Examining the Diabetic Patient: What Matters Most

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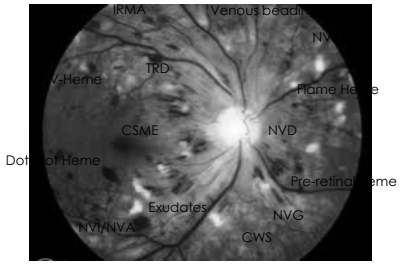
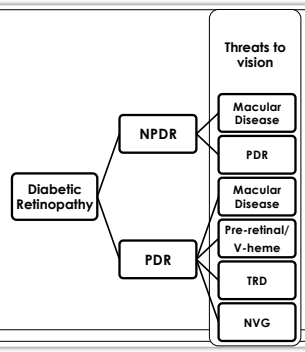
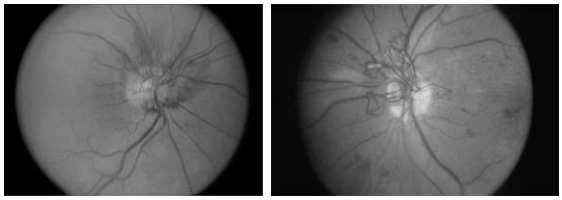
Objectives

- Simplify strategy for evaluating the eyes of diabetics
- Identify the threats to vision and treatments
- Develop patient education that helps diabetics understand the importance of controlling their disease

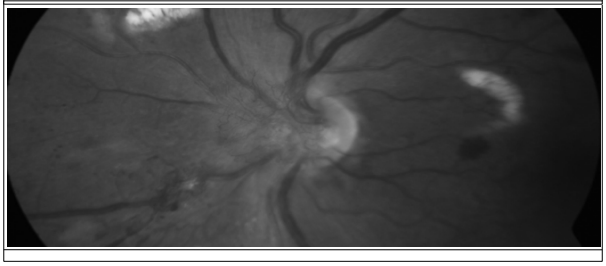




Preretinal Neovascularization = Proliferative Disease



Proliferative Diabetic Retinopathy (PDR)



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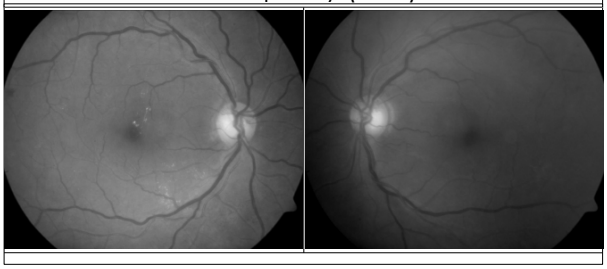

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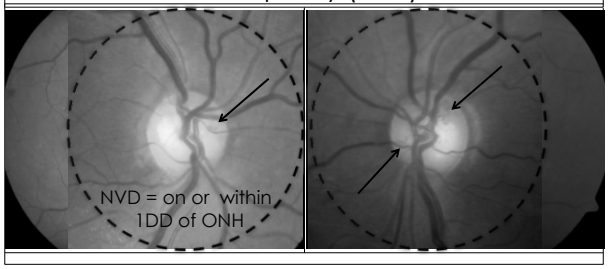

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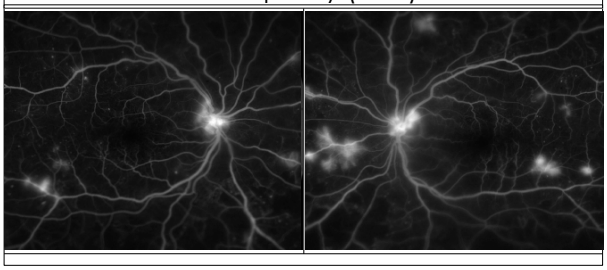
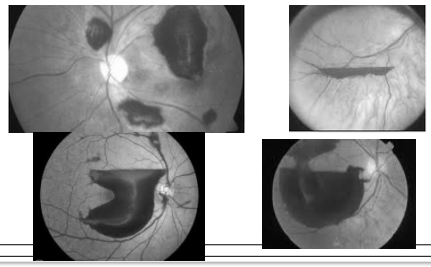
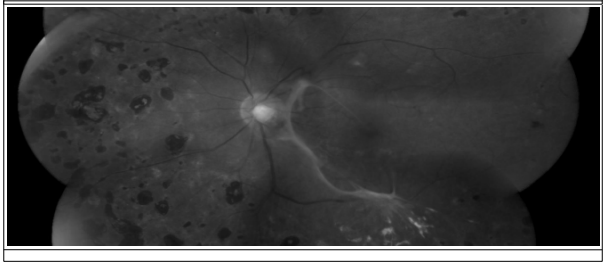


