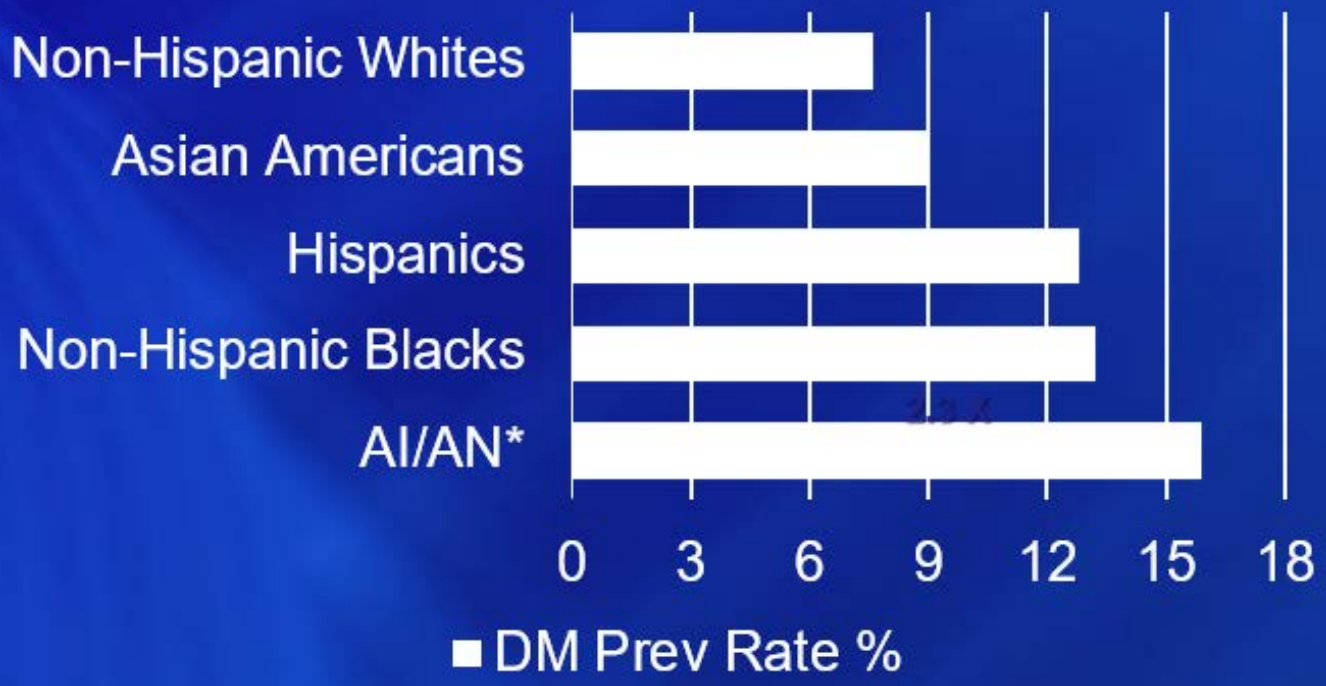
IHS Division of Diabetes
Advancements in Diabetes Seminar

Clinical Advancements in Diabetes Eye Care

Mark B. Horton, OD, MD
Director, IHS/JVN Teleophthalmology Program

Diabetes Mellitus in Indian Country



*6%-24% by region

CDC National Diabetes Statistics Report 2014

http://www.cdc.gov/diabetes/pubs/statsreport14.htm

Endemic nature of diabetes paralleled by diabetic eye disease

Ocular Complications of DM (1 of 3)

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	3rd, 4th, 5th, 7th CN palsies
CNS	CVA associated vision loss

Ocular Complications of DM (2 of 3)

Ocular Tissue	Conditions
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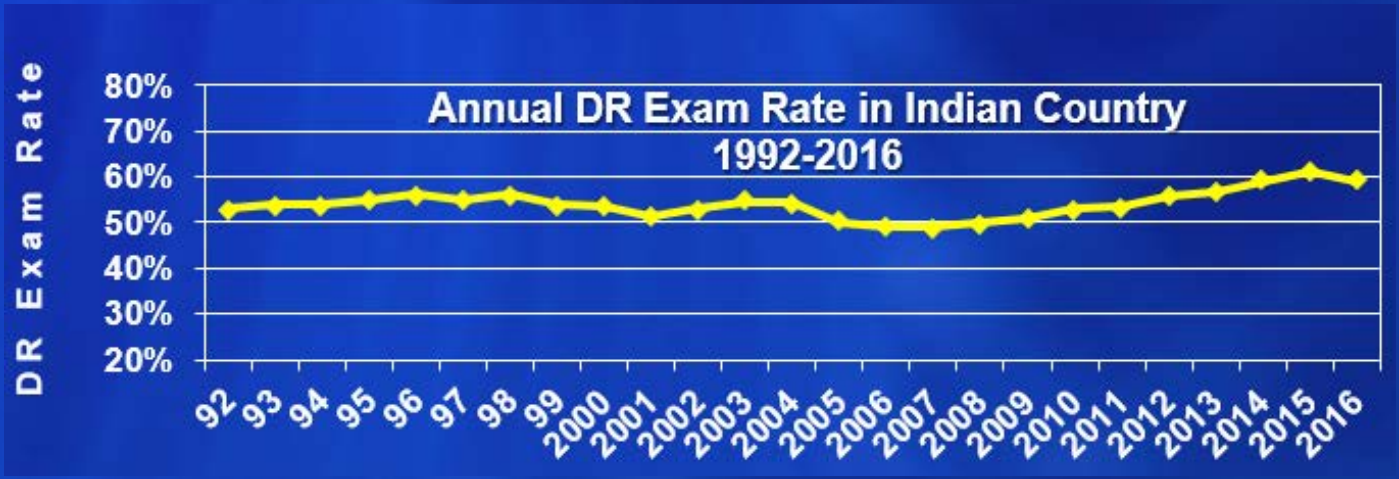
CNS	CVA associated vision loss

Diabetic Retinopathy (DR) (1 of 2)

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



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

Diabetic Retinopathy (DR) (2 of 2)

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

Clinical Management

Primary Care Diabetes Team
+
Ophthalmologist / Optometrist

↓

Systemic control

Timely (Early?) diagnosis

Timely (Early?) 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 (1 of 4)

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

Diabetic Retinopathy (2 of 4)

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 (3 of 4)

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 (4 of 4)

Standard of Care

AAO Preferred Practice Guidelines

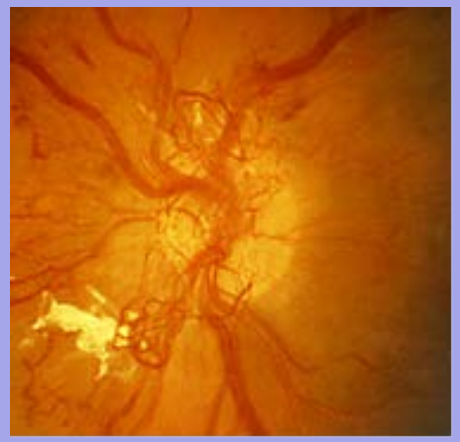
DR severity	CSME	f/u (mths)	Laser Tx	Focal
Minimal NPDR	No	12	No	No
Mild-Moderate NPDR	No	6-12	No	No
	Yes	2-4	No	Usually
Severe NPDR	No	2-4	Maybe	No
	Yes	2-4	Maybe	Usually
Low Risk PDR	No	2-4	Maybe	No
	Yes	2-4	Maybe	Usually
High Risk PDR	No	3-4	Usually	No
	Yes	3-4	Usually	Usually

