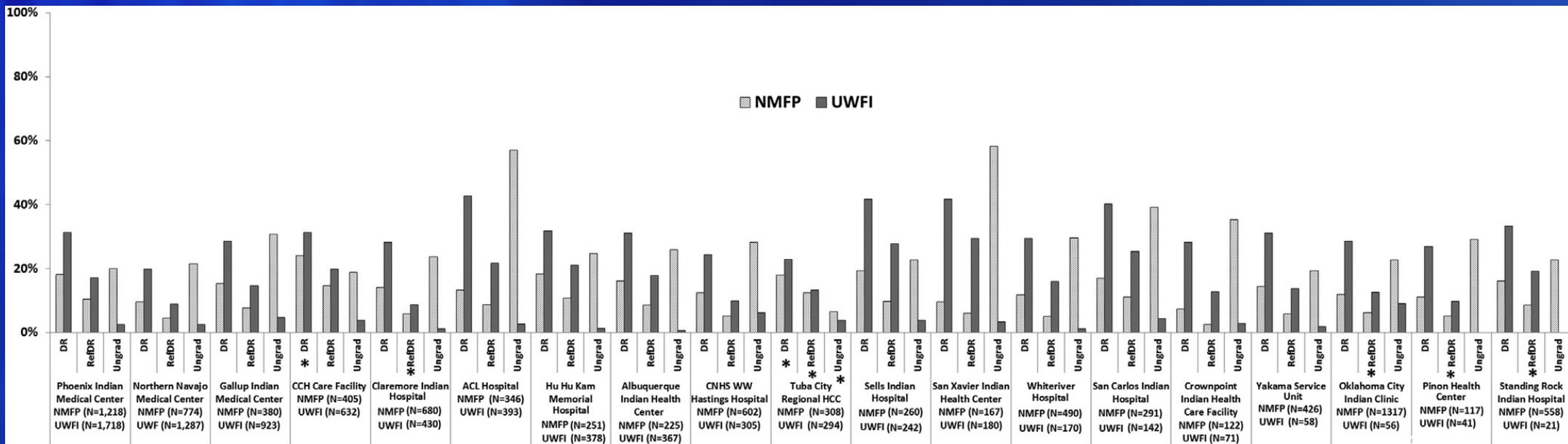
ETDRS 7 standard 30-degree fields



First Year Experience of UWFI in IHS-JVN

25,635 patients: 17,526 NMFP, 8109 UWFI

- Reduction in ungradeable rate (3-4%)
- 2X increase in rate of diagnosed DR
- More severe level of DR in 9%
- Reduction in unnecessary referral in ~ 4,000 pts/yr



JVN Validation Studies Ultrawidefield Imaging (UWFI)

Predominately Peripheral DR Lesion



Peripheral Lesions Identified on Ultrawide Field Imaging Predict Increased Risk of Diabetic Retinopathy Progression over 4 Years

