Eye Disease in Diabetes
ABCD conference
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Financial disclosures

- Lecture fees, conference and travel grants

- Bayer
- Roche
- Allergan
- Heidelberg

What we will cover

- How the Diabetic Eye Screening Programme (DESP) works
- Stages/ Classification of Diabetic Retinopathy
- How to treat Retinopathy and Maculopathy
- When to involve Ophthalmology in GLP1-RA and HCL treatment.
- Key points in NICE Guidance- Treatment and Monitoring of Diabetic Retinopathy and Maculopathy

Risk of blindness

- Diabetic Retinopathy no longer the leading cause of blindness in the working age population
- Contributing factors - National Diabetic eye screening service and improved glycaemic control
- Still a significant cause of visual impairment-especially post COVID-19.

Open Access Research

BMJ Open

A comparison of the causes of blindness certifications in England and Wales in working age adults (16–64 years), 1999–2000 with 2009–2010

Gerald Liew,[1,2] Michel Michaelides,[1,3] Catey Bunce[4]

To cite: 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. doi:10.1136/bmjopen-2013-004015

► Prepublication history for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2013-004015).

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ABSTRACT

Objectives: To report on the causes of blindness certifications in England and Wales in working age adults (16–64 years) in 2009–2010; and to compare these with figures from 1999 to 2000.

Design: Analysis of the national database of blindness certificates of vision impairment (CVIs) received by the Certifications Office.

Setting and participants: Working age (16–64 years) population of England and Wales.

Main outcome measures: Number and cause of blindness

Results: blindness inclusive main cau retinal dis the total) persons, 14.1%). for almos April 199 blindness maculopa (15.8%)

Conclus diabetic r cause of England a retinal dis including screening glycaemic representing the commonest cause of certification in the

Strengths and limitations of this study

- Strengths of the data include nationwide coverage, collection of uniform data fields with prespecified tick boxes, and clear and consistent definitions of sight impairment.
- Limitations include comparisons across two slightly different data collection forms.

through use of a designated certificate, the

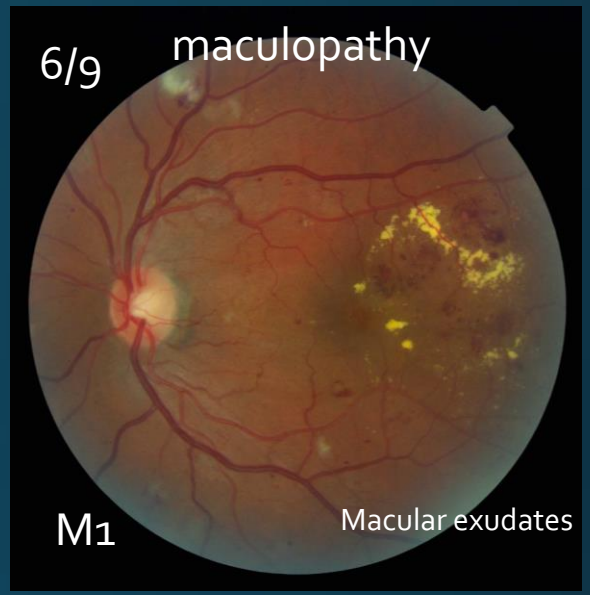
permits access to certain state benefits and

Table 1 Numbers of working age adults (age 16–64) with severe sight impairment (blindness) in England and Wales: certifications 2009–2010

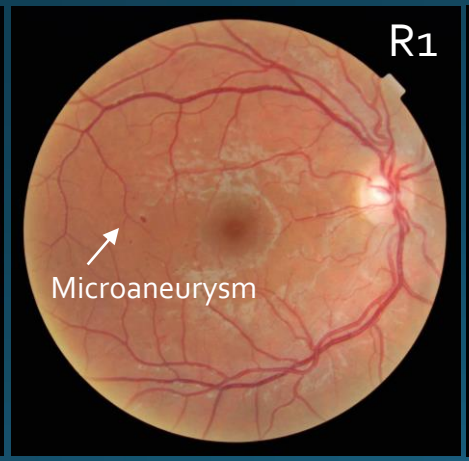
ICD-9 codes	Diagnosis	Main cause (% total)	Contributory cause (% total)	Combined (% total)
362.7	Hereditary retinal disorders	354 (20.2)	29 (6.6)	383 (20.0)
362/34 000	Diabetic retinopathy/maculopathy	253 (14.4)	56 (12.8)	309 (16.2)
377.1	Optic atrophy	248 (14.1)	46 (10.5)	294 (15.4)
365	Glaucoma	104 (5.9)	60 (13.7)	164 (8.6)
743–760	Congenital abnormalities of the eye	89 (5.1)	32 (7.3)	121 (6.3)
377.7	Disorders of the visual cortex	72 (4.1)	24 (5.5)	96 (5.0)
430–438	Cerebrovascular disease	56 (3.2)	21 (4.8)	77 (4.0)
362.5	Degeneration of the macula and posterior pole	52 (3.0)	14 (3.2)	66 (3.5)
360.2	Myopia	49 (2.8)	23 (5.2)	72 (3.8)

Diabetic Retinopathy Stages

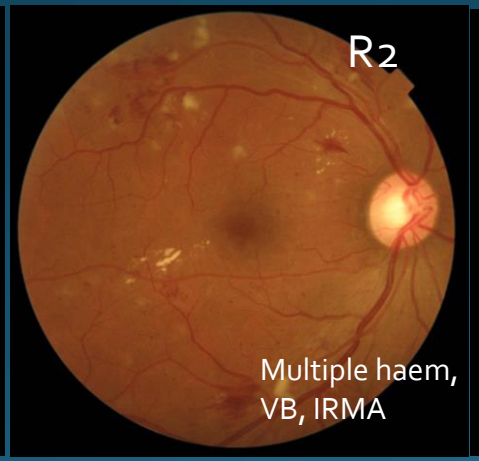
- Progressive Retinal condition from R0 → R1 → R2 → R3A → R3 (S)
- Only symptomatic in late stages- more difficult to treat.
- Retinopathy only detected by systematic photographic screening/ slit lamp examination
- Maculopathy (M1) can occur at any stage with minimal symptoms initially
- Why screening so important