Proliferative Disease: Preretinal hemorrhage

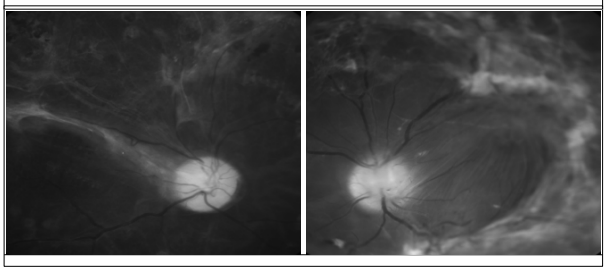


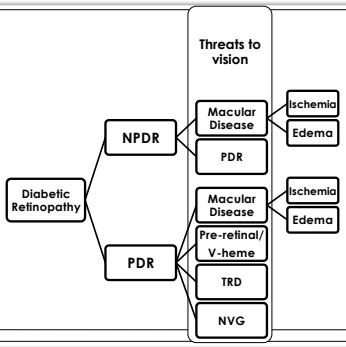
Proliferative Disease: Vitreous Hemorrhage

Proliferative Disease: Tractional Retinal Detachment



Proliferative Disease: Tractional Retinal Detachment





Clinically Significant Macular Edema

CSME	Retinal thickening within 500 microns of fovea
	Exudate within 500 microns of fovea with adjacent thickening
	Retinal thickening of at least one disc area any part within one disc diameter of center of fovea

ETDRS. Ophthalmology. 1985; 103:1796-1806
ETDRS. Ophthalmology. 1987; 94: 761-774

Clinically Significant Macular Edema

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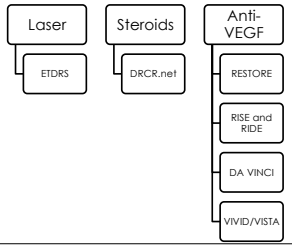
What are the chances?

No Tx	Tx	RRR	ARR	NNT
90%	45%	50%	45%	2
25%	12.5%	50%	12.5%	8
10%	5%	50%	5%	20
2/million	1/million	50%	0.0001%	1,000,000

ETDRS: Focal laser for CSME
DRS: PRP for High Risk PDR

Treatments DME



Early Treatment Diabetic Retinopathy Study (ETDRS)

Moderate vision loss (15 letters on ETDRS) at 3 years

24% untreated	12% treated

ARR 12%

NNT 8

Few (<3%) had improvement of 15 letters or more

ETDRS. Ophthalmology. 1985; 103:1796-1806
ETDRS. Ophthalmology. 1987; 94: 761-774

Diabetic Retinopathy Clinical Research Network (DRCR.net)

DME
20/40 – 20/320
N = 840

1mg triamcinolone	4mg triamcinolone	Macular laser
N = 256	N = 254	N = 330

DRCR.net. Ophthalmology. 2008:115(9):1447-1459

DRCR.net

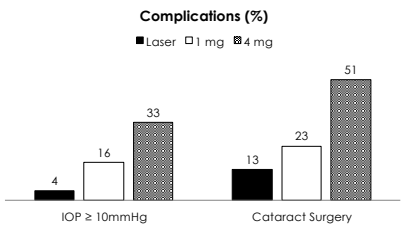
4 mg > 1 mg/laser • 4 months

4 mg = 1 mg = laser • 1 year

laser > 4 mg/1 mg • 2 years

DRCR.net. Ophthalmology. 2008:115(9):1447-1459

DRCR.net



DRCR.net. Ophthalmology. 2008:115(9):1447-1459

RESTORE

DME
20/32 – 20/160
N = 345

Ranibizmab + sham laser	Ranibizumab + active laser	Active laser + sham injections
N = 116	N = 118	N = 111

RESTORE study. Ophthalmology 2011;118:615-25

RESTORE

Average change in visual acuity from baseline to month 12

Ranibizumab + sham laser: +6.1 ± 6.4 letters (p<.0001)	Ranibizumab + active laser: +5.9 ± 7.9 letters (p<.0001)	Active laser + sham injections: +0.8 ± 8.6 letters

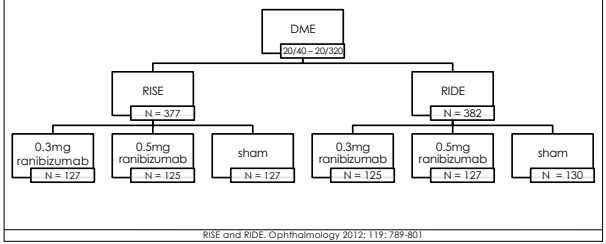
20/40 BCVA or better in patients with mild visual loss