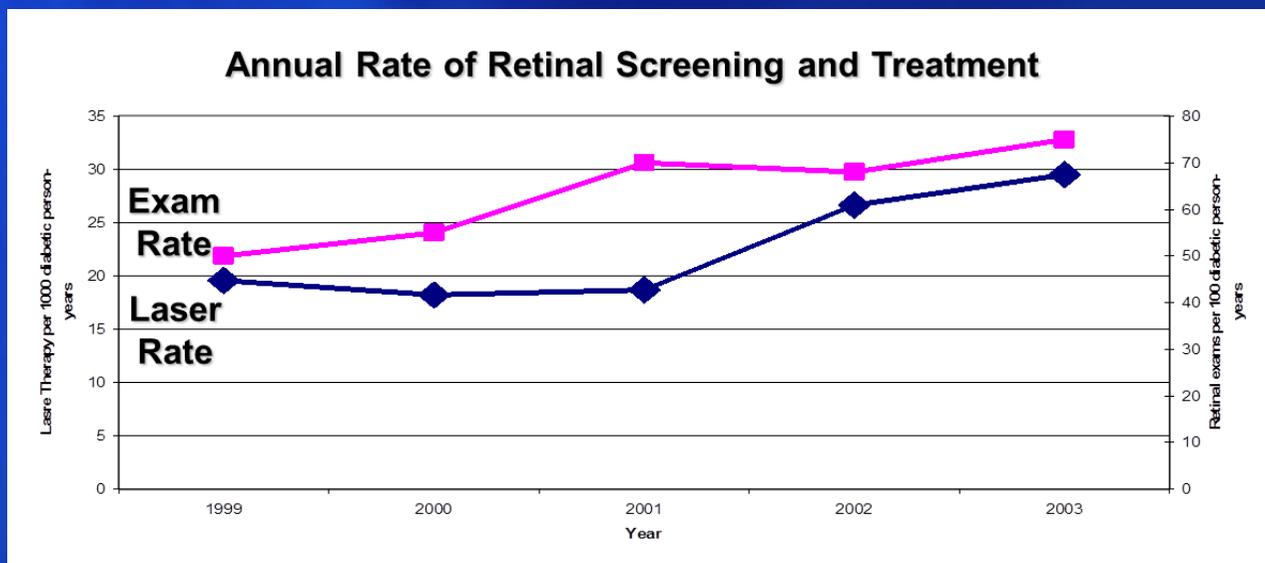
Paolo S. Silva, MD,^{1,2} Jerry D. Cavallerano, OD, PhD,^{1,2} Nour Maya N. Haddad, MD,¹ Hanna Kwak, BS,¹
Kelli H. Dyer, DO,¹ Ahmed F. Omar, MD,^{1,3} Hasanain Shikari, MD,¹ Lloyd M. Aiello, MD,^{1,2}
Jennifer K. Sun, MD, MPH,^{1,2} Lloyd Paul Aiello, MD, PhD^{1,2}

3.2X risk for progression of DR
4.7x risk for PDR

Outcome Linked to Intervention (prevention of vision loss)

- Diabetes Care- Feb 2005 (28:318-322)

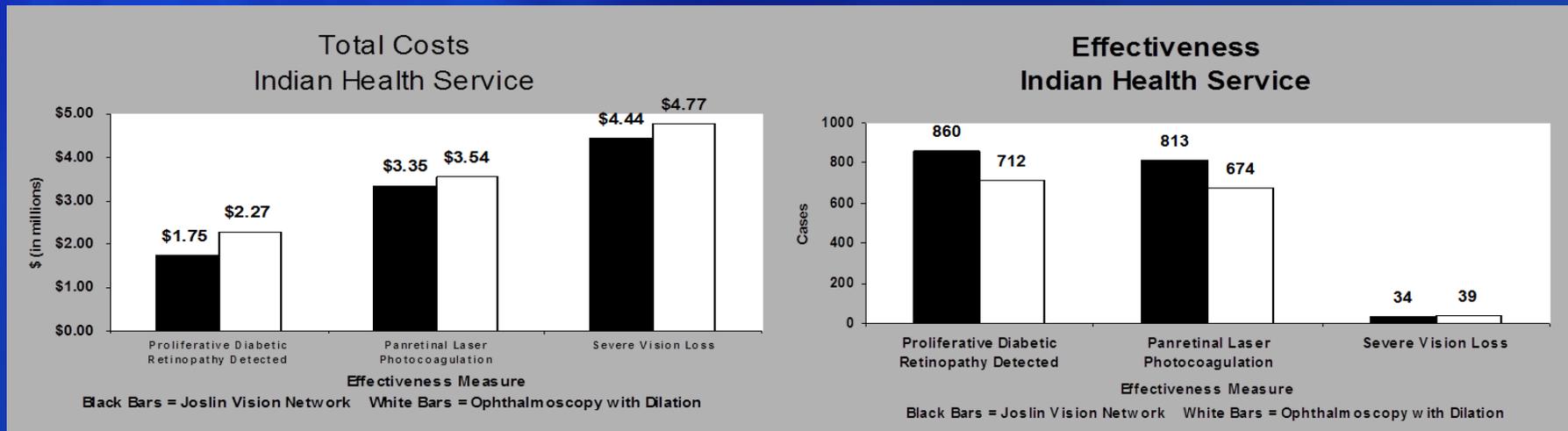
JVN resulted in a 50% increase in DR surveillance and 51% increase in laser treatment for DR (2000-2003)