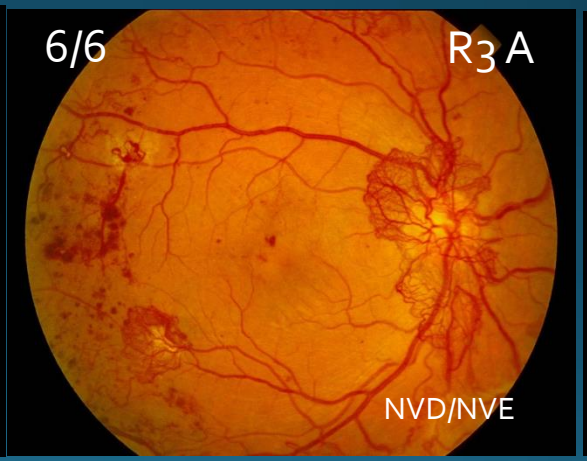
No retinopathy



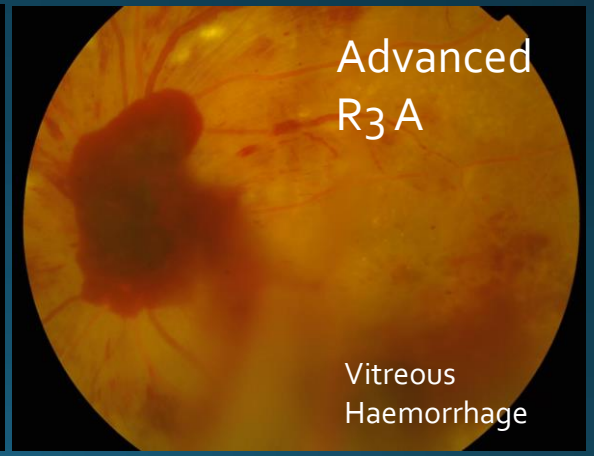
R1- mild NPDR



R2-mod-severe NPDR



R3 A- proliferative DR

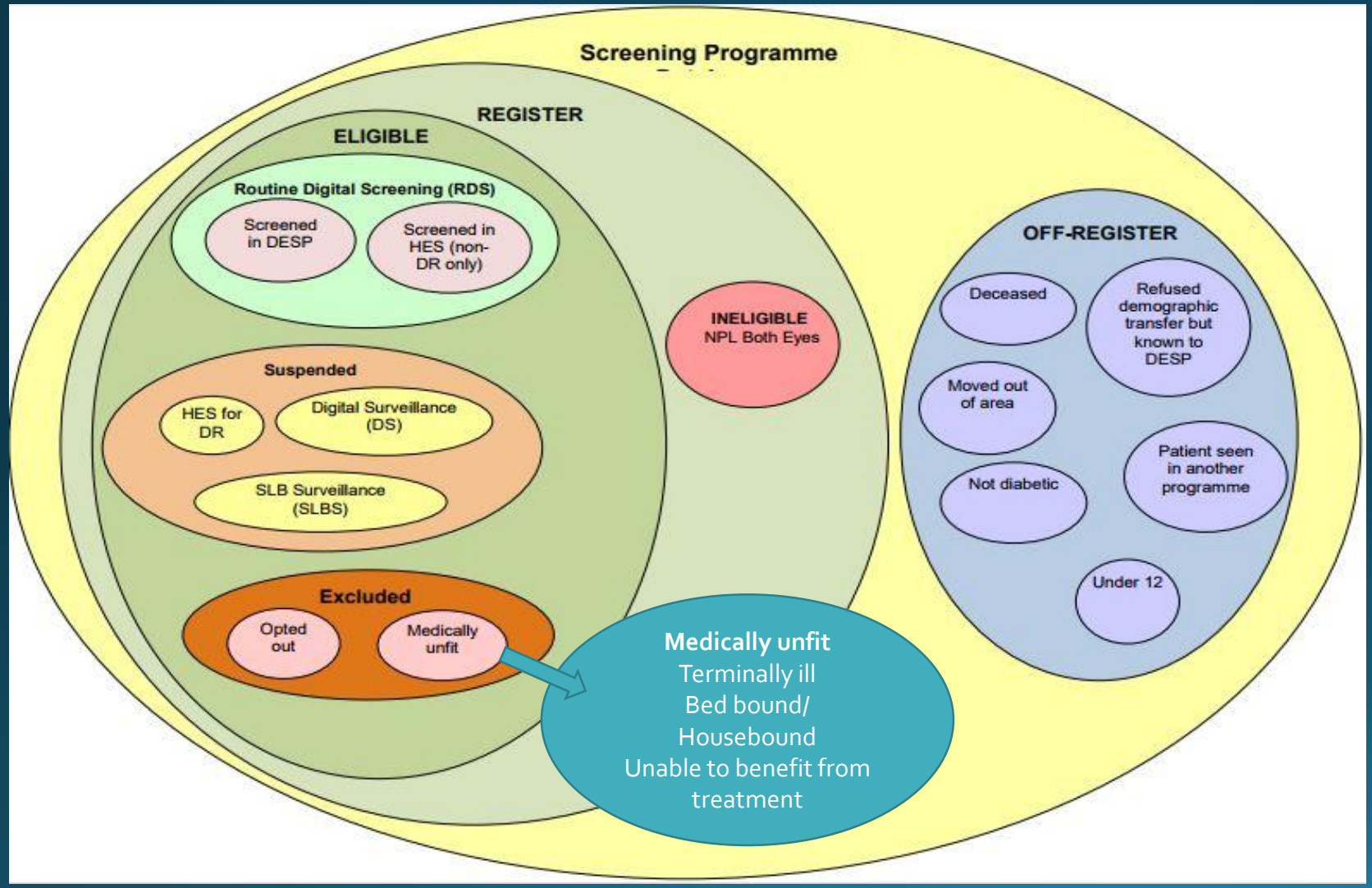


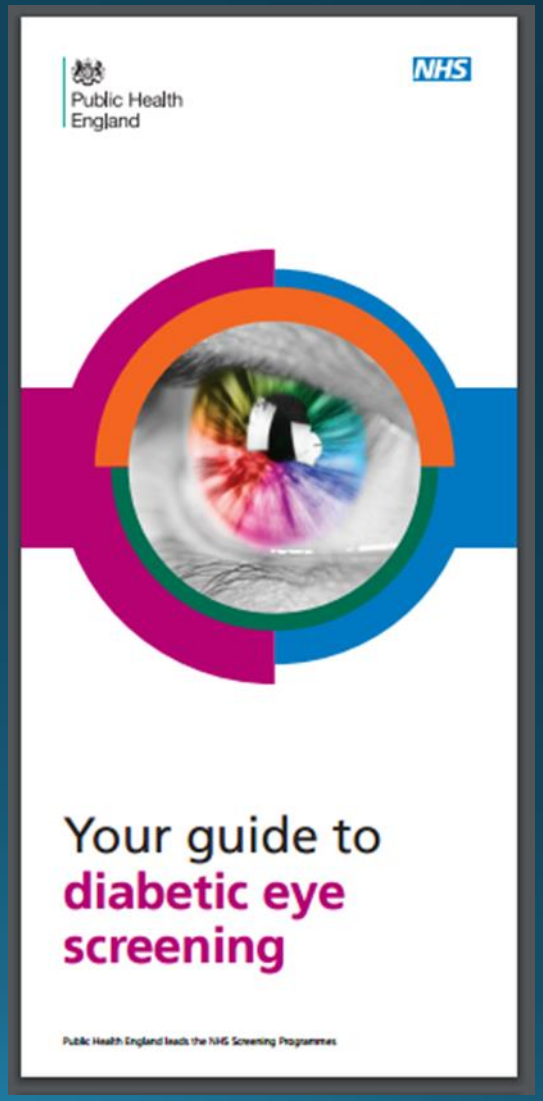
R3 A- vitreous haem

asymptomatic

Symptomatic
With blurred vision

How Eye Screening Works?





Those eligible for screening

- Type 1 or 2 diabetes
- 12 years
- Registered with a GP

Digital monthly GP2DRS extraction

Invited for screening 1-2 yearly to community site

Vision tested, drops instilled, 4 digital photos taken (2 per eye)- Optomize

RoMo, R1Mo

DESP team

Images graded by trained technicians (1°,2 °, arbitration, Referral Outcome grading)

R3a/ R2H Hospital Eye Service

R2L/R1M1 Surveillance Pathway (OCT, more images)

Slit lamp pathway (Unassessables)

Hospital Eye Clinic

Urgent Retinopathy requiring Treatment (R3A)

Advanced maculopathy/ retinopathy requiring treatment/ monitoring (R2HM1, R1M1)

Patients with Non-DR requiring Treatment (AMD)

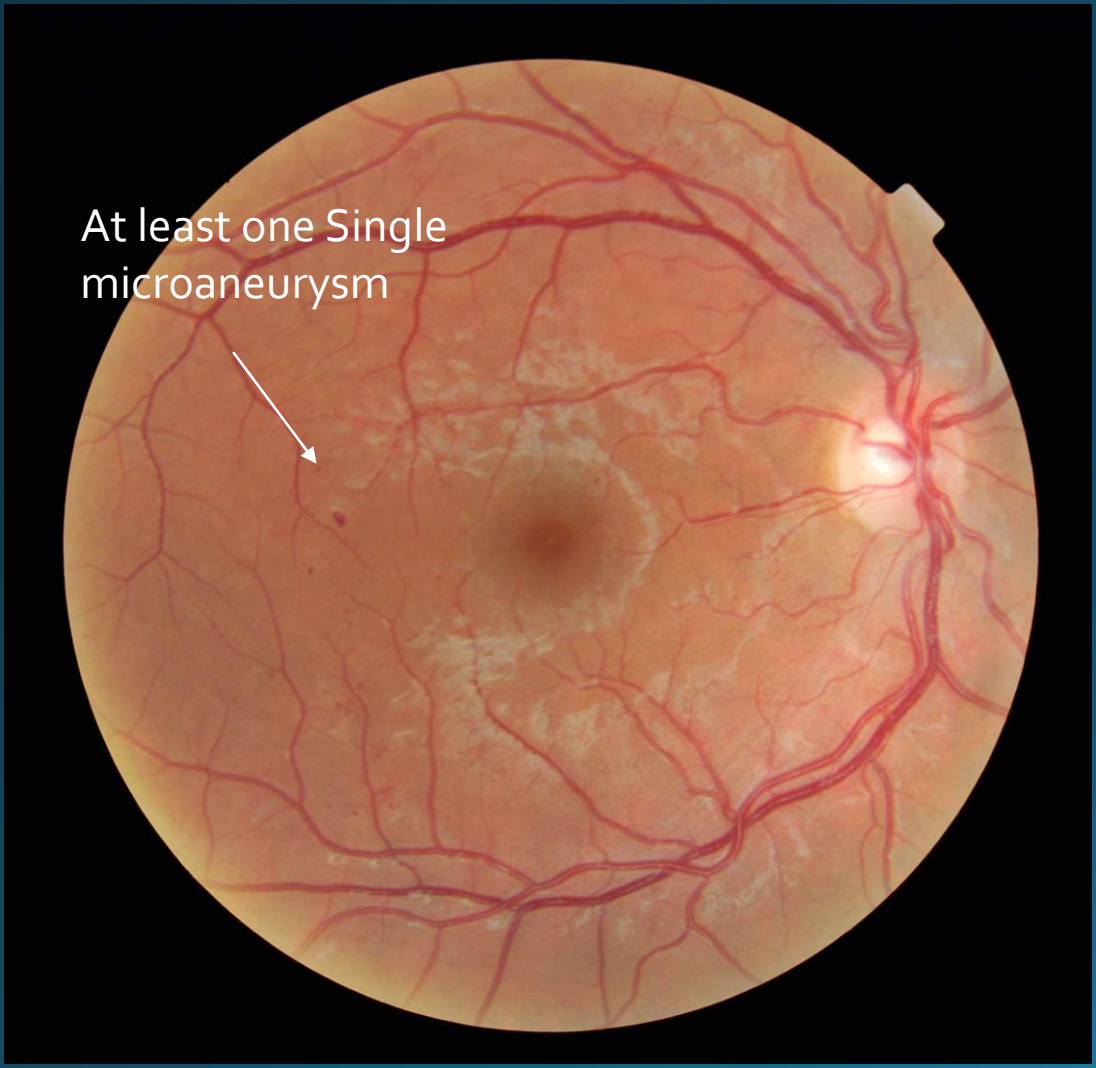
DESP

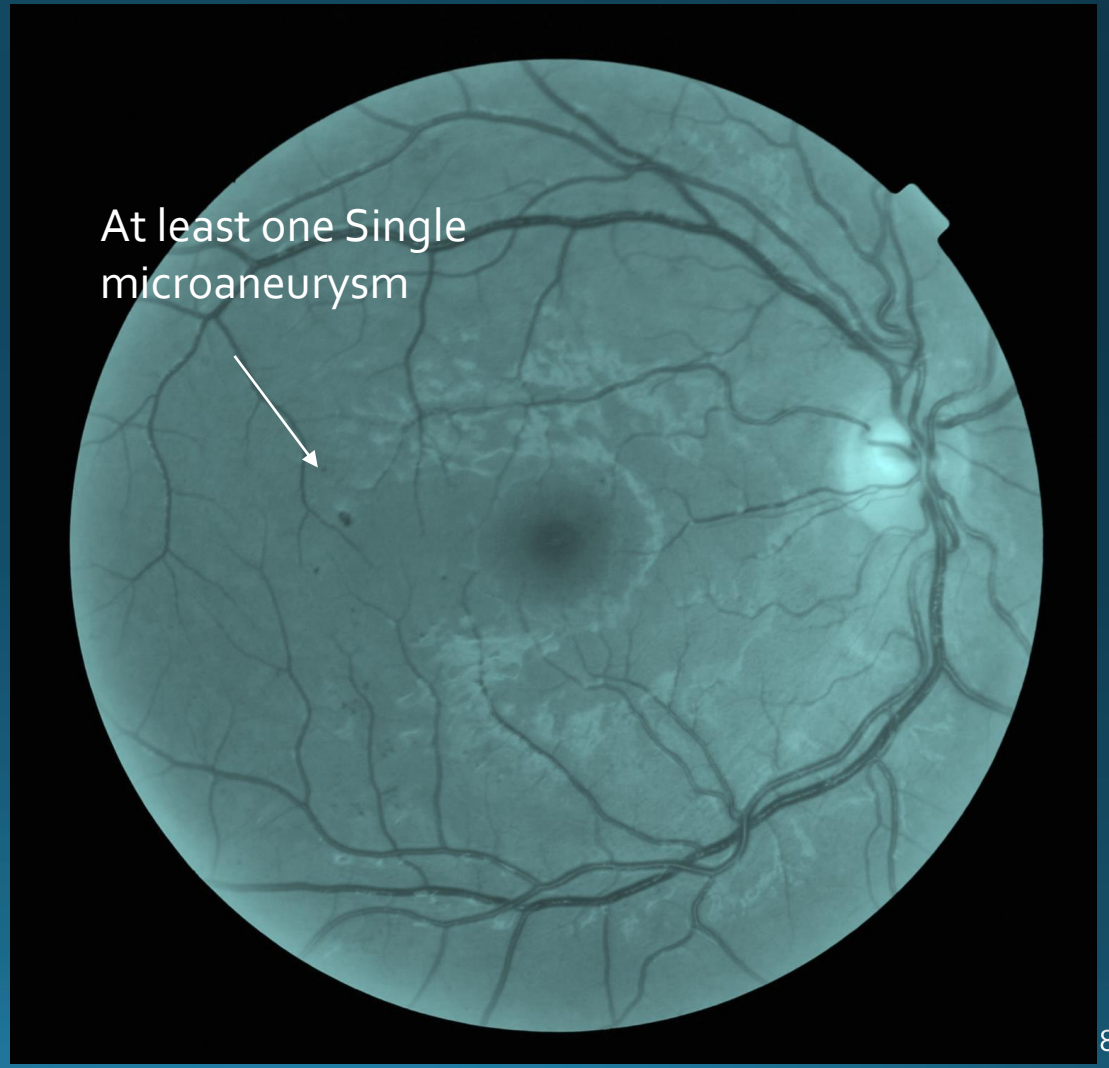
Pt requiring more frequent monitoring -pregnancy -R2L, R1M1, R2LM1