FARSITED Protocol
Retinal Imaging

Mild nonproliferative DR

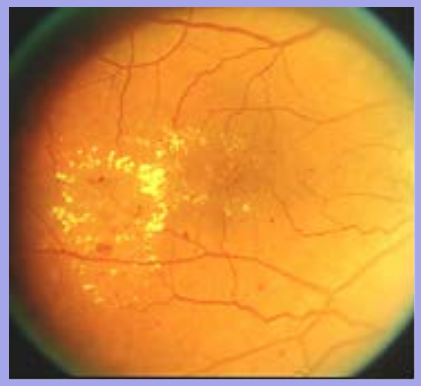
Moderate nonproliferative DR

Severe nonproliferative DR



Proliferative DR

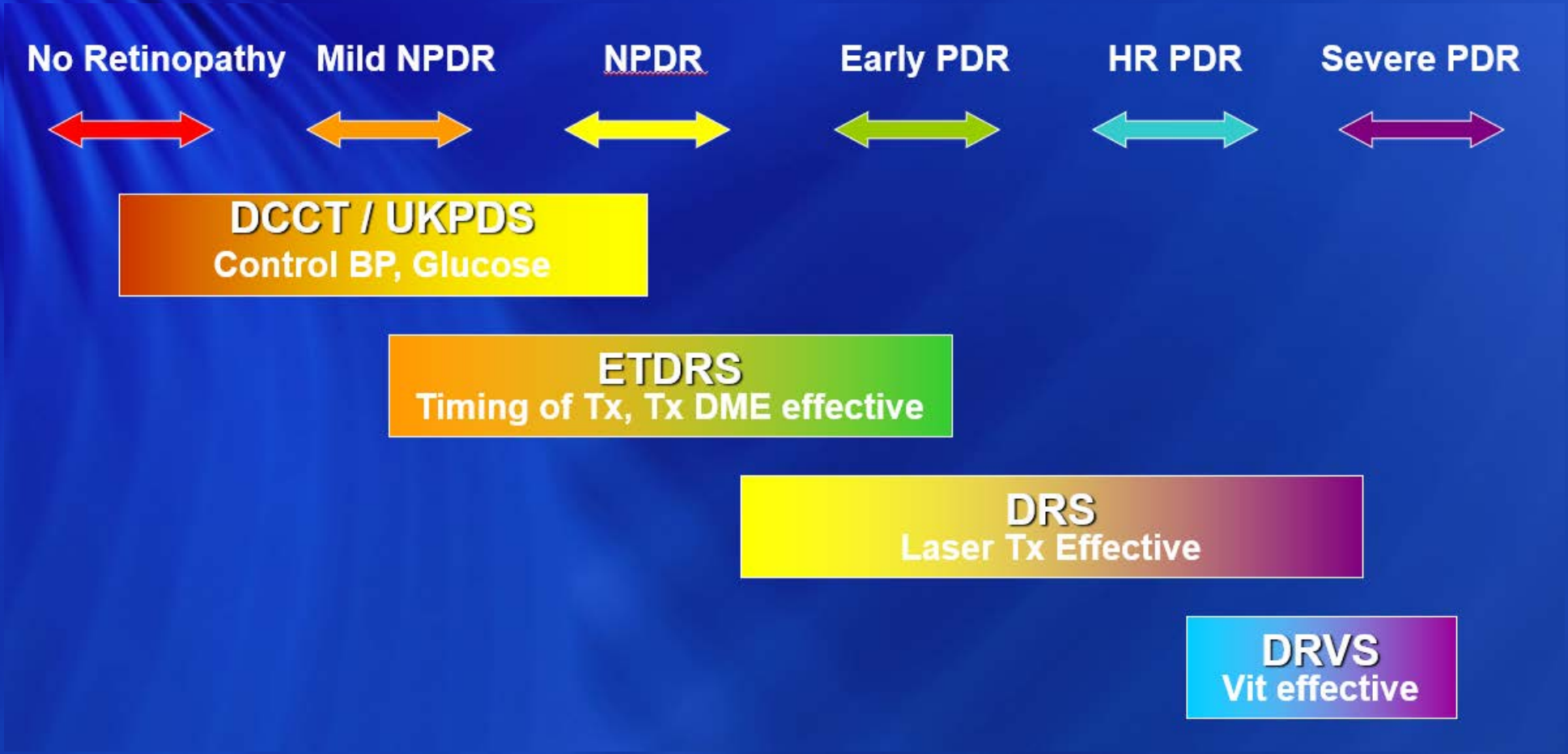
Proliferative DR



Diabetic macular edema

Diabetic Eye Exam and Tx

Standards of Care



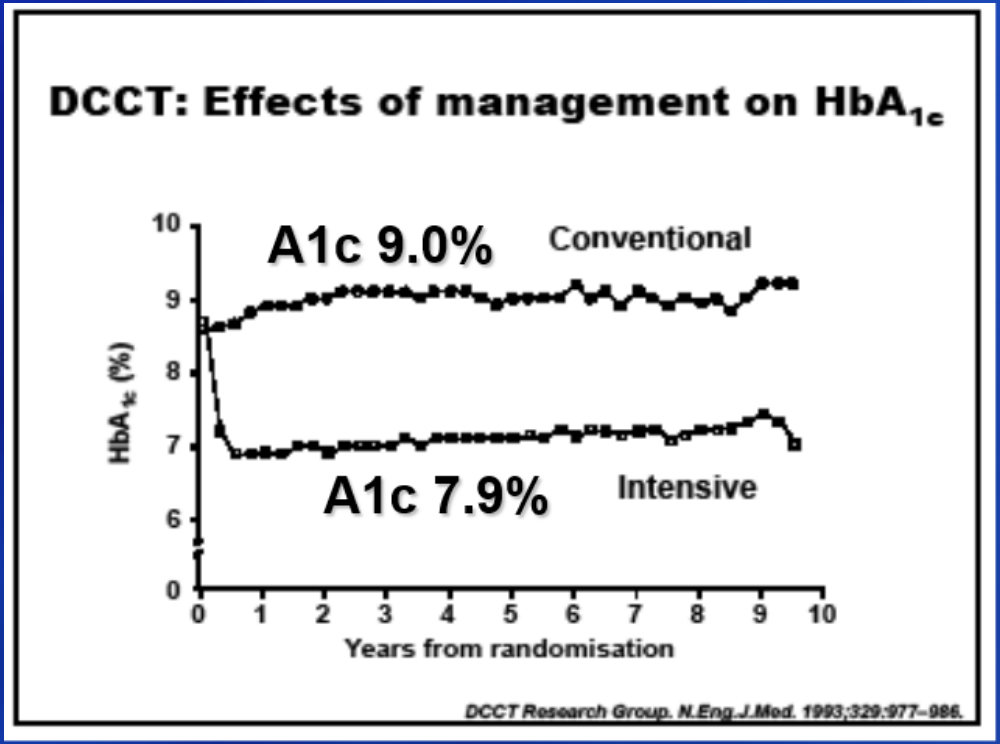
Diabetic Retinopathy

Diabetes Control and Complication Trial (DCCT) 1983-1993

- DM I
- Standard control

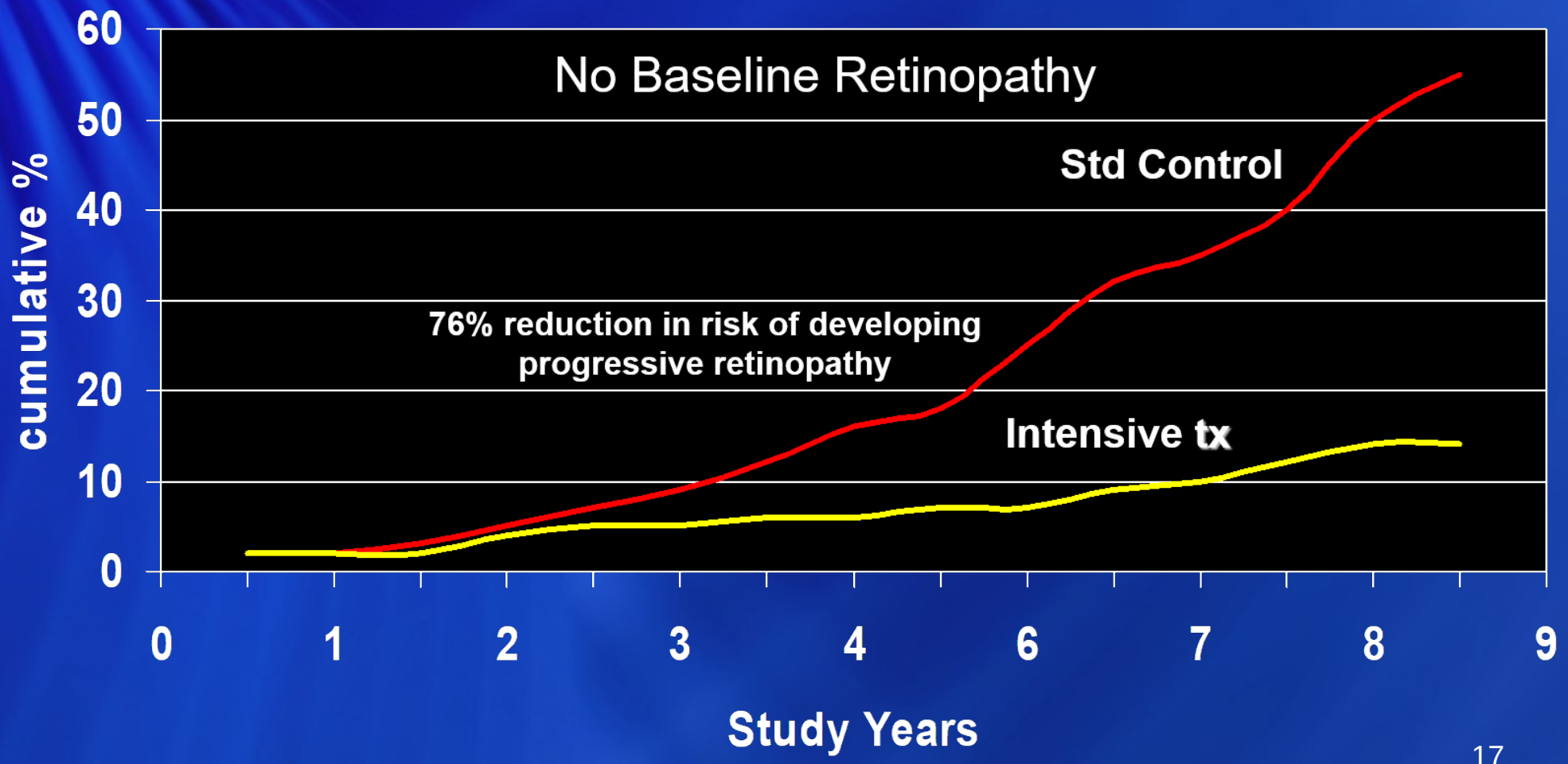
  vs

  Intensive control
  A1c 9.0 vs 7.9
  - Glucose levels qid
  - Insulin qid or pump
  - Diet and exercise