Diabetic Retinopathy Cost Effectiveness

Whited JD, et al. A Modeled Economic Analysis of the Joslin Vision Network as used by Three Federal Healthcare Agencies for Detecting Proliferative Diabetic Retinopathy. *Telemedicine Journal and e-Health*

- IHS/JVN is both less costly and more effective for:
- Detecting DR
- Identifying IHS patients that require laser tx
- Preventing severe vision loss



Diabetic Retinopathy Surveillance

IHS-JVN Teleophthalmology Program

96 Fixed/Hybrid sites + 13 Portable Sites in 25 States

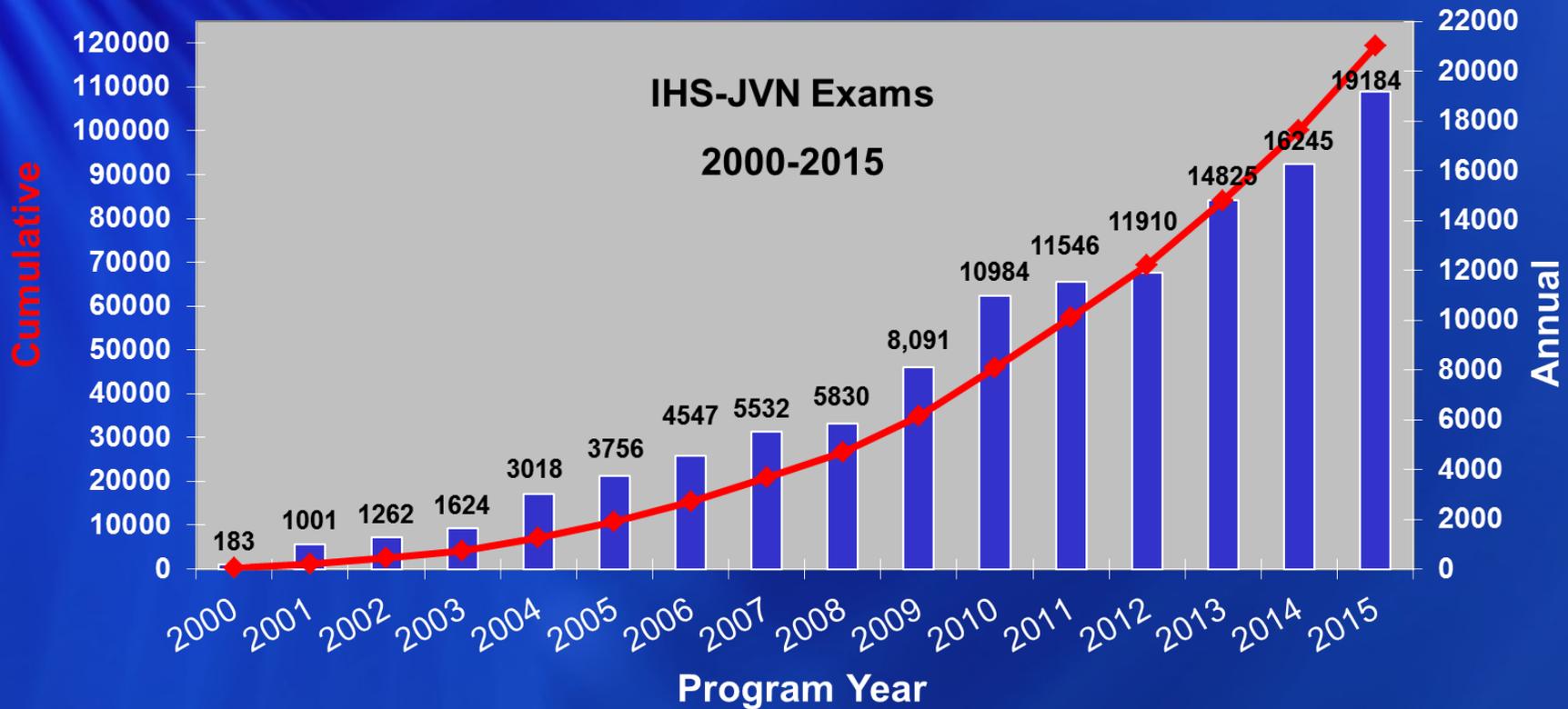
- Phoenix, AZ
- Sacaton, AZ
- Polacca, AZ
- Pinon, AZ
- San Carlos, AZ
- Salt River, AZ
- Ft. Yuma, AZ
- Whiteriver, AZ
- Sells-, AZ
- Tuba City, AZ
- Tucson, AZ
- Parker, AZ
- Peach Springs, AZ
- San Xavier, AZ
- Kayenta, AZ
- Chinle, AZ
- Flagstaff, AZ
- Inscription House, AZ
- Navajo Mountain, AZ
- Elko, NV
 - Goshute, NV
 - Ely, NV
 - Duckwater, NV
- Owyhee, NV
- Reno Sparks, NV
- Fallon, NV
- Claremore, OK
- Wewoka, OK