Ranibizumab + sham laser: 20% → 53%	Ranibizumab + active laser: 16% → 45%	Active laser + sham injections: 15% → 24%

ARR 33%, NNT 3	ARR 29%, NNT 3	ARR 9%, NNT 11

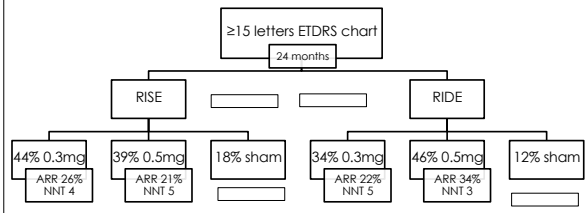
RESTORE study. Ophthalmology 2011;118:615-25

RISE and RIDE



RISE and RIDE. Ophthalmology 2012; 119: 789-801

RISE and RIDE



RISE and RIDE. Ophthalmology 2012; 119: 789-801

RISE and RIDE

Mean change from baseline BCVA

+8.5-9.9 letters more in ranibizumab vs. sham

% with BCVA ≥20/40

60% ranibizumab	36% sham	ARR 24% NNT 4

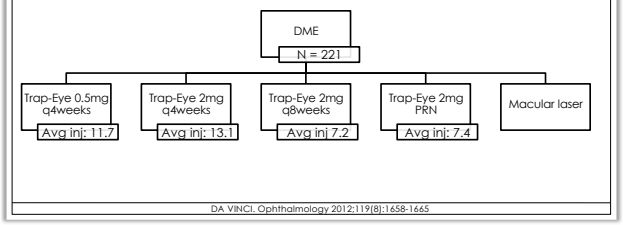
Progression to PDR and needing PRP

< 1% ranibizumab	11% sham

RISE and RIDE. Ophthalmology 2012; 119: 789-801

Lucentis® (ranibizumab) FDA approved for treatment of DME in 2012

DA VINCI



DA VINCI. Ophthalmology 2012;119(8):1658-1665

DA VINCI

Mean change in BCVA from baseline at 1 year

Trap-Eye: +11 letters	Laser: -1 letter

Eyes gained ≥ 3 lines BCVA

Trap-Eye: 38%	Laser: 11%

ARR 27%

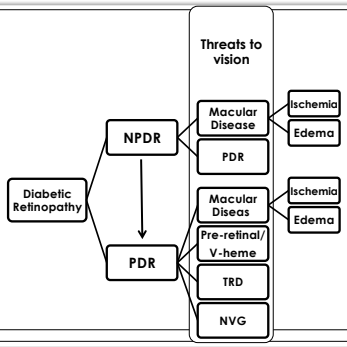
NNT 3

DA VINCI. Ophthalmology 2012;119(8):1658-1665

Trap-Eye (aflibercept) was FDA approved for treatment of DME in 2014

Summary DME Treatment

DME Tx	Laser maintains vision rather than improving it
	Steroids work as well as laser but the side effects are worse
	Anti-VEGF has shown to improve vision although requires a lengthy course of treatment of monthly injections



4-2-1 Rule: Raising the (Risk) Bar

4 Severe retinal hemorrhages in 4 quadrants

2 Venous beading in 2 quadrants

1 IRMA in 1 quadrant

NPDR → PDR in 1 year

Mild	• 5% risk of progression to PDR
Moderate	• 15% risk of progression to PDR
Severe	• **52% risk of progression to PDR** • Meets ONE criteria of 4-2-1 Rule
Very Severe	• **75% risk of progression to PDR** • Meets TWO criteria of 4-2-1 rule

Klein R, et al. Arch Ophthalmol. 1984;102(4):527-532

Follow-up intervals in months

Severity of NPDR	American Academy of Ophthalmology	American Optometric Association
None	12	12
Mild	6-12	12
Moderate	6-12	12
Severe	2-4	3-4
Very Severe	2-4	2-3

4-2-1 Rule

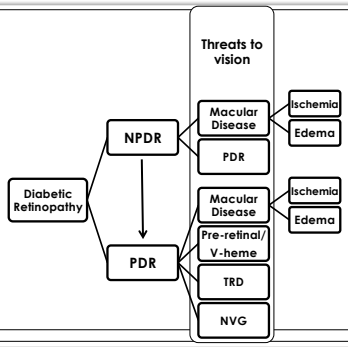
AAO. Preferred Practice Pattern. Diabetic Retinopathy. 2013.
AOA. Evidence-Based Clinical Practice Guidelines. Eye Care of the Patient with Diabetes Mellitus. 2014

8-year Incidence of CHD and Stroke as a Hazard Ratio (HR) in Japanese Type 2 Diabetics (N=2033)

Retinal Finding	Coronary Heart Disease	Stroke
Mild-Mod NPDR	1.69 (95% CI 1.17-2.97)	2.69 (95% CI 1.03-4.86)
Retinal hemes/MA	1.63 (95% CI 1.04-2.56)	Not associated (P=0.06)
CWS	Not associated (P=0.66)	2.39 (95% CI 1.35-4.24)

Communicate Diabetic Eye Exam Results to PCP!