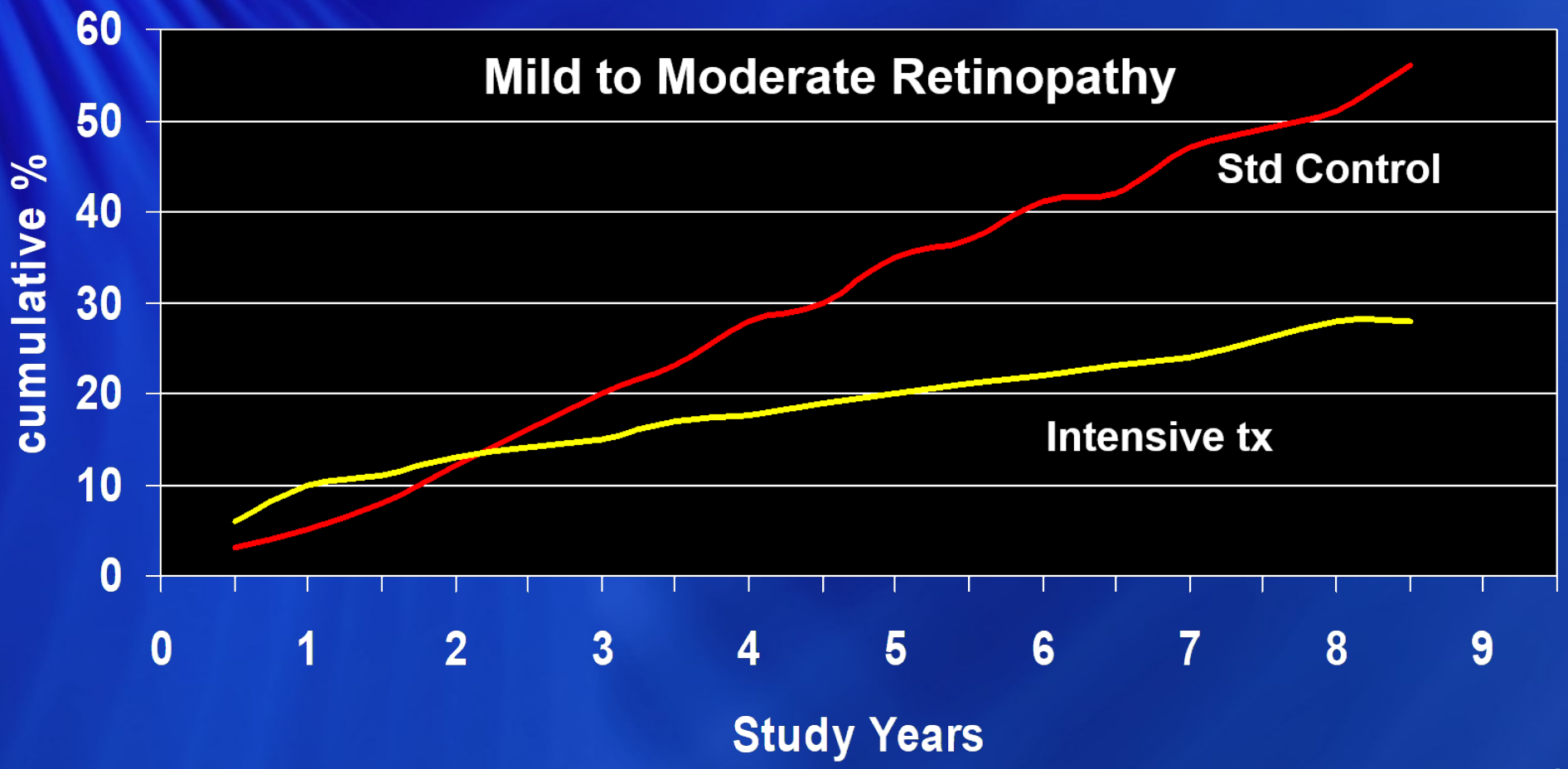
Diabetic Retinopathy (1 of 2)

Impact of Intensive DM control



Diabetic Retinopathy (2 of 2)

Impact of Intensive DM control



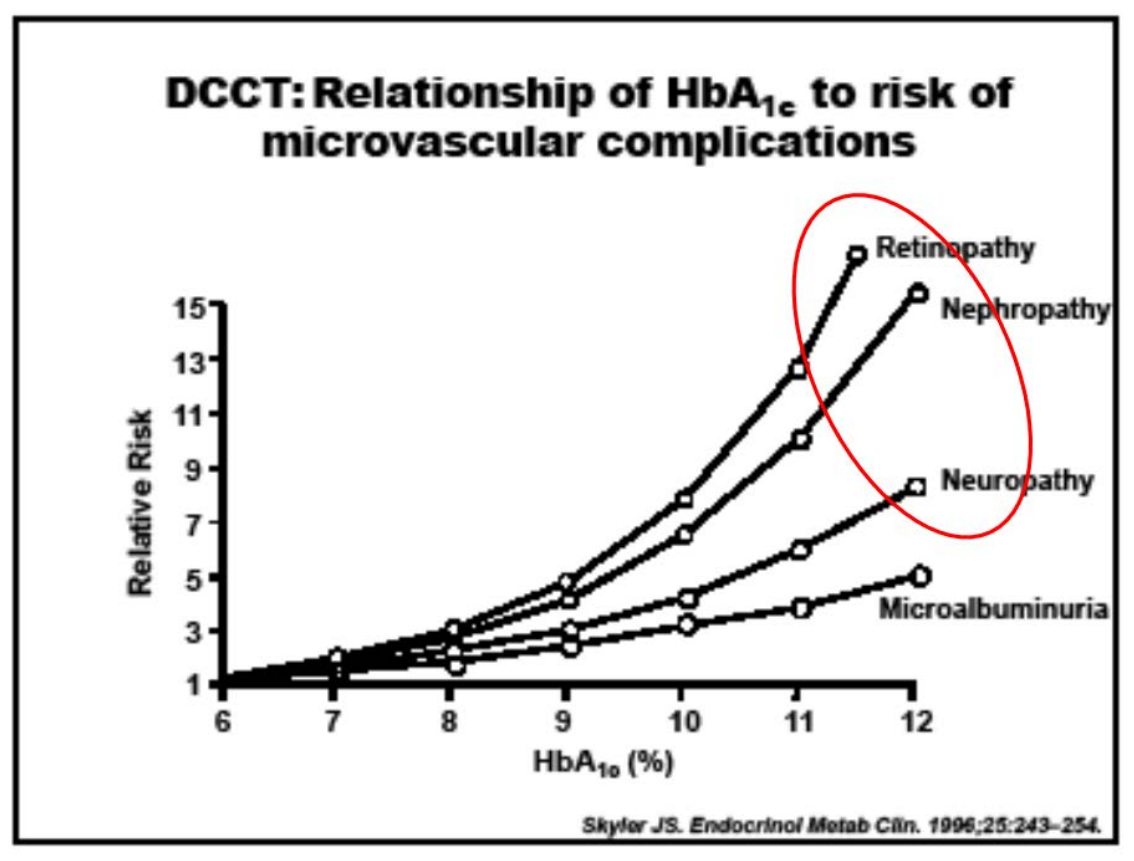
Diabetic Retinopathy

Intensive Glucose Control – mild to 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 (Slide 1 of 2)

- 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 (Slide 2 of 2)

- 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 (UKPDS) (1977-1997) (1 of 2)

- 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 (2 of 2)

- 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 within 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

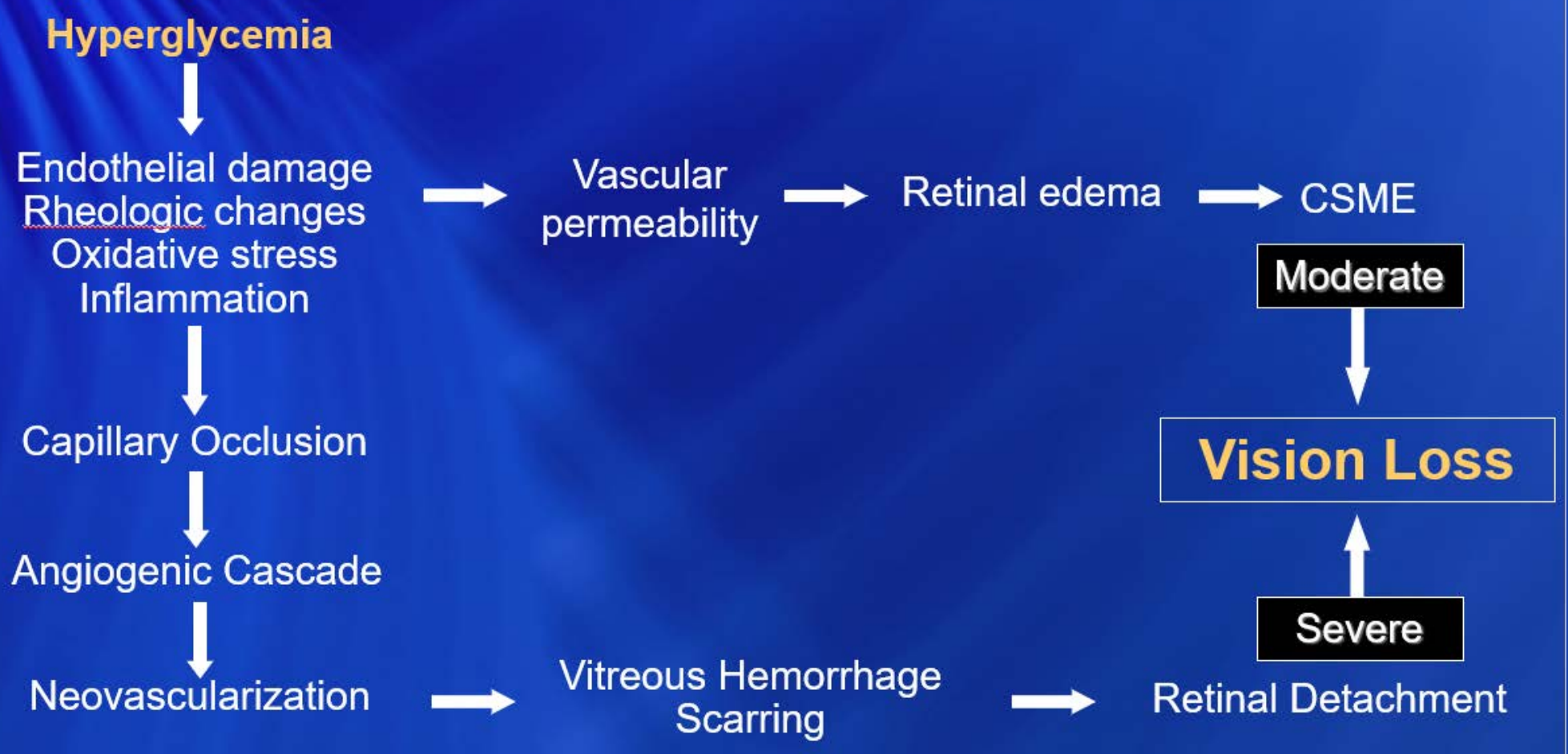
- Control
  - Blood Pressure- 130/85
  - Blood Glucose- A1c 6.5%-7.0% (↑ risk of compl)
  - Blood lipids
- Decrease risk of DR development
- Decrease risk of DR progression
- Decrease need for laser surgery