- Eufaula, OK
- Okmulgee, OK
- Oklahoma City, OK
- Tahlequah, OK
- Lawton, OK
- Carnegie, OK
- Miami, OK
- Anadarko, OK
- Portland, OR
- Warm Springs, OR
- Salem, OR
- Cow Creek, OR
- Klamath, OR
- Pendelton, OR
- Nespelem, WA
- Yakama, WA
- Wellpinit, WA
- Tacoma, WA
- Fort Hall, ID
- Lapwai, ID
- Plummer, ID
- Pine Ridge, SD
- Rosebud, SD
- Rapid City, SD
- Sisseton, SD
- Wagner, SD
- Eagle Butte, SD
- Spirit Lake, ND
- Ft. Yates, ND
- Belcourt, ND
- Ft. Peck, MT
- Ft Belknap, MT
- Crow Agency, MT
- Lame Deer, MT
- Browning, MT
- Ft Washakie, WY
- Red Lake, MN
- Cass Lake, MN
- White Earth, MN
- Lawrence, KS
- Mayetta, KS
- Shiprock, NM
- Santa Fe, NM
- Albuquerque, NM
- Mescalero, NM
- Crown Point, NM
- Jicarilla, NM
- San Fidel, NM
- Dallas, TX
- Winnebago, NE
- Hayward, WI
- Mt Pleasant, MI
- Oneida, NY
- Charlestown, RI
- Fairbanks, AK
- Bristol Bay, AK
- Ketchikan, AK
 - Metlakatla, AK
- Rock Hill, SC
- Cherokee, NC
- U&O, UT
- Presque Isle, ME
- Indian Island, ME
- Philadelphia, MS