SLB

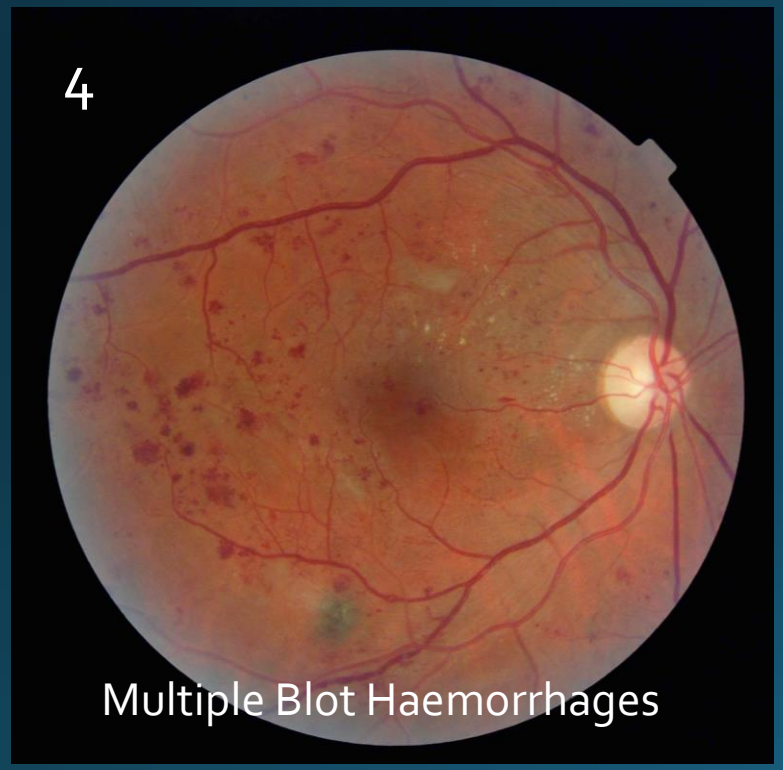
Those with cataract

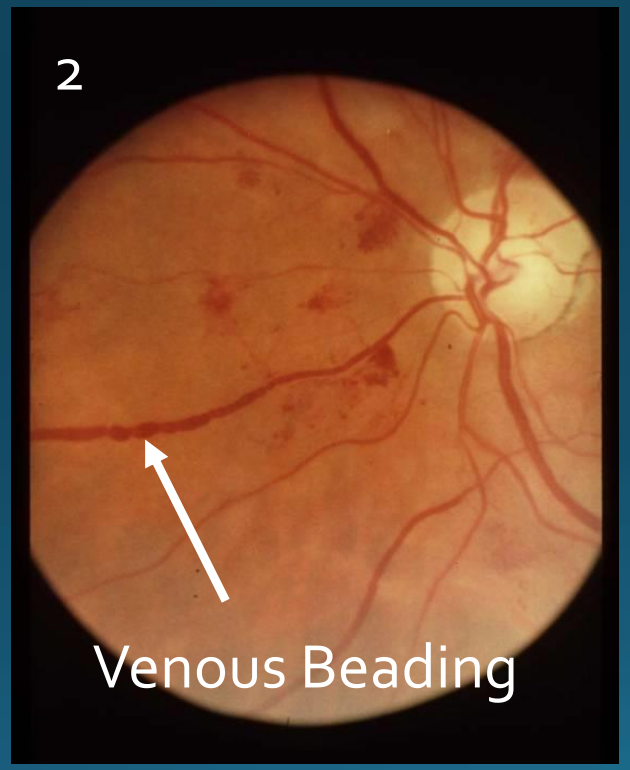
R1 – example – at least 1 microaneurysm

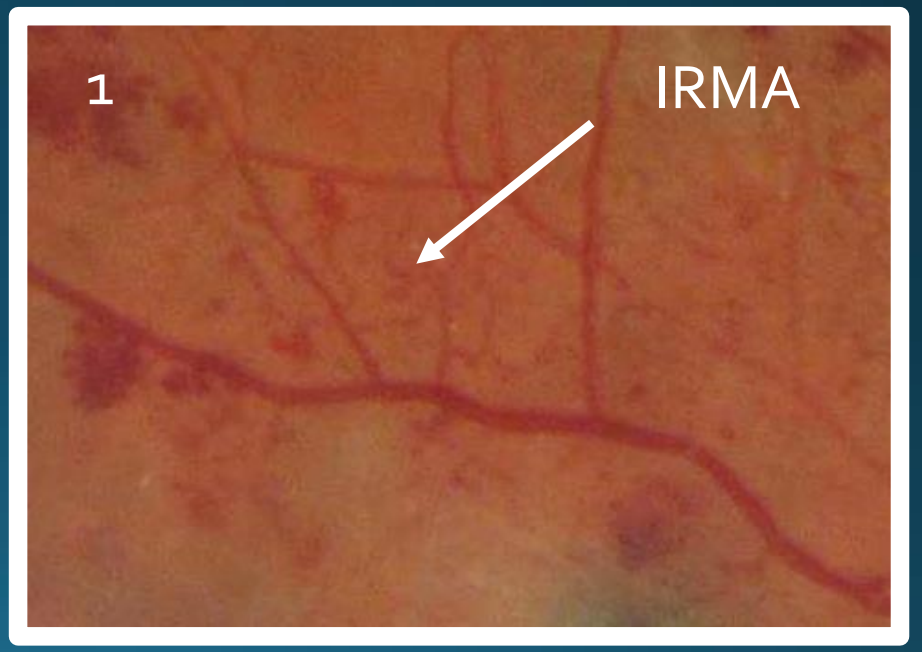




R2 example – MBH, Venous Beading & IRMA- signs of ischaemia (R2L & H: 4:2:1 rule)