Diabetic Retinopathy

Pathophysiology of Vision Loss (1 of 2)

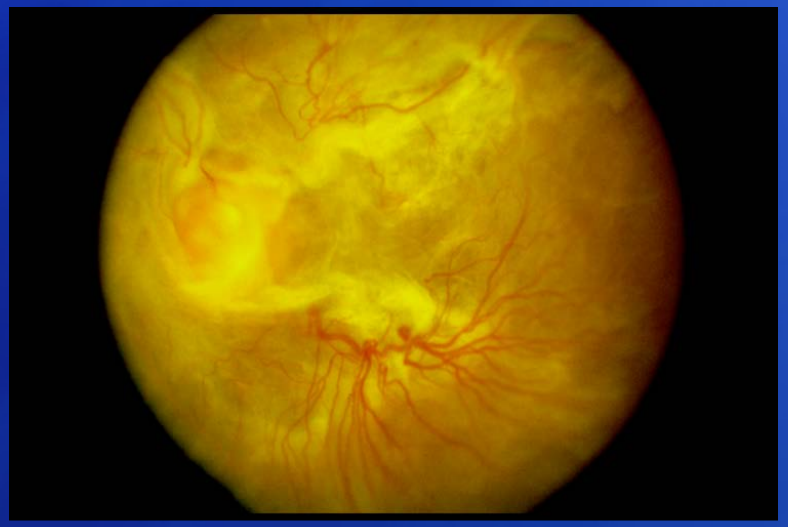
Diabetic Retinopathy

Pathophysiology of Vision Loss (2 of 2)



Vision Loss From Diabetes

Vitreous Hemorrhage



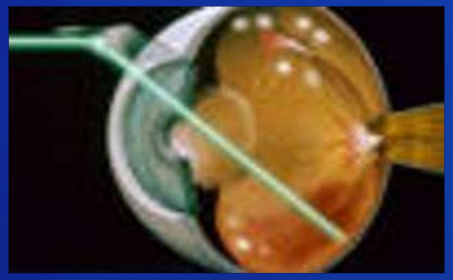
Traction Retinal Detachment

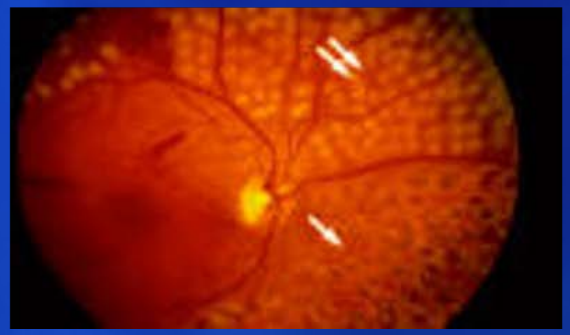
Macular Edema

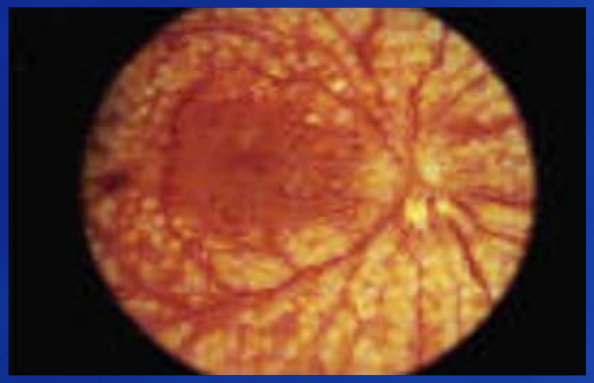
Diabetic Retinopathy

Current Ophthalmic Treatment

- Proliferative DR (PDR)-
  - Laser photocoagulation (PRP)

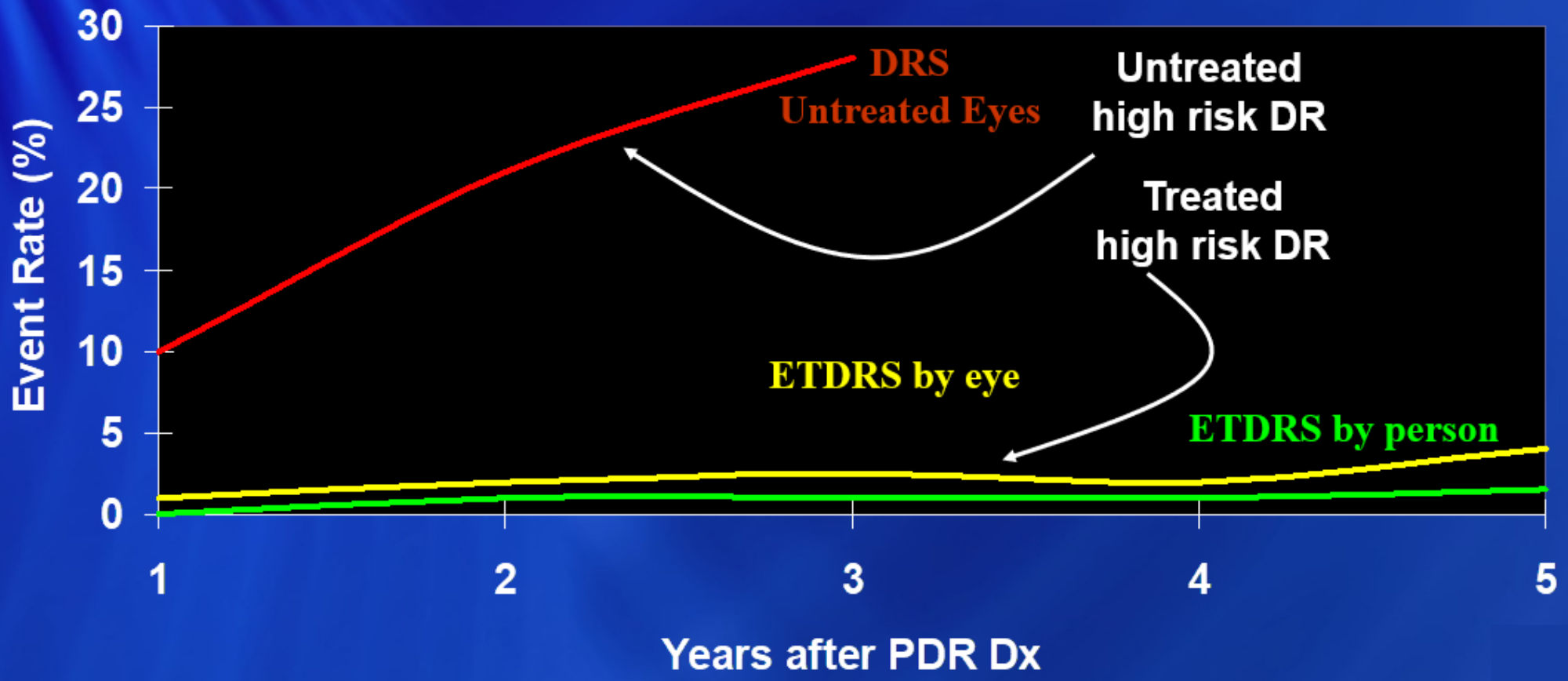






Visual Acuity Less than 20/800

Proliferative Diabetic Retinopathy



Diabetic Retinopathy

Current Ophthalmic Treatment (1 of 3)

Diabetic Macular Edema (DME)-

- Intravitreal injections

Diabetic Retinopathy

Anti-VEGF and Steroids for DR

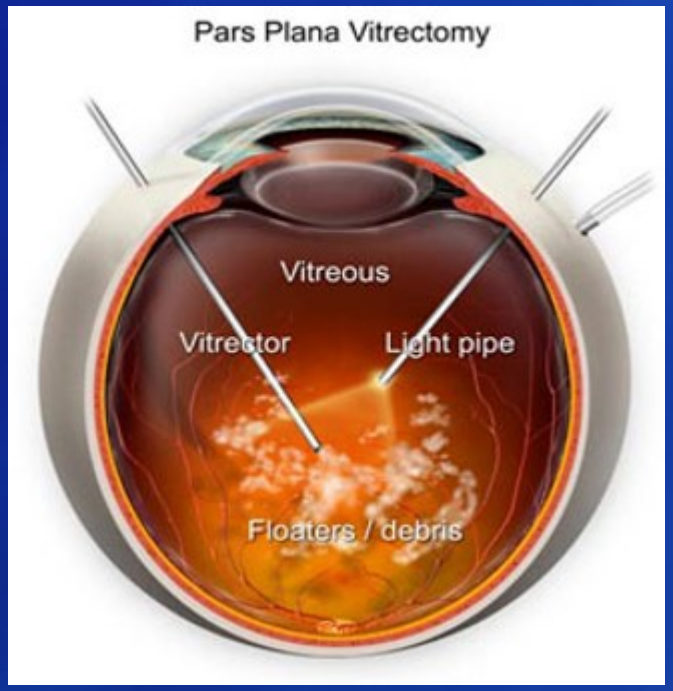
- Lucentis (Genetech) $1,200/dose
- Eylea (Regeneron) $1,850/dose
- Avastin (Genetech) $60/dose
- Ozurdex (Allergan) $1,300/dose 3-4 months
- Iluvien (Alimera Sciences) $8,800/dose 36 months

Diabetic Retinopathy

Current Ophthalmic Treatment (2 of 3)

Vitreous hemorrhage/Retinal Detachment

- Vitrectomy (PPV)



Diabetic Retinopathy- PDR / VH / RD

Vitrectomy

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

Diabetic Retinopathy

Primary Care Management of DR

- ~ 50% reduction in the prevalence of DR among AI/AN over the past two decades:
  - NPDR 17.7%
  - PDR 2.3%
  - DME 2.3%
  - STR 4.2%
- Similar reduction in prevalence of diabetes-related ESRD over the same period, which aligns temporally with SDPI implementation.