Kawasaki R, et al. Ophthalmology 2013;120(3)574-582



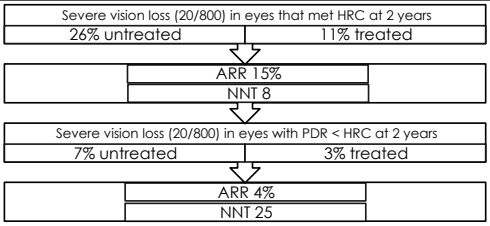
High Risk Characteristics

HRC

NVD ≥ ¼ disc area

Any NVD or NVE with pre-retinal or vitreous hemorrhage

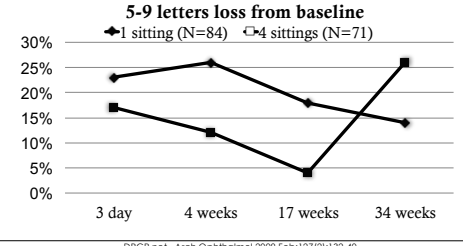
Diabetic Retinopathy Study (DRS)



DRS. Am J Ophthalmol. 1976;81:383-396
DRS Report No. 8. Ophthalmology. 1988;88:583-600

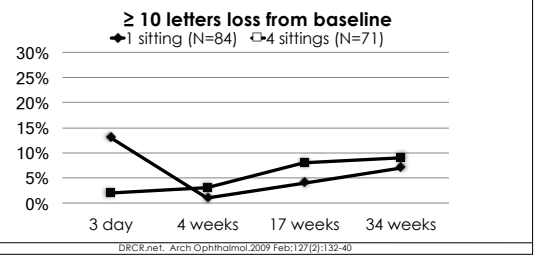
"My vision was fine until you sent me to that retinal specialist for laser"

PRP for PDR



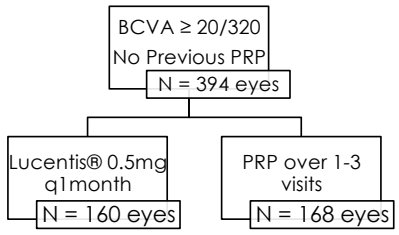
DRCR.net. Arch Ophthalmol.2009 Feb;127(2):132-40

PRP for PDR



DRCR.net. Arch Ophthalmol.2009 Feb;127(2):132-40

Anti-VEGF for PDR



DRCR.net. JAMA 2015;314(20):2137-2146

Anti-VEGF for PDR: 2 Year Results

Mean change in visual acuity	Lucentis: +2.8 letters	PRP: +0.2 letters
Change in visual field total point score	Lucentis: -23 dB	PRP: -422 dB
DME development	Lucentis: 9%	PRP: 28%
Eyes without PDR on fundus photos	Lucentis: 35%	PRP: 30%

DRCR.net. JAMA 2015;314(20):2137-2146

"Every time a doctor sees a patient, the patient should feel better as a result"
-Anonymous MD

Recorded at

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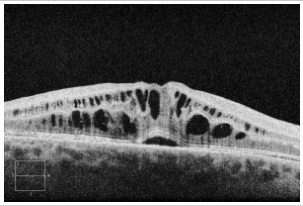

After 20 years of known diabetes the prevalence of DME was approximately 28% in both type 1 and type 2 diabetes

The Wisconsin Epidemiologic Study of Diabetic Retinopathy. IV. Diabetic macular edema. Ophthalmology. 1984;91:1464–74

The most widely accepted methods to reduce vision loss from DME and reduce progression of DR are:

1) Intensive glycemic control
2) Blood pressure control
3) Lipid management

Diabetes Control and Complication Trial (DCCT). N Engl J Med. 1993;329:977–86.
UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998;352:837–53

UK Prospective Diabetes Study (UKPDS). BMJ. 2002;325:860.
UK Prospective Diabetes Study (UKPDS). Diabetologia. 2006;49:1761–9

ACCORD Study Group. N Engl J Med. 2010;362(17):1563-1574
FIELD Study Group. Cardiovasc Diabetol. 2005;4:13

ORIGINAL CONTRIBUTION

Association of an Intensive Lifestyle Intervention With Remission of Type 2 Diabetes

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Context The frequency of remission of type 2 diabetes achievable with lifestyle intervention is unclear.