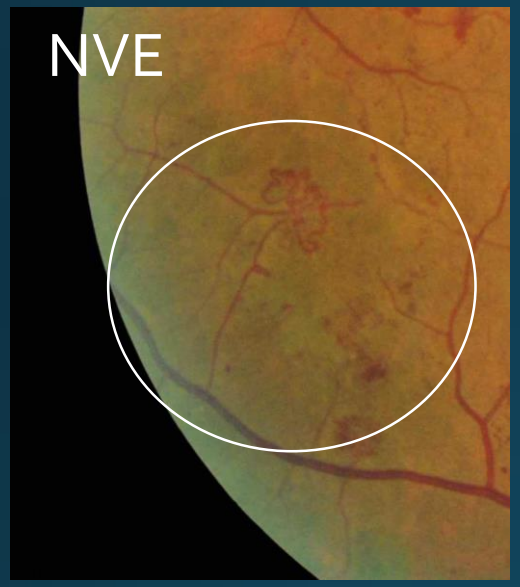


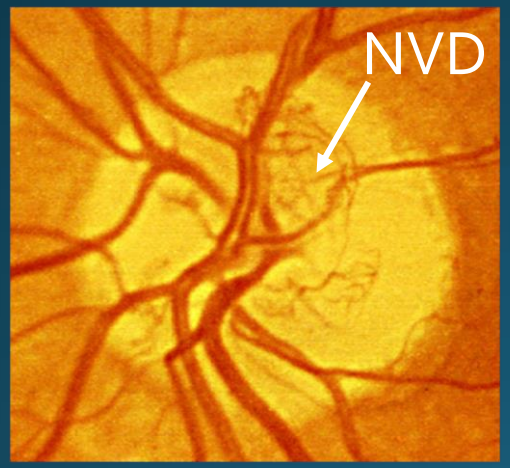


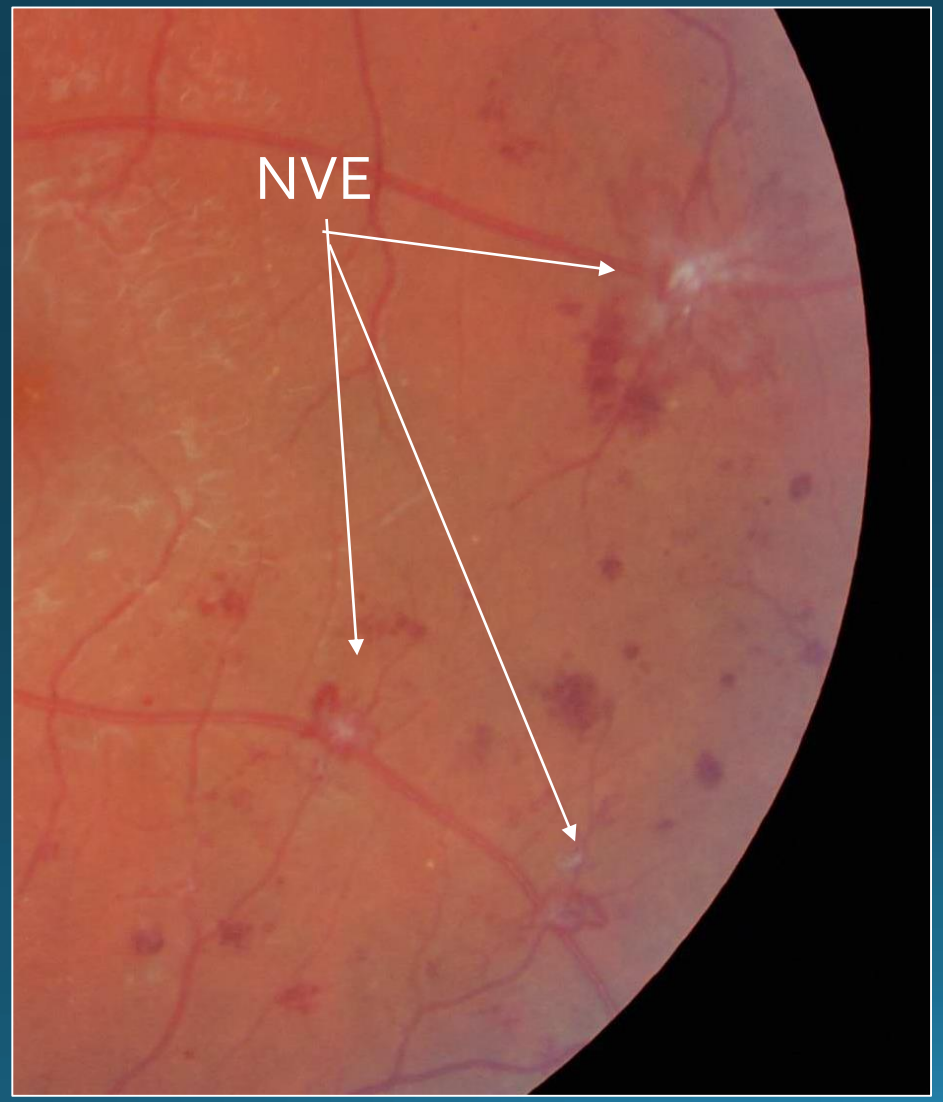


Severe R2/ R2H changes have 50% risk of progression to R3A (PDR) within 1 year

R3A example- Proliferative DR





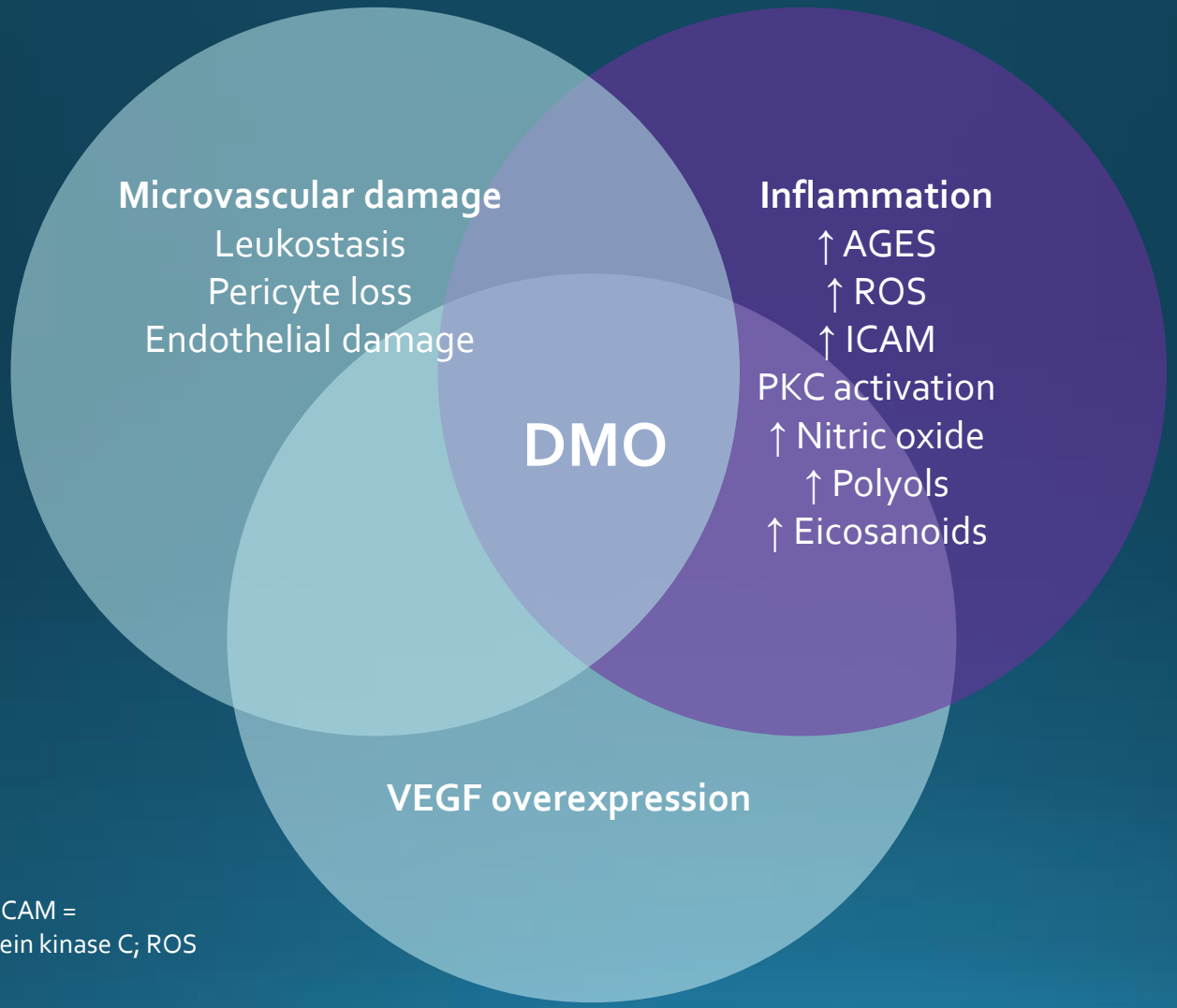


Features:

1. New Vessel formation
2. Elsewhere (NVE) or on the Disc (NVD)
3. Vision often normal
4. Can be subtle to spot
5. High risk characterisitcs increased risk of sight loss

Need Urgent Referral for Laser Treatment

Chronic hyperglycaemia initiates a number of inter-related pathways that lead to Diabetic Retinopathy/ Maculopathy



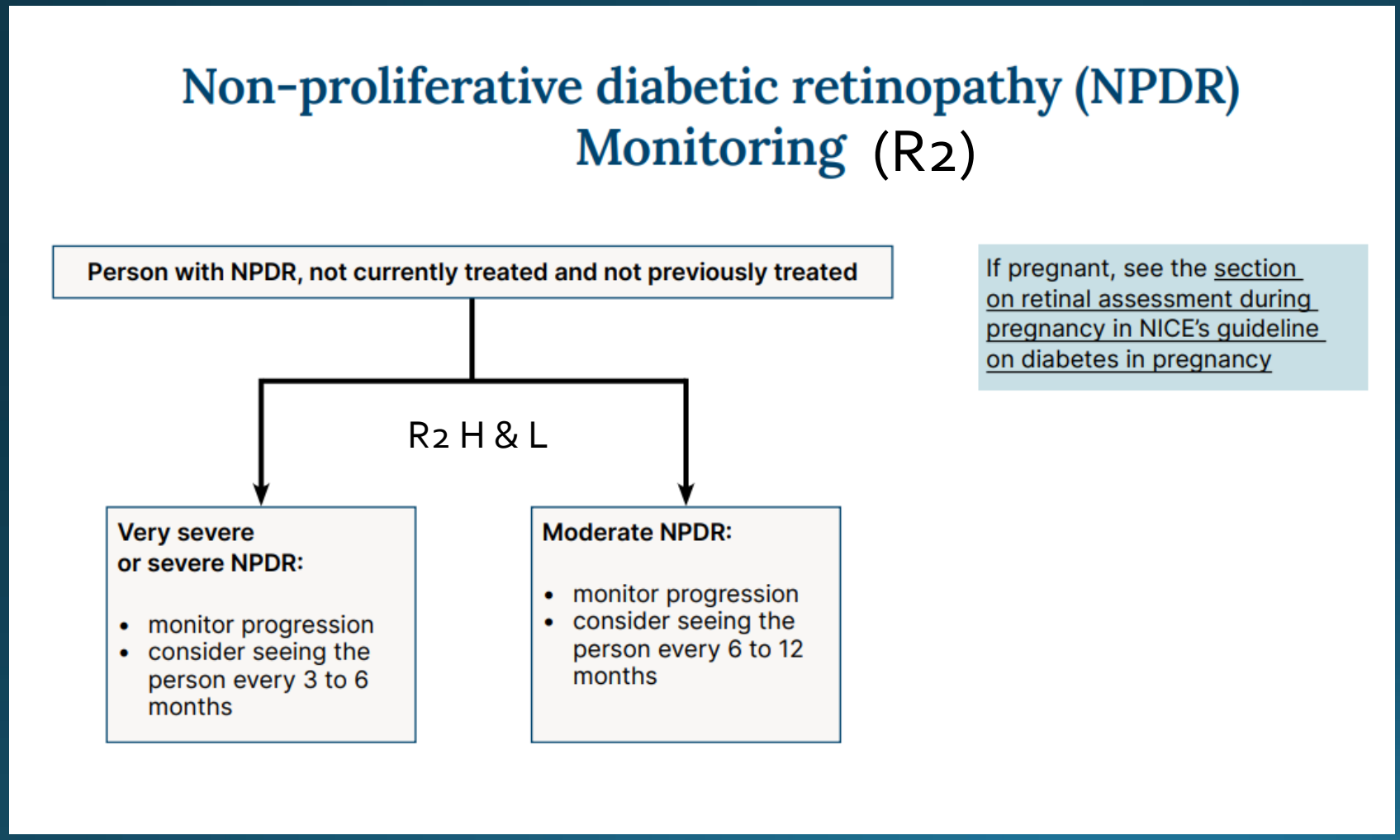
AGES = advanced glycation end-products; ICAM = intercellular adhesion molecule; PKC = protein kinase C; ROS = reactive oxygen species.

Boyer DS, et al. *Ther Adv Endocrinol Metab.* 2013;4(6):151–169.

Summary of Retinopathy Grades

Retinopathy Grade		OUTCOME
R0	No retinopathy	Stay in DESP (2 yearly screening)
R1	Mild Non-proliferative retinopathy	Stay in DESP (yearly screening)
R2 (Low risk)	Mod Non- proliferative	Stay in DESP Surveillance (6-12 monthly)
R2 (High risk)	Severe Non-proliferative retinopathy	Stay in Hospital clinics for monitoring (3-6 monthly)
R3 (A)	Active Proliferative retinopathy	Refer Urgently to Hospital within 6 weeks For Tx with PRP
R3 (S)	Stable treated Proliferative retinopathy	Discharge back to DESP Screening
M1	Referable Maculopathy - Can occur at any stage	Refer to Hospital for treatment or OCT surveillance clinic in DESP depending on severity (2-3 months)
U	Unassessable (SLB)	Slit lamp clinic/ cataract surgery

NICE Guidance (Aug 2024)



No Evidence for active treatment of R2:

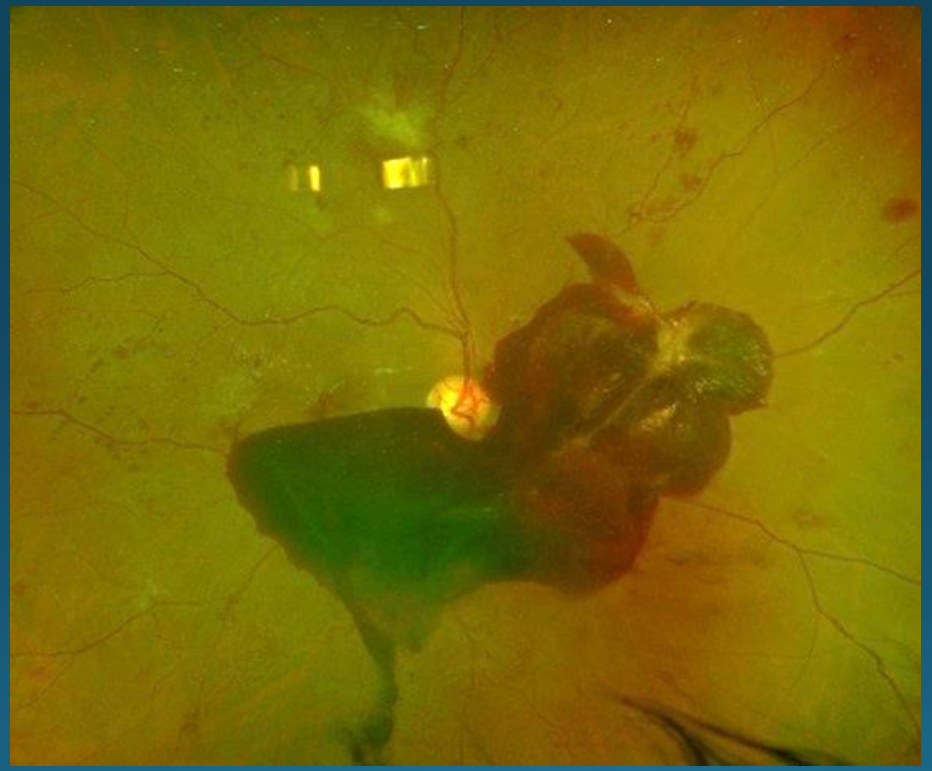
- PANORAMA study
- Protocol W

Wells JA, Glassman AR, Ayala AR, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema: two-year results from a comparative effectiveness randomized clinical trial. *Ophthalmology*. 2016;123(6):1351-1359.
Maturi RK, Glassman AR, Josic K, et al. Effect of intravitreous anti-vascular endothelial growth factor vs sham treatment for prevention of vision-threatening complications of diabetic retinopathy: The Protocol W Randomized Clinical Trial. *JAMA Ophthalmol*. 2021;139(7):701-712.

Treatment of Proliferative Diabetic Retinopathy (R3A)

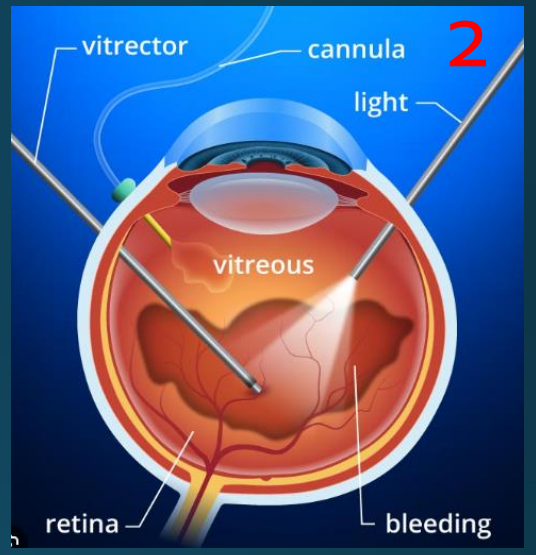
1

PRP laser



Vitrectomy/ Surgery

2



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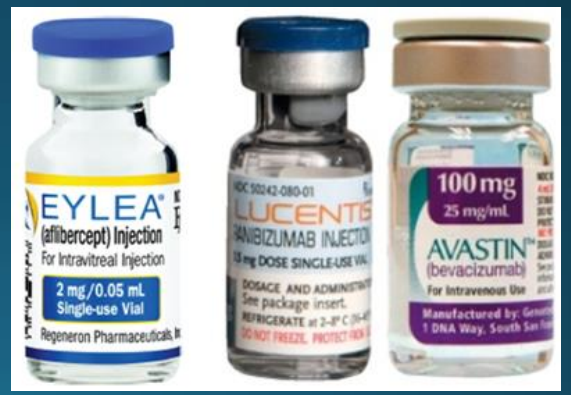
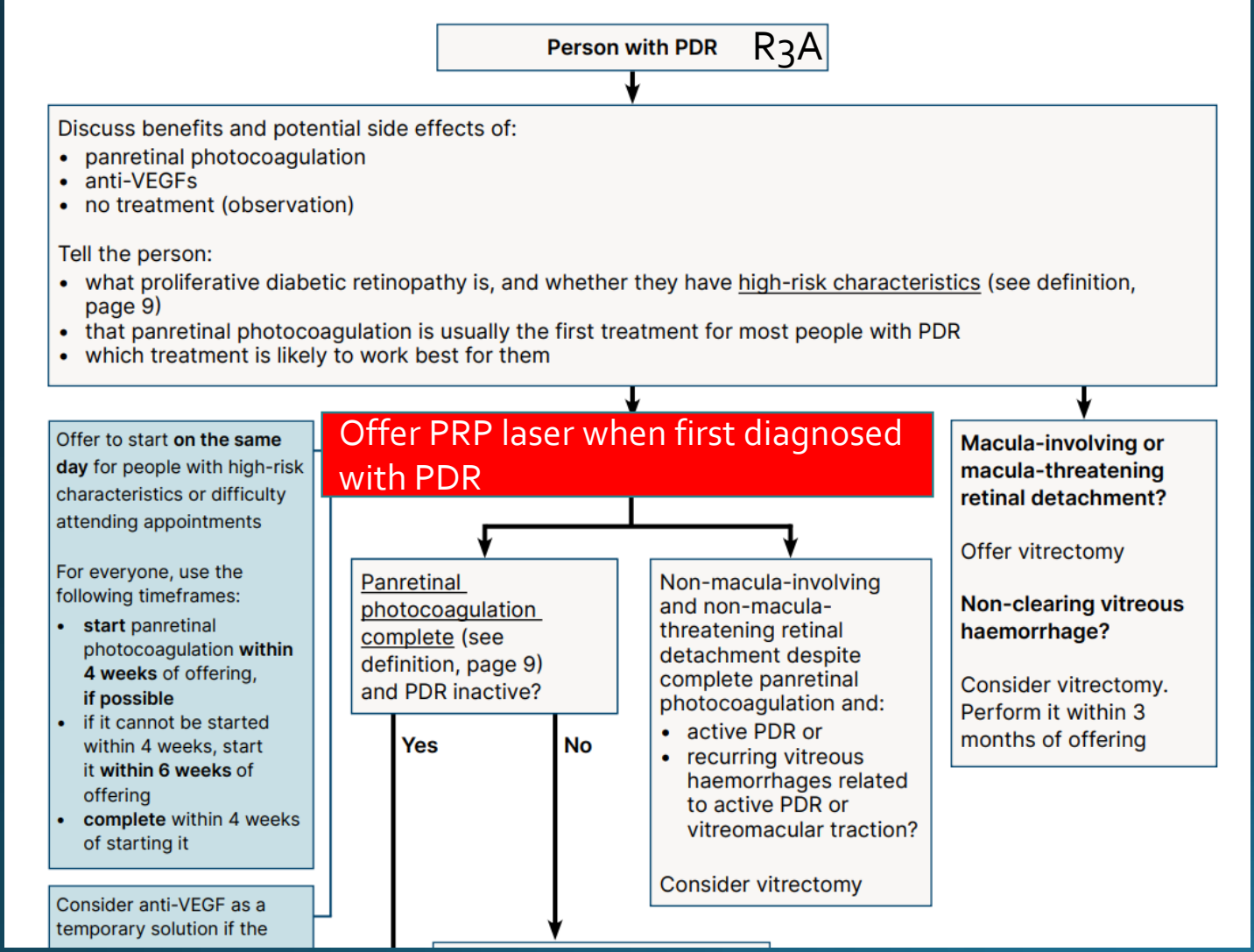


Anti-VEGF injections

NICE Guidance (Aug 2024)



NG242 Diabetic retinopathy: Visual summary 13/08/2024 (nice.org.uk)

PRP laser

- Reduces the 5 year risk of blindness by 90%
  Start on the same day if high risk R3A or within 4-6 weeks
- Complete PRP laser within 4 weeks of starting

Consider Vitrectomy surgery

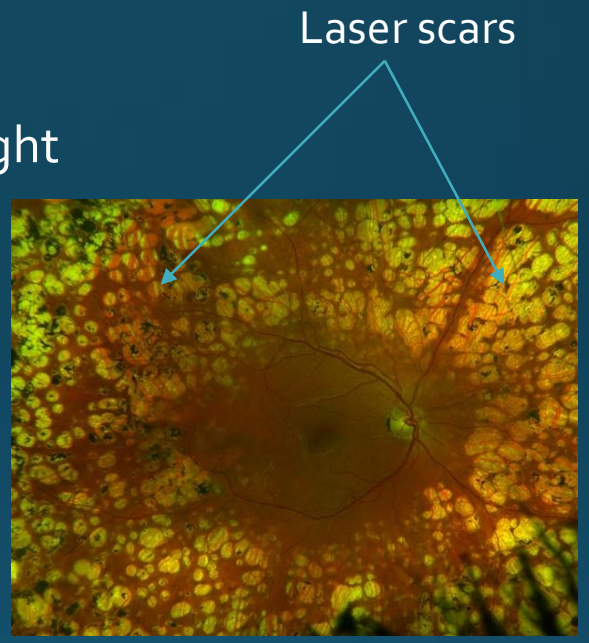
- In advanced cases especially with vitreous haemorrhage (VH) or tractional detachment.

Consider Anti-VEGF injections

- As a temporary measure in those with VH or cataract

What does PRP laser treatment involve?