Diabetic Retinopathy

Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) 2005

- 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) 2010

- 36% reduction of progression (all cases)
- 78% reduction of progression (mild NPDR)

Fenofibrate

Mechanism of Action

- Not related to lipid effects.
- Treat early in the course of DR, but precise timing is not determined.
- Possible collateral benefits to other microvasculopathic end organ processes:
  - Renal
  - Peripheral neuropathy
- High patient safety.

Fenofibrate

Patient Safety

- Long history 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 statins:
  - .5% vs .8% serious ADE (placebo : fenofibrate)

Fenofibrate

Clinical Use

- On label use for DR in Australia and other countries
- DM clinical practice guidelines:
  - Canadian Diabetes Association, 2016: "Though not recommended for CVD prevention or treatment, fenofibrate, in addition to statin therapy, may be used in patients with type 2 diabetes to slow the progression of established retinopathy."
  - American Diabetes Association, 2017: "… collaboration between the ophthalmologists (eye care providers) and the medical physician to consider this treatment for people affected with diabetic retinopathy."

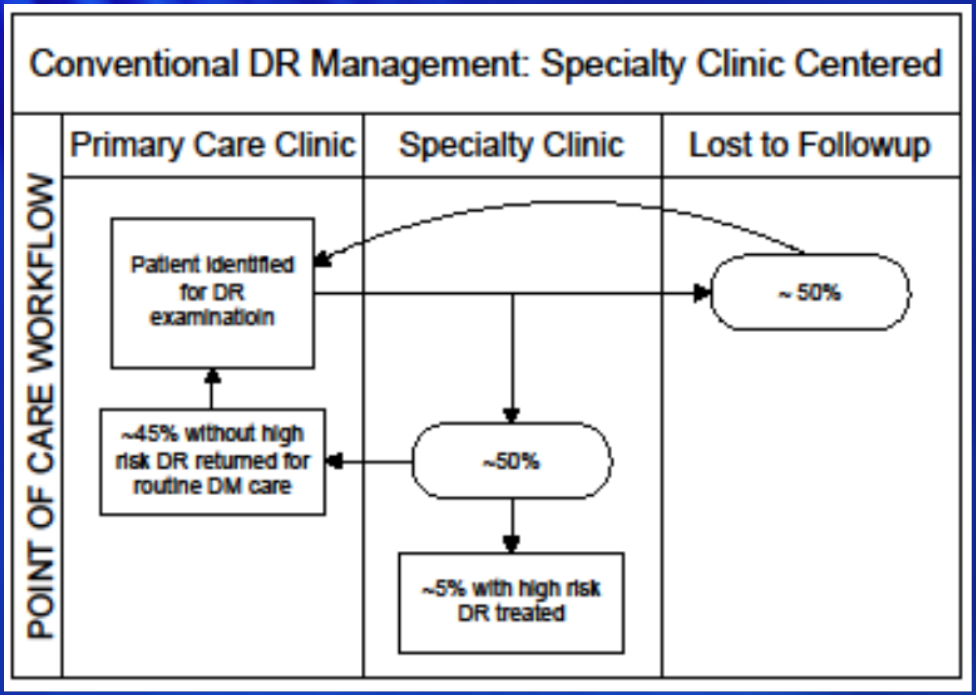
Diabetic Retinopathy

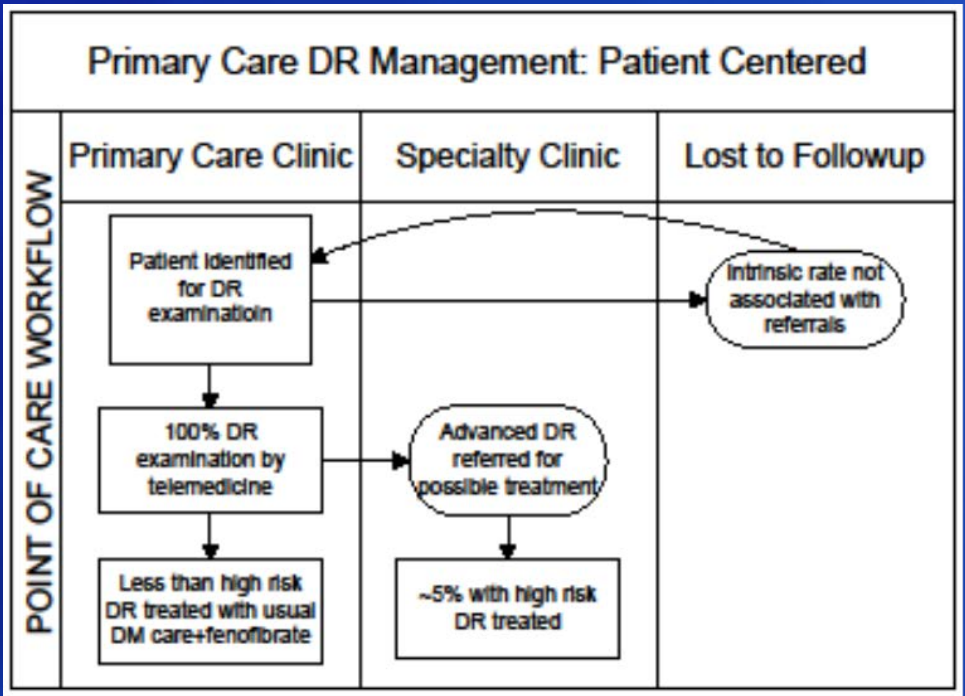
Primary Care Treatment with Fenofibrate

- Treat early in the course of DR.
  - Treat by PCP without specialty referral
  - Reduced need for difficult and costly travel to subspecialty eye care
- Naturally incorporated into a primary care-based teleophthalmology-DR program for combined benefits of pt recruitment, DR Dx, and treatment.

Diabetic Retinopathy

Possible Early Fenofibrate DR Tx Best Practice in IHS



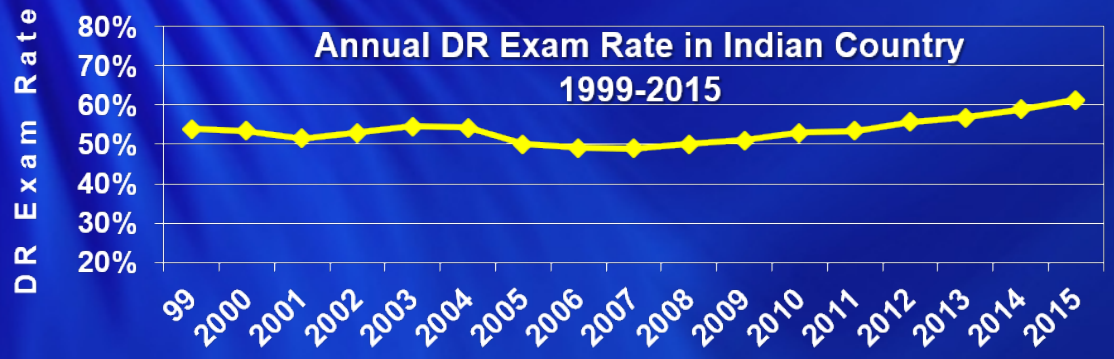


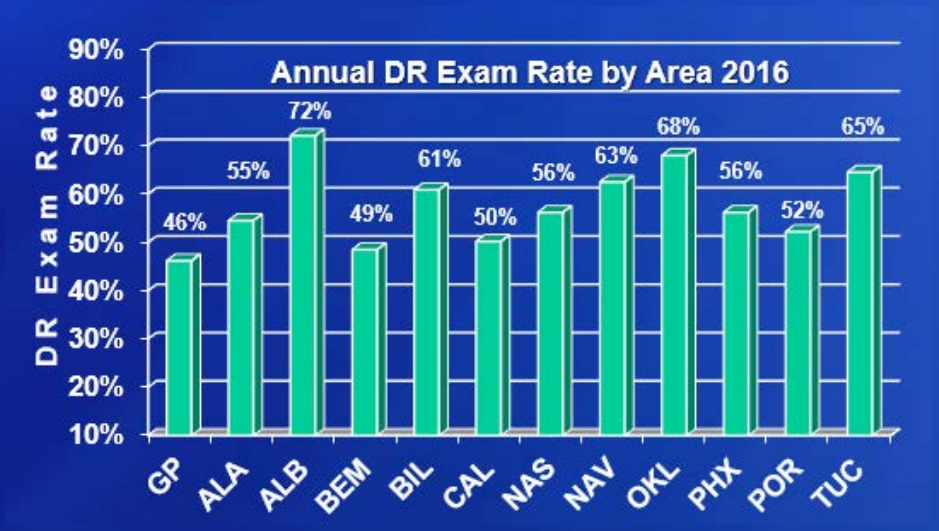
Diabetic Retinopathy

Failure to Meet Standard of Care

40%-60% of patients fail to receive needed treatment to prevent vision loss due to diabetic retinopathy.