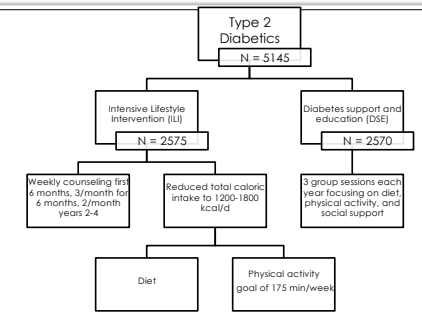
Objective To examine the association of a long-term intensive weight-loss intervention with the frequency of remission from type 2 diabetes to prediabetes or normoglycemia.

Design, Setting, and Participants Ancillary observational analysis of a 4-year randomized controlled trial (baseline visit, August 2001–April 2004; last follow-up, April 2008) comparing an intensive lifestyle intervention (ILI) with a diabetes support and education control condition (DSE) among 4503 US adults with body mass index of 25 or higher and type 2 diabetes.

Interventions Participants were randomly assigned to receive the ILI, which included weekly group and individual counseling in the first 6 months followed by 3 sessions per month for the second 6 months and twice-monthly contact and regular refresher group series and campaigns in years 2 to 4 (n=2241) or the DSE, which was an offer of 3 group sessions per year on diet, physical activity, and social support (n=2262).

Main Outcome Measures Partial or complete remission of diabetes, defined as transition from meeting diabetes criteria to a prediabetes or nondiabetic level of glycemia (fasting plasma glucose <126 mg/dL and hemoglobin A_{1c} <6.5% with no antihyperglycemic medication).

Results Intensive lifestyle intervention participants lost significantly more weight than DSE participants at year 1 (net difference, −7.9%; 95% CI, −8.3% to −7.6%) and at year 4 (−3.9%; 95% CI, −4.4% to −3.5%) and had greater fitness increases at year 1 (net difference, 15.4%; 95% CI, 13.7%–17.0%) and at year 4 (6.4%; 95% CI, 4.7%–8.1%) (P< .001 for each). The ILI group was significantly more likely to experience any remission (partial or complete), with prevalences of 11.5% (95% CI, 10.1%–12.8%) during the first year and 7.3% (95% CI, 6.2%–8.4%) at year 4, compared with 2.0% for the DSE group at both time points (95% CIs, 1.4%–2.6% at year 1 and 1.5%–2.7% at year 4) (P< .001 for each). Among ILI participants, 9.2% (95% CI, 7.3%–10.4%)



Association of an Intensive Lifestyle Intervention with Remission of Type 2 Diabetes.
JAMA. 2012;308(23):2489-2496

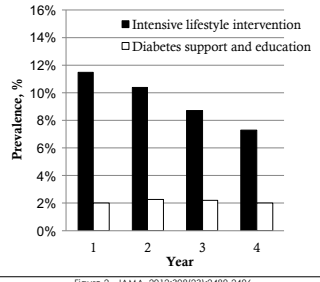


Figure 2. JAMA. 2012;308(23):2489-2496

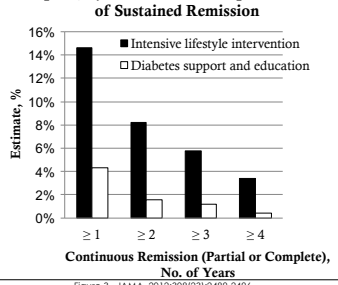


Figure 3. JAMA. 2012;308(23):2489-2496

Highest probabilities of 1-year remission

Less than 2-year history of diabetes	• **21.2%**; 95% CI, 18.0%-24.7%
More than 6.5% weight loss	• **16.4%**; 95% CI, 14.5%-18.6%
Fitness improvements	• **15.6%**; 95% CI, 13.3%-18.1%
Low initial HbA_{1c}	• **17.1%**; 95% CI, 14.4%-20.3%
Not taking antihypertensive medications	• **15.2%**; 95% CI, 12.3%-18.6%

Gregg EW, et al. JAMA. 2012;308(23):2489-2496

Avoid words that maim

Encourage with words that heal

Teach well

Summary

- Inquire about blood sugar, HbA_{1c}, year of diagnosis, blood pressure, cholesterol, PCP visits (send a report to them), diet/exercise
- Look carefully for the threats to vision
- Engage in conversation with empathy, compassion and educate well

Contact Information
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