- Outpatient procedure
- Drops to numb the eye, Lens to stop blinking
- Laser machine like a camera on a slit lamp with bright light
- Takes 15-20 minutes per eye
- **PROS**
- Effective, long term treatment
- Reduces risk of severe visual loss in long term
- No risk of infection
- **CONS**
- Bright flash sensation/twinge sensation/ some discomfort during laser
- May need to complete over several sessions
- Can cause restriction in peripheral field/ reduced night vision/ worsen maculopathy
- May have headache, visual disturbance for 1-3 days following procedure

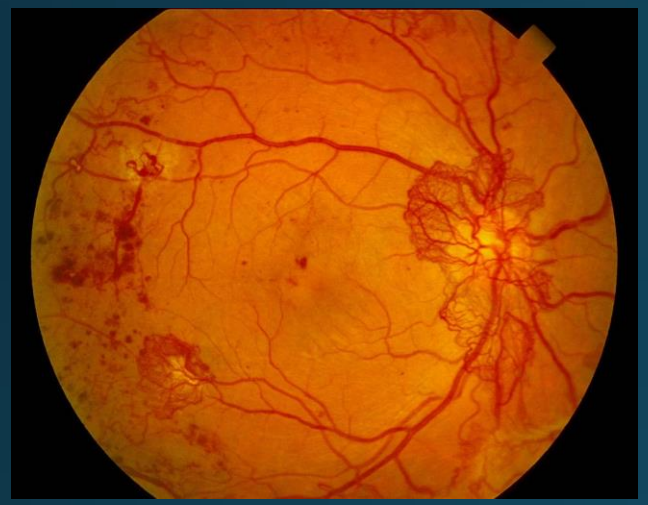


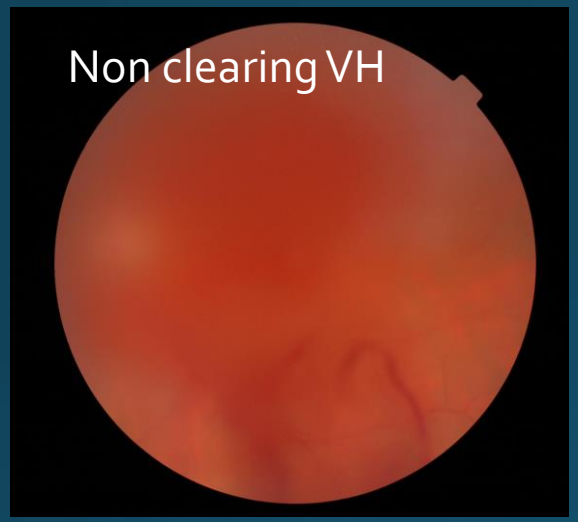
QR code

Diabetic retinal laser. Pt experience video

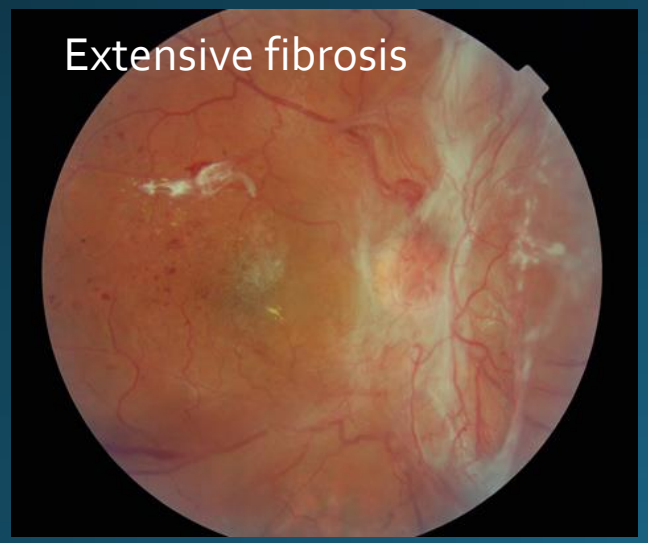
Photocoagulation treatment for proliferative retinopathy: report 2. Ophthalmology. 1978; 85:82-106

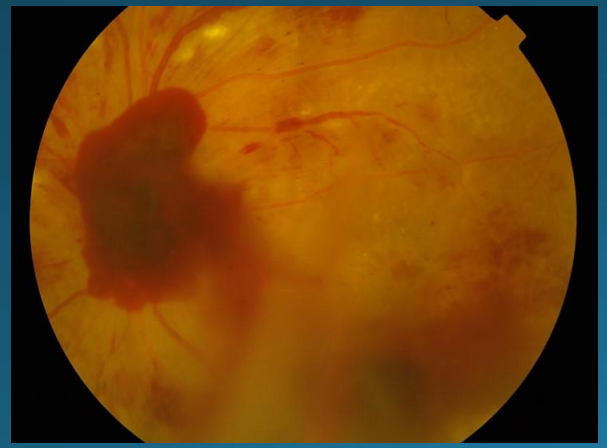
Advanced/ High risk Proliferative DR- R3A Often too late for PRP/- often need Vitrectomy surgery

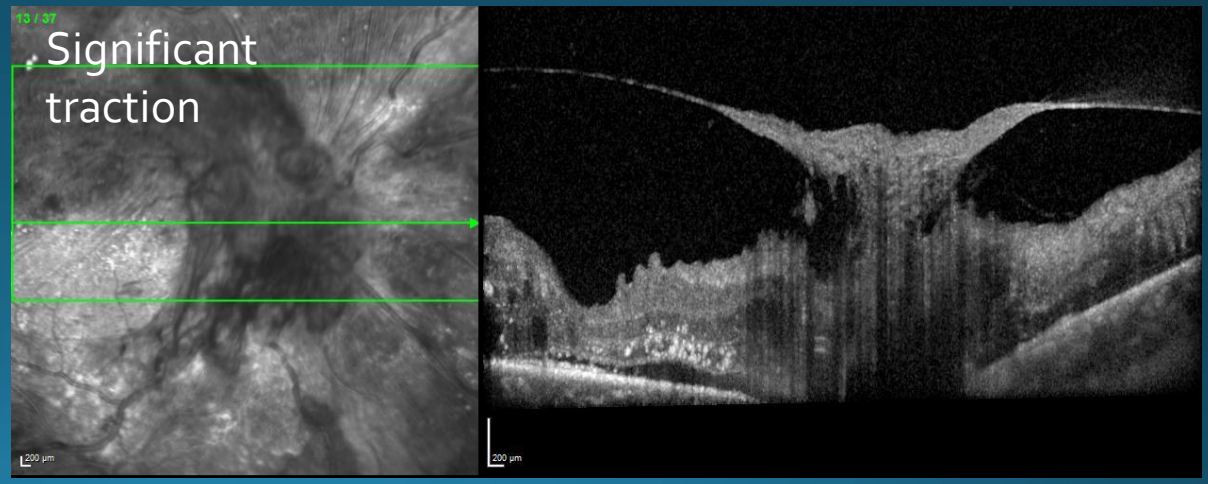




- If left untreated, high risk of visual loss due to bleeding, fibrosis and development of a tractional detachment.

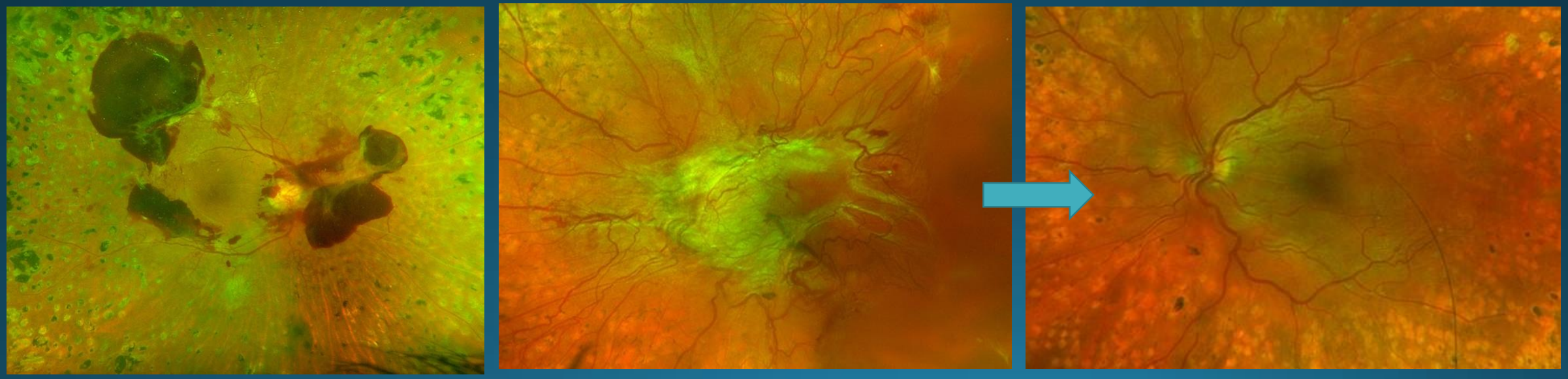




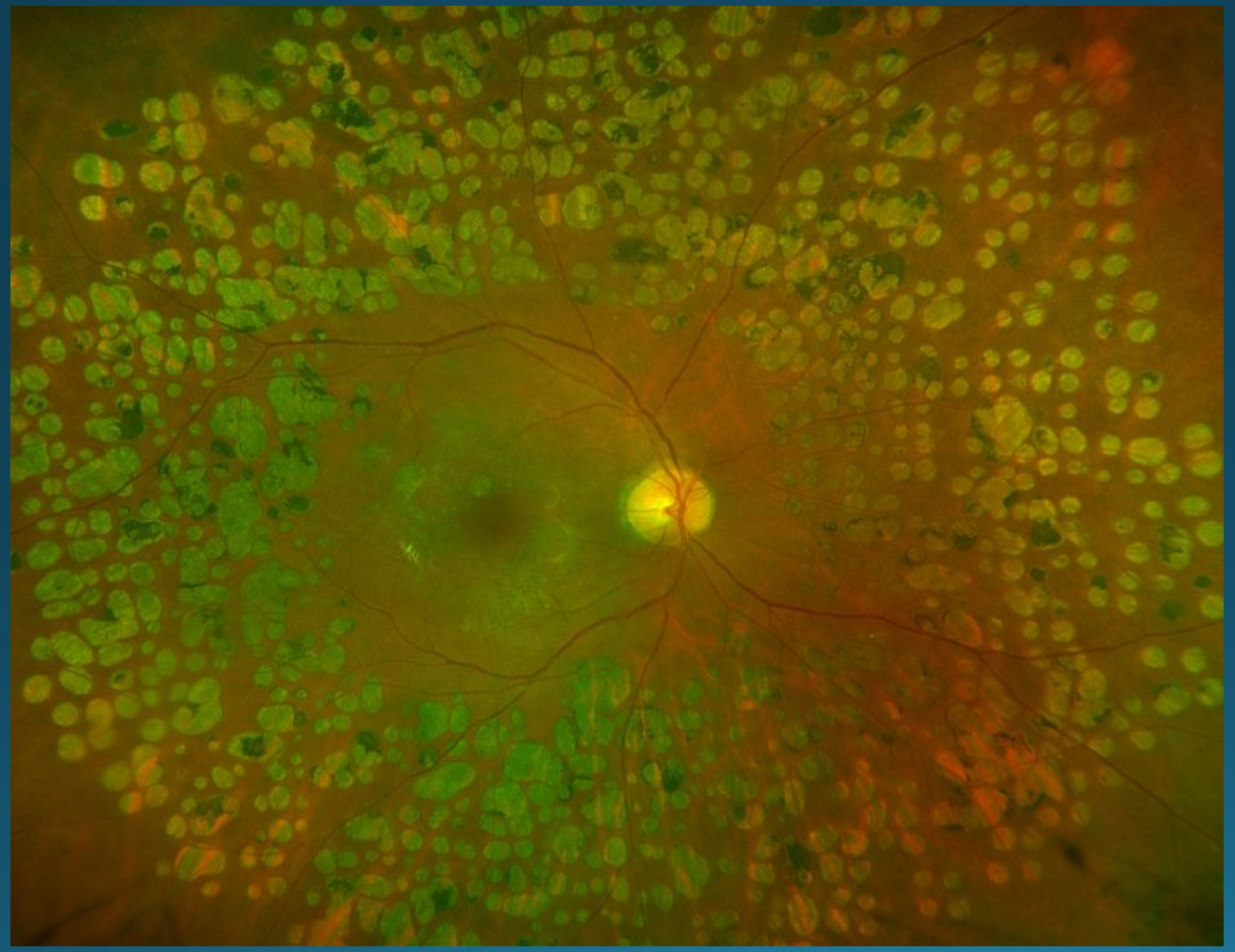


2. Vitrectomy Surgery –For Advanced Retinopathy with traction/ vitreous haemorrhage

- Example of 21 yr old, with type 1 diabetes since age 2, had floaters and reduced vision.
- Didn't see any doctors over COVID-19.
- Very poor control- Had dramatic worsening of retinopathy with bleeding/ fibrosis and traction
- Required Vitrectomy surgery.