Half of AI/AN population with DM does not get timely Dx and Tx (1 of 2)



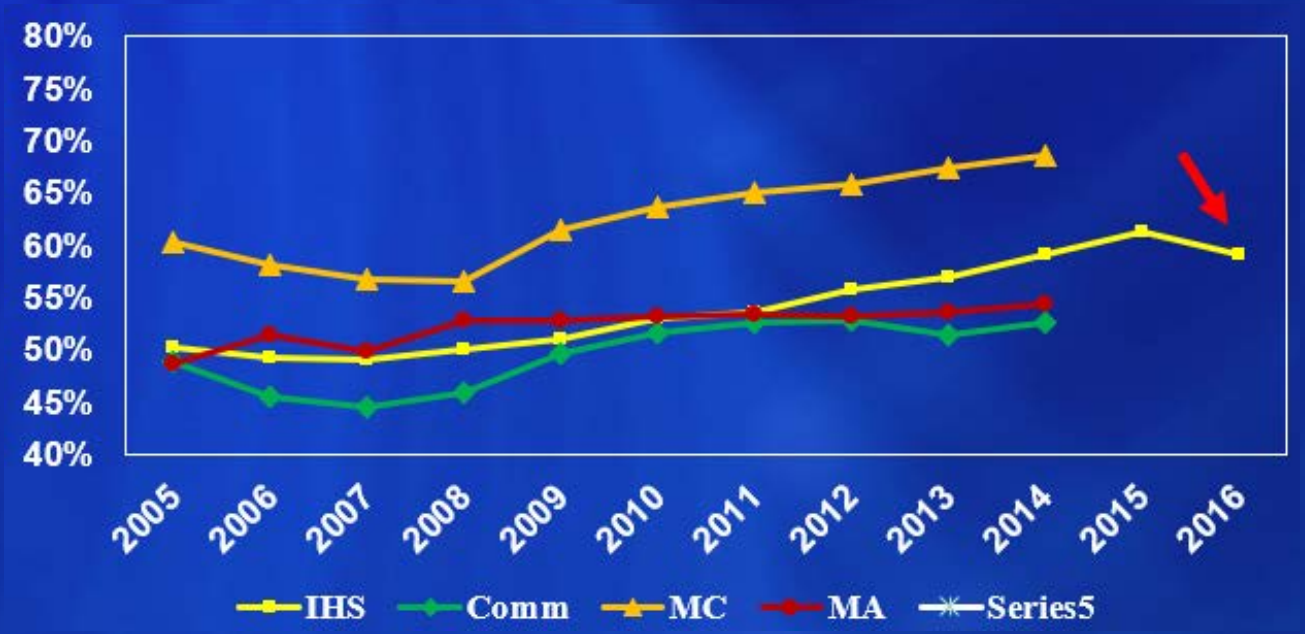


"Every system is perfectly designed to achieve the results it gets."

Donald Berwick
Director CMS
CEO, IHI

Half of AI/AN population with DM does not get timely Dx and Tx (2 of 2)

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 2015 Report
State of Health Care Quality
http://www.ncqa.org/report-cards/health-plans/state-of-health-care-quality

EYE EXAMS					
	COMMERCIAL		MEDICAID	MEDICARE	
YEAR	HMO	PPO	HMO	HMO	PPO
2014	56.2	48.7	54.4	68.5	68.4
2013	55.7	46.9	53.6	68.5	66.0
2012	56.8	48.8	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	–	–	–	–

Diabetic Retinopathy
Surveillance Best Practices

- This is not a problem with eye doctors
  - Patients with an asymptomatic chronic condition
  - Inconvenient examination
- A primary care diabetes management problem
  - Programs that depend upon appointed visits to an eye doctor usually fail standard of care for 40%-50% of DM patients
- Must be smarter than the disease
- Must understand the patient

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.

DR Surveillance Methods (1 of 2)

- 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 (2 of 2)

- 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

Indian Health Service-Joselin Vision Network (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