Portable Deployments

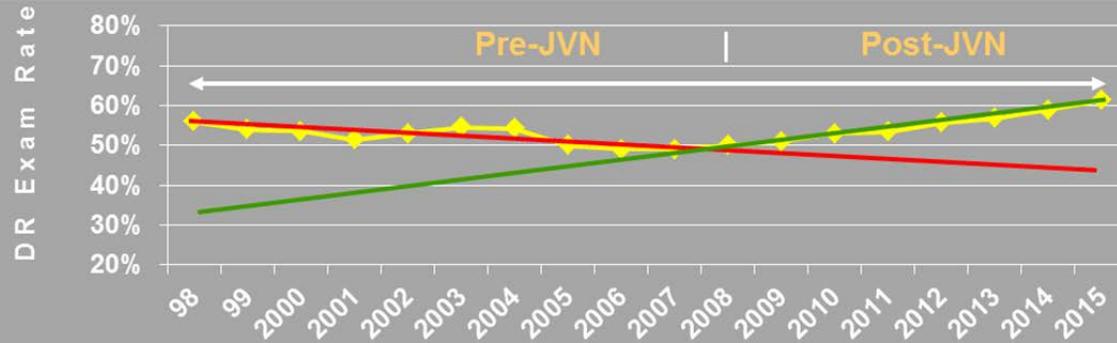
- Alaska- EAT, APIA
- North Carolina
- Oklahoma- Redbird
Sam Hider Jay
- Arizona- Supai
- Nevada- Schurz, Loveloc
Yerington
- Maine- Littleton,
Princeton, Pleasant
Point

IHS/JVN Experience

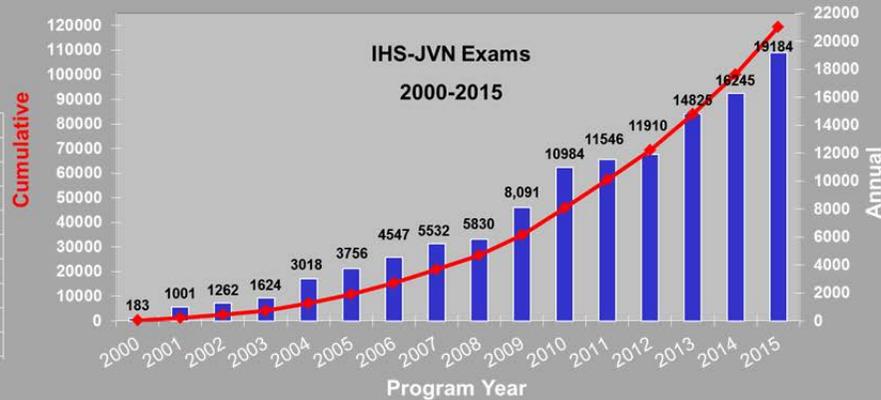
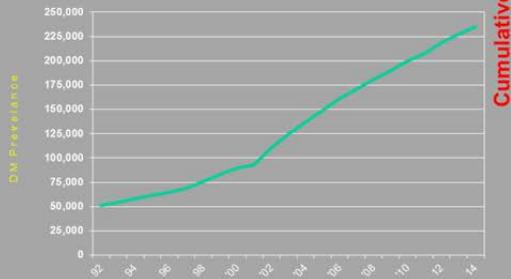


Clinical Outcome

IHS DR Exam Rate pre/post JVN Ramp-up



~10 year doubling rate of DM prevalence



Public Health Case

Compliance with DR Standards of Care

- **Re-tasking of recovered resources**
 - Staff
 - \$
- **Targets of opportunity**
- **Person-years of sight preserved**
- **secondary impact**
 - Family, Society, Health Care System

Telemedicine-DR: A better tool to address this universal public health problem

- **VHA**
 - 1.3 million veterans with DM (25%)
 - 400 Tmed-DR deployments / 500,000 annual exams
- **UK**
 - ~2.9 million with DM
 - 2.1 million annual tmed DR exams
 - 2014- For the first time in 5 decades of survey, DR is no longer the leading cause of new blindness among working age adults in UK

Liew G, Michaelides M, Bunce C.A Comparison of the causes of blindness certifications in England and Wales in working age adults (16-64 years), 1999-2000 with 2009-2010. *BMJ Open* 2014;4:e004015.

Best Practices Strategy for preventing vision loss due to DM

- Patient Education
- Control confounding factors:
 - Glucose
 - Lipids
 - BP
 - Smoking
- Fenofibrate ??
- Annual DR exams for timely DX and Tx

IHS Division of Diabetes Advancements in Diabetes Seminar

Thank you;

Questions?

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