Once treated - R3(S) Stable treated proliferative Retinopathy- with PRP scars- back to DESP

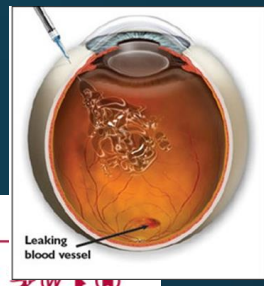


3. Anti-VEGF injections for R3/Proliferative Retinopathy?

- We know that Anti-VEGF injections reduce retinopathy progression (protocol W/ PANORAMA studies*)
- Protocol S (USA) and Clarity Studies (UK) looked at injections for Proliferative Retinopathy
- These Anti-VEGF injections reduce new vessel growth and potentially can preserve field of vision (in short term) and can reduce the need for surgery.
- Huge Cost burden/ treatment burden- regular treatments- ongoing with risk of infections
- Worse outcome in anti-VEGF group in those that were lost to follow up

- Only approved by NICE in cases of vitreous haemorrhage or cataract awaiting surgery

CLARITY



Clinical efficacy of intravitreal aflibercept versus panretinal photocoagulation for best corrected visual acuity in patients with proliferative diabetic retinopathy at 52 weeks (CLARITY): a multicentre, single-blinded, randomised, controlled, phase 2b, non-inferiority trial

Sobha Sivaprasad, A Toby Prevost, Joana C Vasconcelos, Amy Riddell, Caroline Murphy, Joanna Kelly, James Bainbridge, Rhiannon Tudor-Edwards, David Hopkins, Philip Hykin, on behalf of the CLARITY Study Group*

Summary

Background Proliferative diabetic retinopathy is the most common cause of severe sight impairment in people with diabetes. Proliferative diabetic retinopathy has been managed by panretinal laser photocoagulation (PRP) for the past 40 years. We report the 1 year safety and efficacy of intravitreal aflibercept.

Methods In this phase 2b, single-blind, non-inferiority trial (CLARITY), adults (aged ≥18 years) with type 1 or 2 diabetes and previously untreated or post-laser treated active proliferative diabetic retinopathy were recruited from

Lancet 2017; 389: 2193–203
Published Online May 7, 2017
http://dx.doi.org/10.1016/S0140-6736(17)31193-5
See Editorial page 2163

Protocol S

Randomized Controlled Trial > JAMA. 2015 Nov 24;314(20):2137-2146.
doi: 10.1001/jama.2015.15217.

Panretinal Photocoagulation vs Intravitreous Ranibizumab for Proliferative Diabetic Retinopathy: A Randomized Clinical Trial

Writing Committee for the Diabetic Retinopathy Clinical Research Network; Jeffrey G Gross [1], Adam R

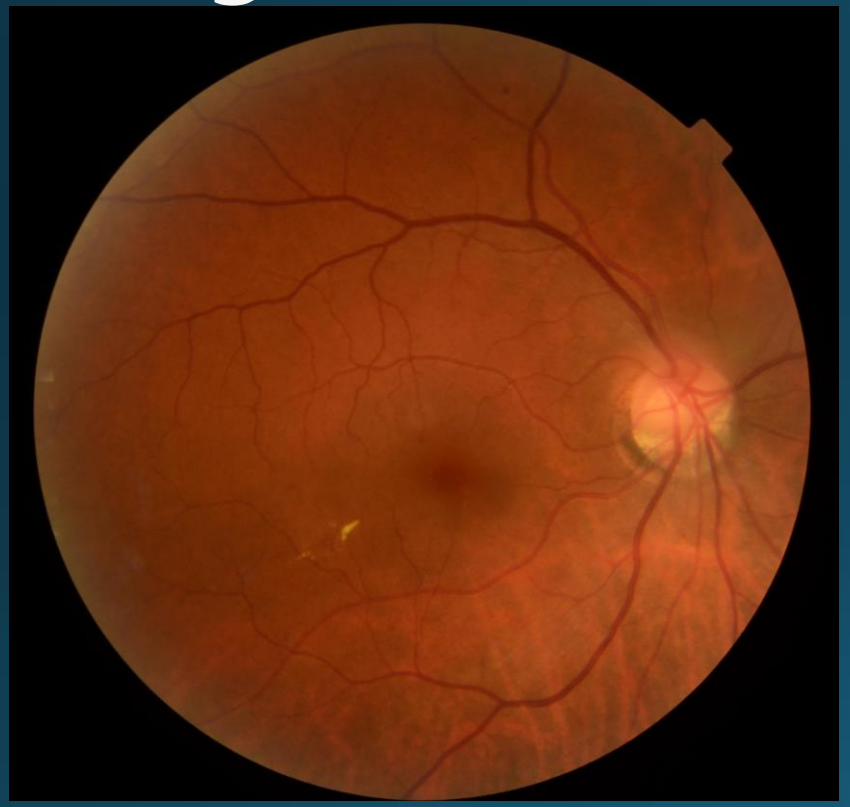
AMERICAN ACADEMY OF OPHTHALMOLOGY®

Outcomes of Eyes Lost to Follow-up with Proliferative Diabetic Retinopathy That Received Panretinal Photocoagulation versus Intravitreal Anti–Vascular Endothelial Growth Factor

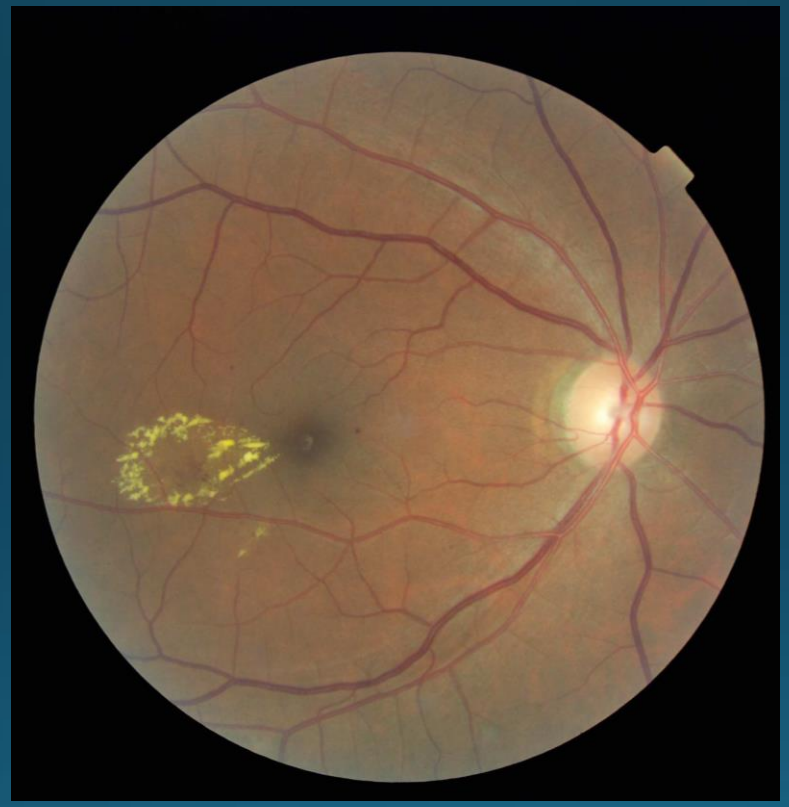
Anthony Obeid, MD, MPH, Daniel Su, MD, Samir N. Patel, MD, Joshua H. Uhr, MD, Durga Borkar, MD, Xinxiao Gao, MD, PhD, Mitchell S. Fineman, MD, Carl D. Regillo, MD, Joseph I. Maguire, MD, Sunir J. Garg, MD, Jason Hsu, MD

* Maturi RK et al. DRCRnet Protocol W. JAMA Ophthalmol 2021; 139 (7): 701-712. Brown D et al. PANORAMA study results. JAMA Ophthalmol 2021; 139 (9):946-955

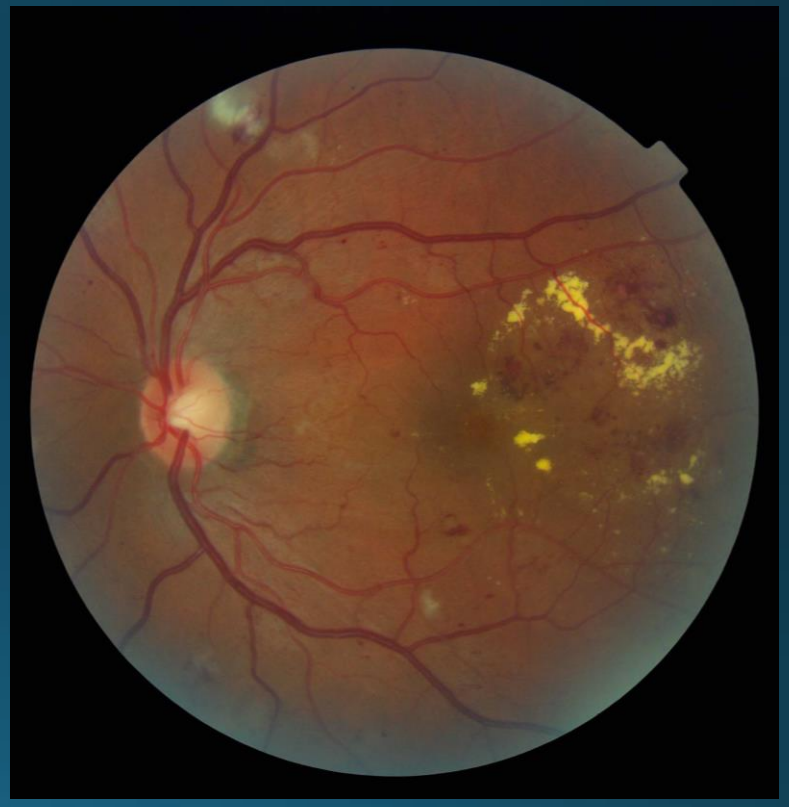
What about M1- referable maculopathy? (huge variation)