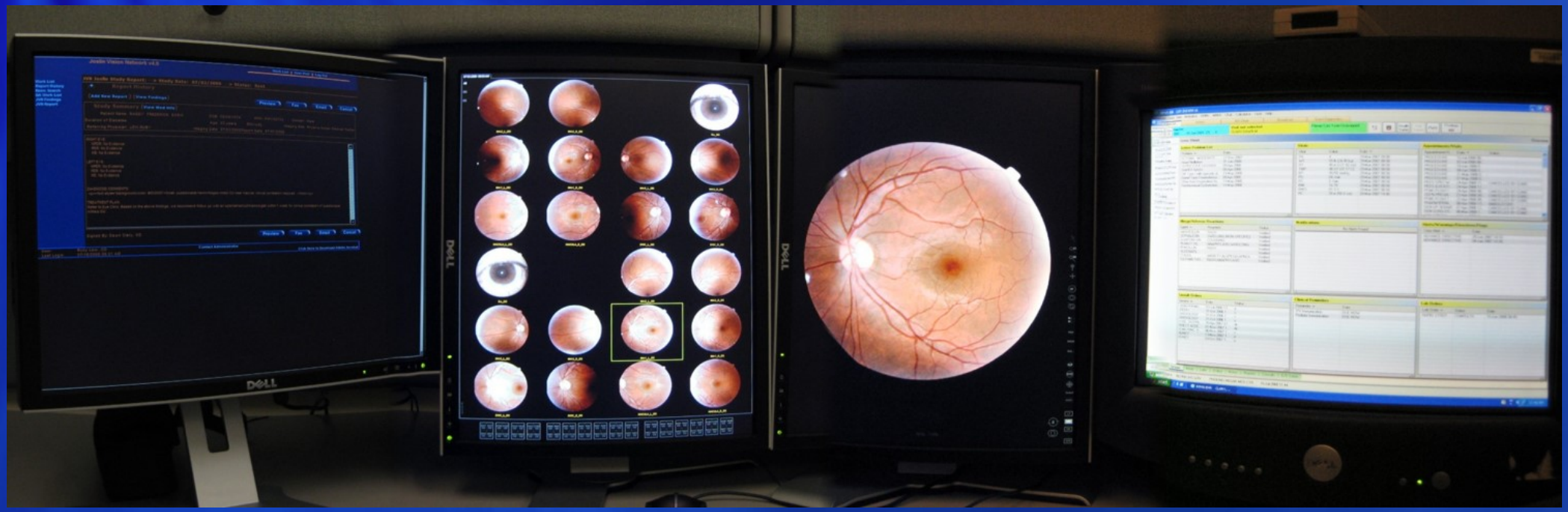
JVN Image Acquisition Station

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

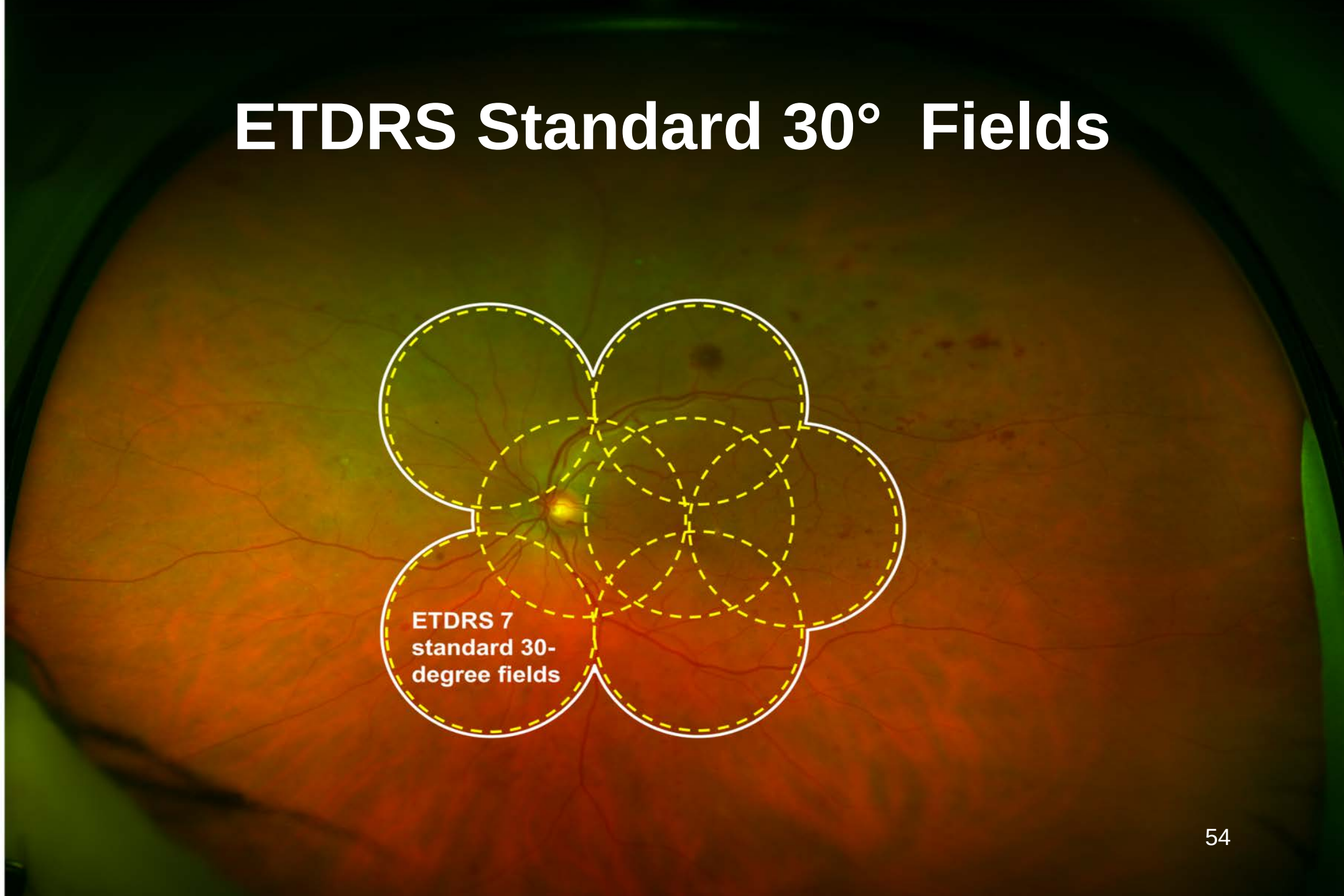
JVN Physical Components

JVN Diagnostic Workstation

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



ETDRS Standard 30° Fields



First Year Experience of UWFI in IHS-JVN

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

- Reduction in ungradable 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

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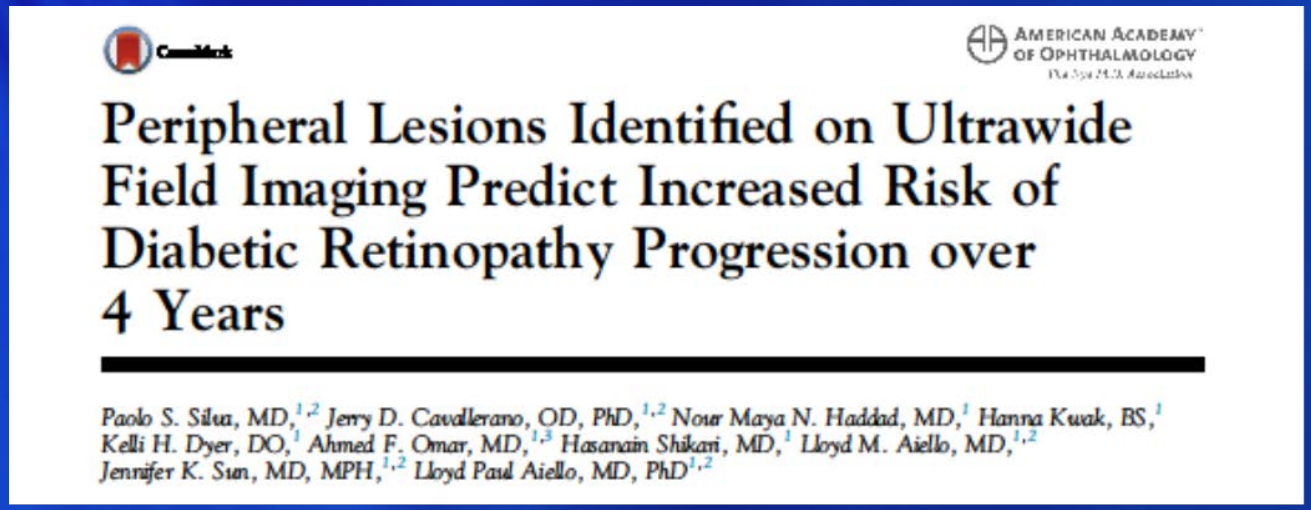
Identification of Diabetic Retinopathy and Ungradable Image Rate with Ultrawide Field Imaging in a National Teleophthalmology Program

Paolo S. Silva, MD,[1,2] Mark B. Horton, OD, MD,[3] Dawn Clary, OD,[3] Drew G. Lewis, BA,[4] Jennifer K. Sun, MD, MPH,[1,2] Jerry D. Cavallerano, OD, PhD,[1,2] Lloyd Paul Aiello, MD, PhD[1,2]

JVN Validation Studies

Ultrawide Field Imaging (UWFI)

- Predominately Peripheral DR Lesions



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

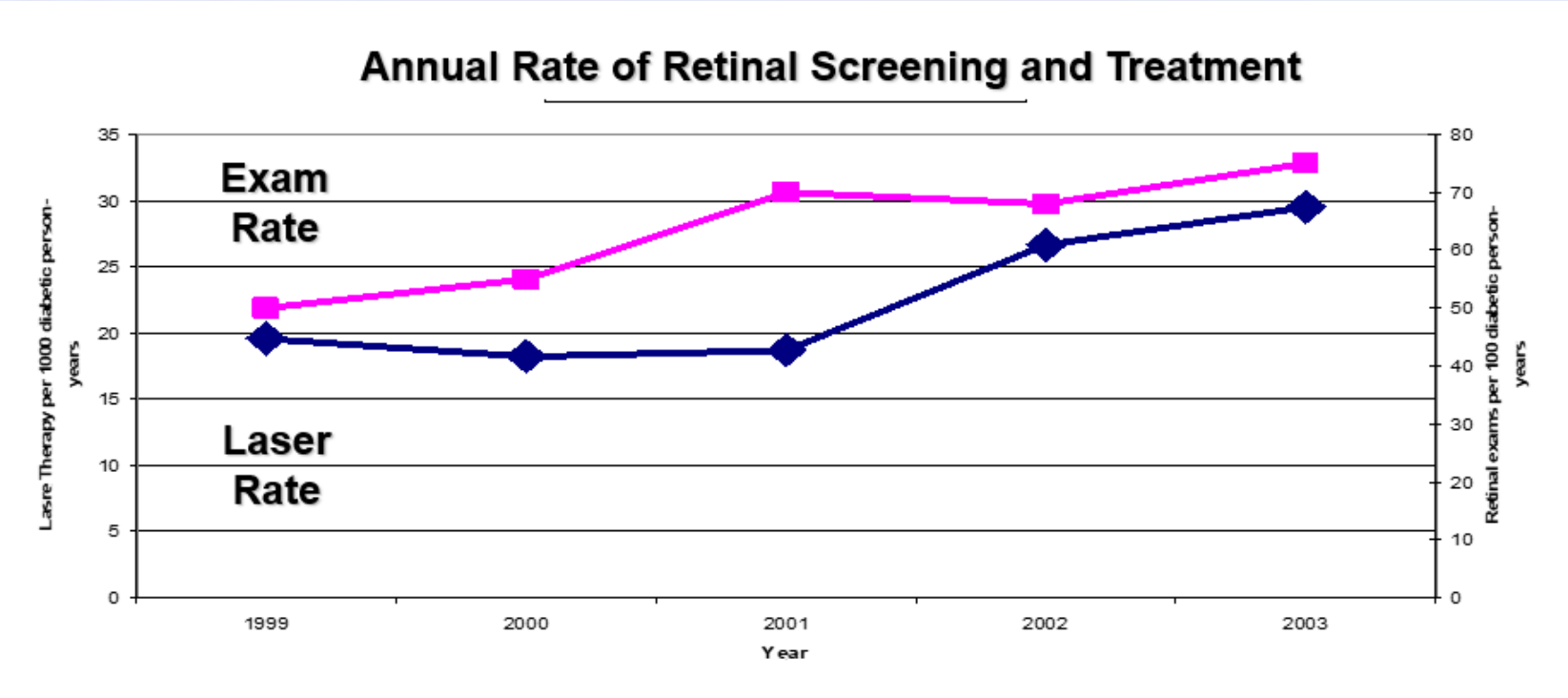
Paolo S. Silva, MD,[1,2] Jerry D. Cavallerano, OD, PhD,[1,2] Nour Maya N. Haddad, MD,[1] Hanna Kwak, BS,[1] Kelli H. Dyer, DO,[1] Ahmed F. Omar, MD,[1,3] Hasanain Shikari, MD,[1] Lloyd M. Aiello, MD,[1,2] Jennifer K. Sun, MD, MPH,[1,2] Lloyd Paul Aiello, MD, PhD[1,2]

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

Addition of Primary Care-Based Retinal Imaging Technology to an Existing Eye Care Professional Referral Program Increased the Rate of Surveillance and Treatment of Diabetic Retinopathy

Charlton Wilson, MD[1]
Mark Horton, OD, MD[2]
Jerry Cavallerano, OD, PhD[3]
Lloyd M. Aiello, MD[3]

Diabetes Care
Feb 2005



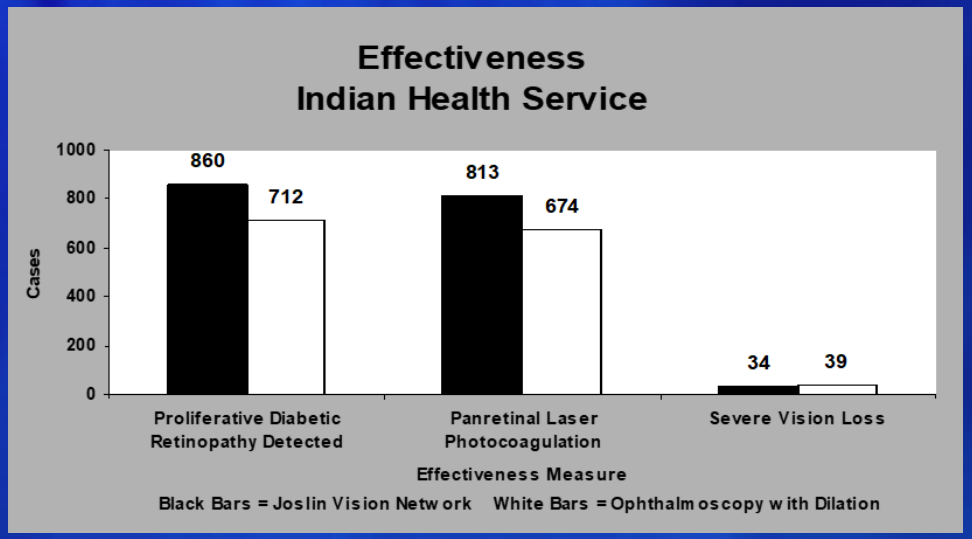
50% increase in DR surveillance and laser treatments

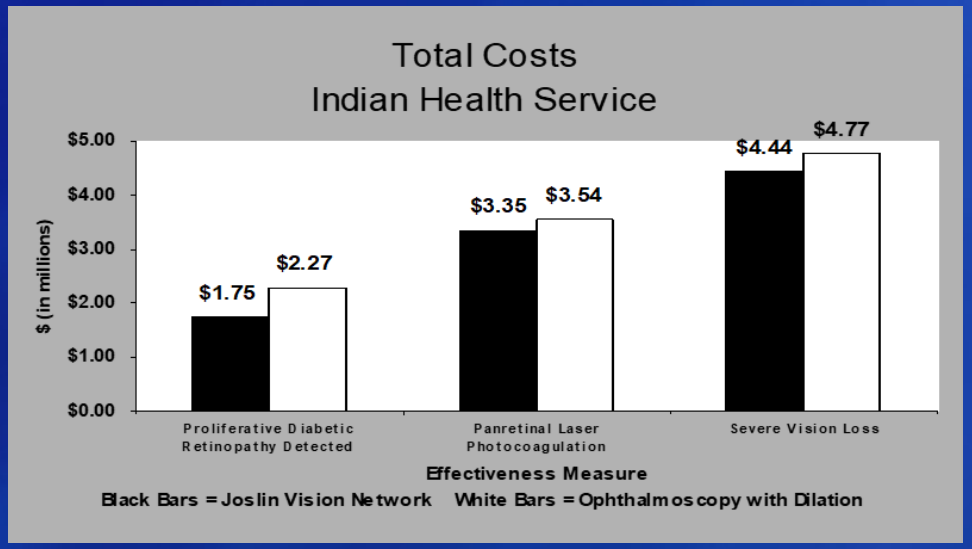
Diabetic Retinopathy

Cost Effectiveness

IHS/JVN is both less costly and more effective for:

- Detecting DR
- Identifying IHS patients who require laser tx
- Preventing severe vision loss





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*

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

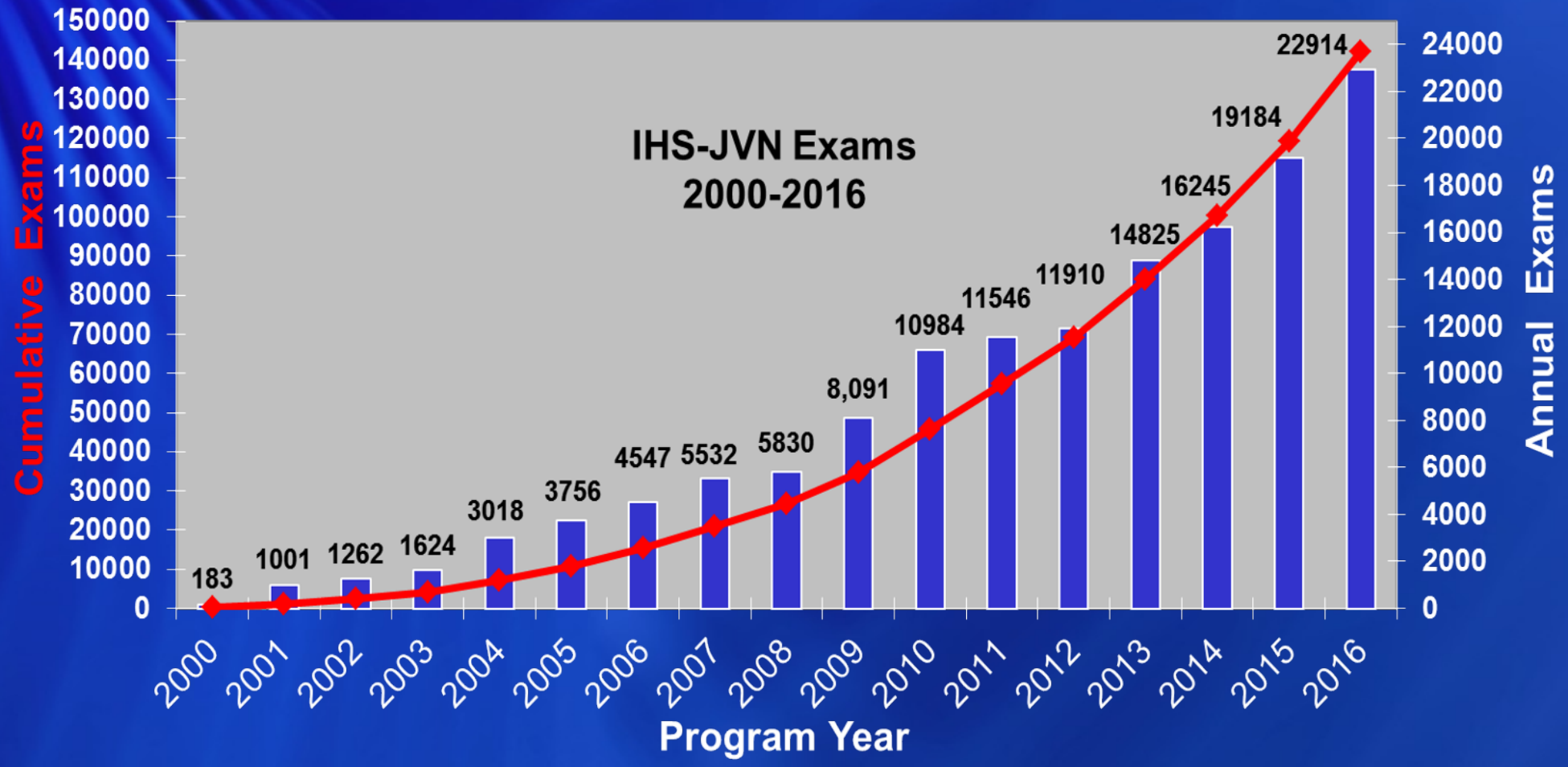
- Spirit Lake, ND
- Ft. Yates, ND
- Belcourt, ND
- Ft. Peck, MT
- Ft Belknap, MT
- Crow Agency, MT
- Lame Deer, MT
- Browning, MT
- Ft Washakie, WY
- Red Lake, MN
- Cass Lake, MN
- White Earth, MN
- Lawrence, KS
- Mayetta, KS
- Shiprock, NM
- Santa Fe, NM
- Albuquerque, NM
- Mescalero, NM
- Crown Point, NM
- Jicarilla, NM
- San Fidel, NM
- Dallas, TX
- Winnebago, NE
- Hayward, WI
- Mt Pleasant, MI
- Oneida, NY
- Charlestown, RI

- Fairbanks, AK
- Bristol Bay, AK
- Ketchekan, AK
  - Metlakatla, AK
- Rock Hill, SC
- Cherokee, NC
- U&O, UT
- Presque Isle, ME
- Indian Island, ME
- Philadelphia, MS

Portable Deployments

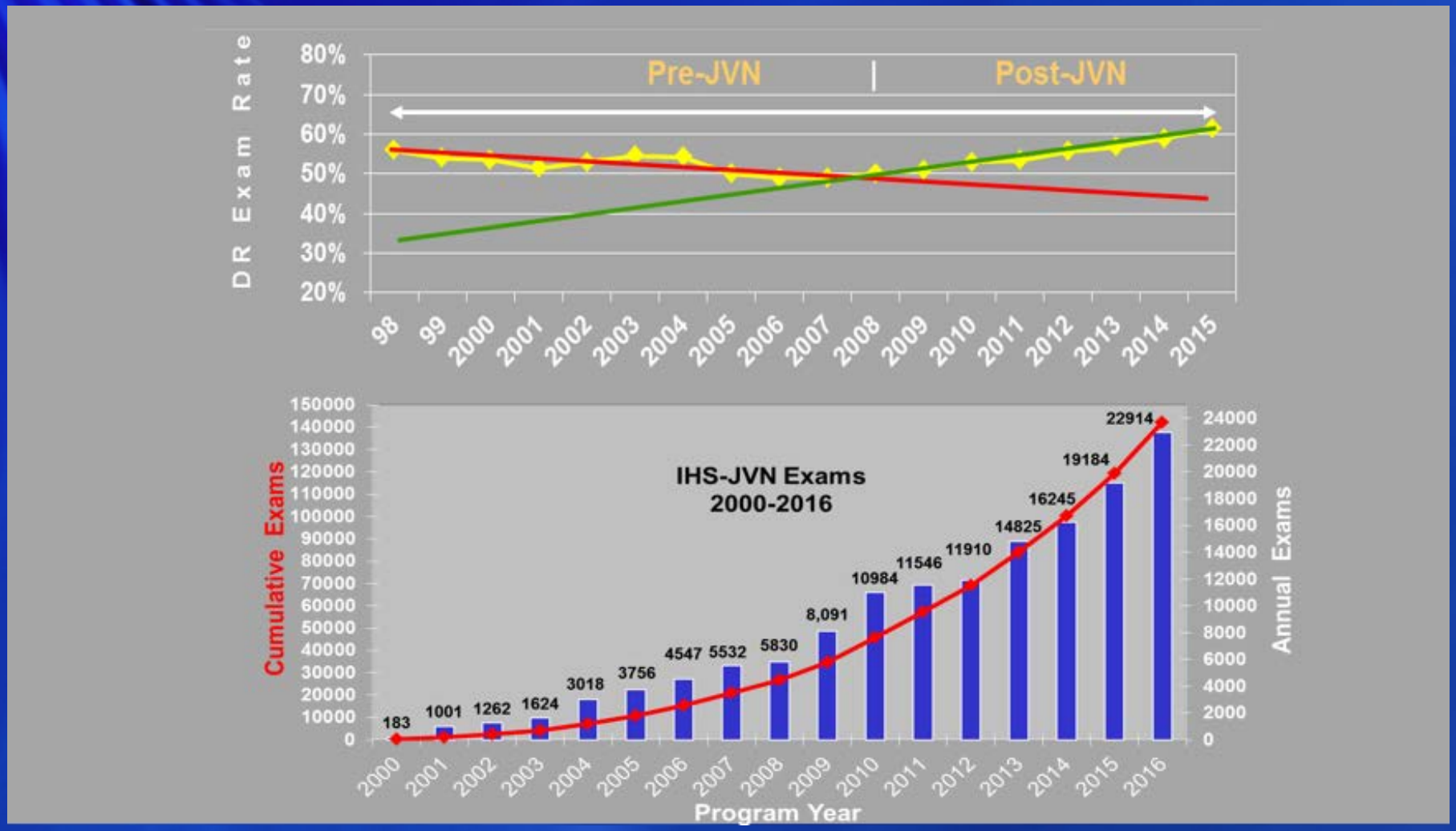
- Alaska- EAT, APIA
- North Carolina
- Oklahoma- Redbird
  Sam Hider Jay
- Arizona- Supai
- Nevada- Schurz, Loveloc
- Yerington
- Maine- Littleton,
  Princeton,
  Pleasant Point

IHS/JVN Experience



Clinical Outcome

IHS DR Exam Rate pre/post JVN Ramp-up



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?

Mark B. Horton, OD, MD
Director, IHS/JVN Teleophthalmology Program

mark.horton@ihs.gov
602 820-7654