Single exudate - Stay in screening surveillance



Group of exudates- Non-Centre involving- Refer to Hospital for macular laser treatment



Centre-involving – refer to Hospital for consideration on Anti-VEGF / injections

NICE Guidance

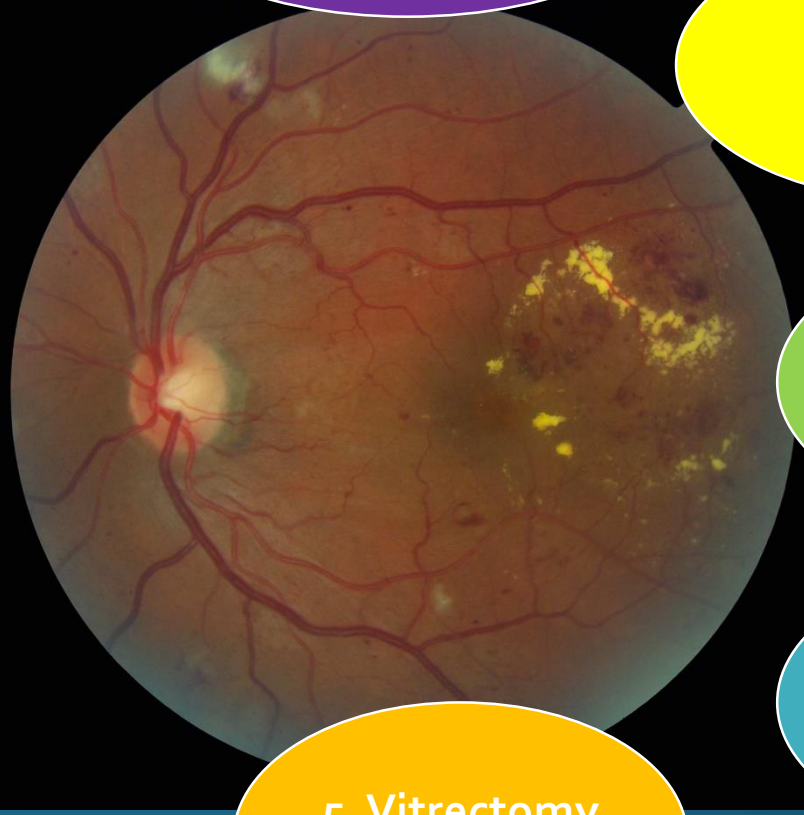
Clinically significant macular oedema (CSMO) Management (1 of 3)

Person with CSMO (see definitions, page 9)

Discuss:
- anti-VEGFs
- macular laser treatment
- steroid treatment
- observation

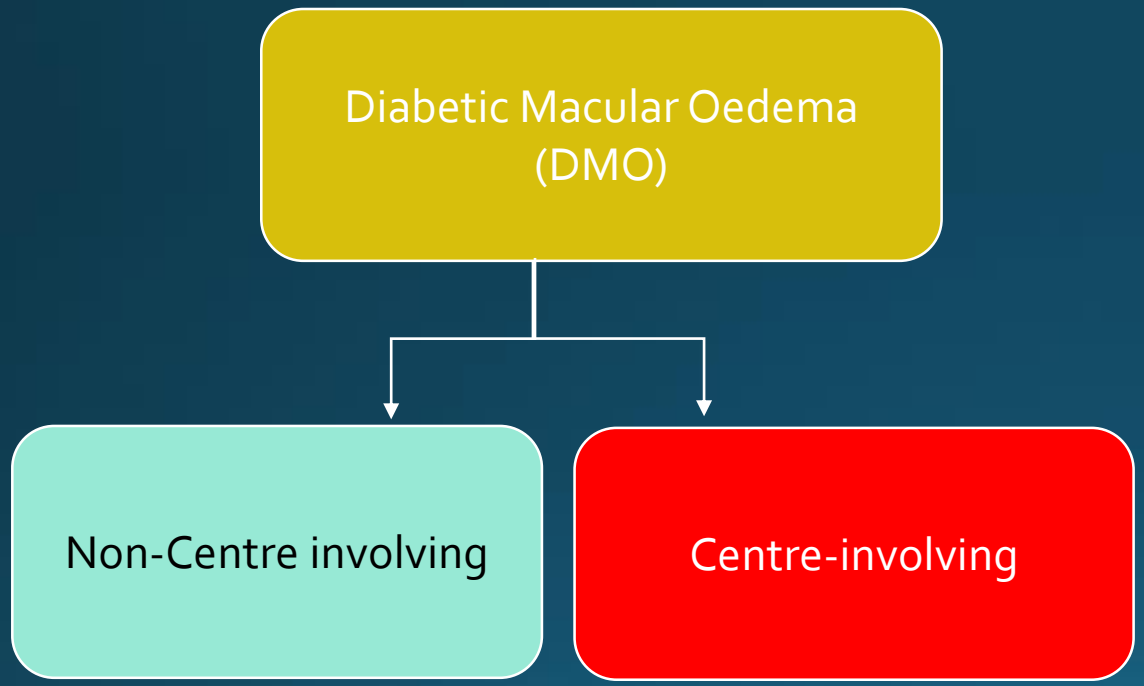
Tell the person if their DMO is centre-involving or not, and which treatment is likely to work best for them

- Centre-involving macular oedema and visual impairment (see page 6)
- Centre-involving macular oedema and good vision (see page 7)
- Non-centre involving CSMO (see page 7)



1. Observation Systemic Control HbA1c / BP/ cholesterol
2. Macular laser
3. Anti-VEGF injections
4. Steroid implant injections
5. Vitrectomy Surgery

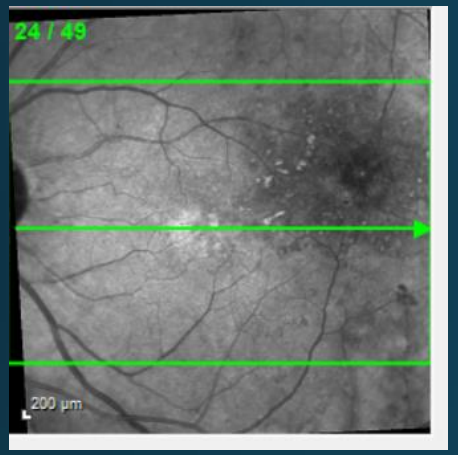
Treatment of Diabetic Maculopathy

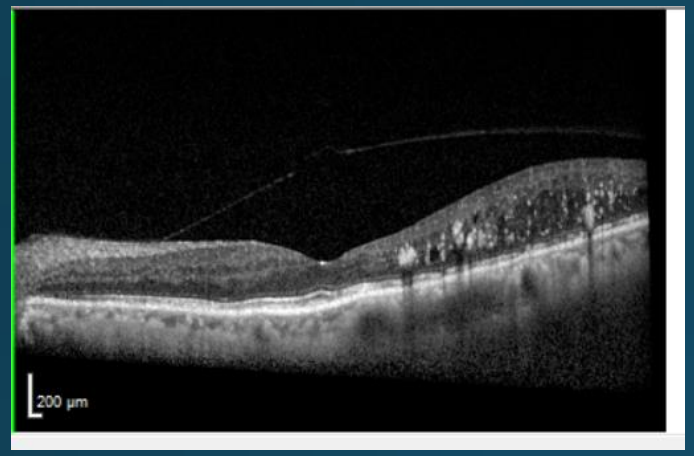


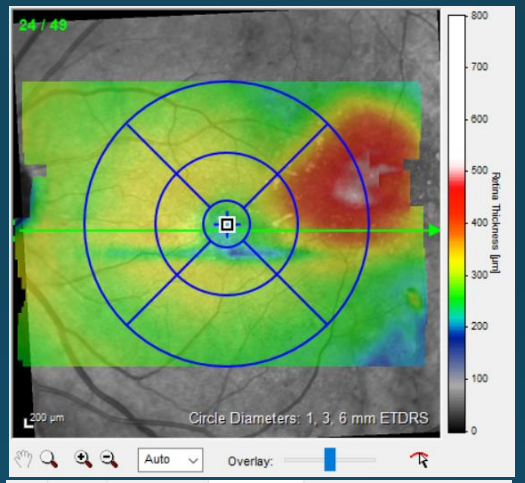
OCT scanning

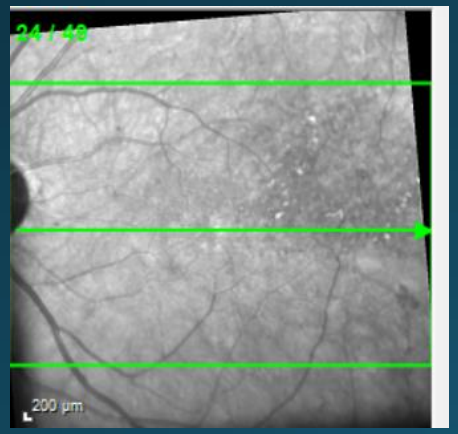
Non-Centre involving

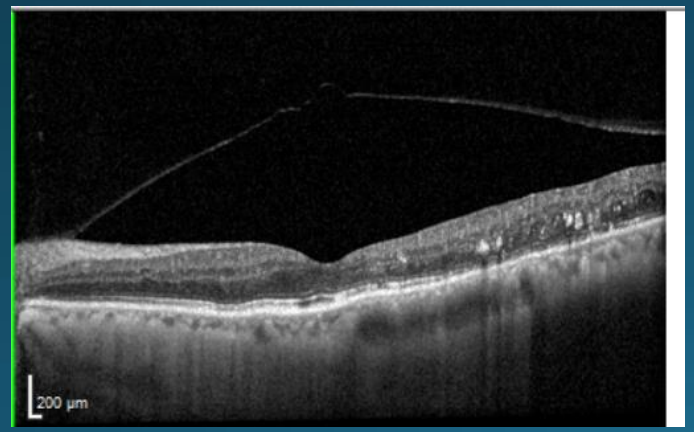
Macular laser

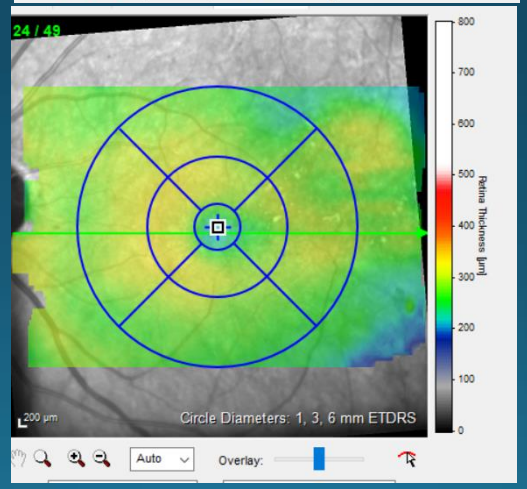












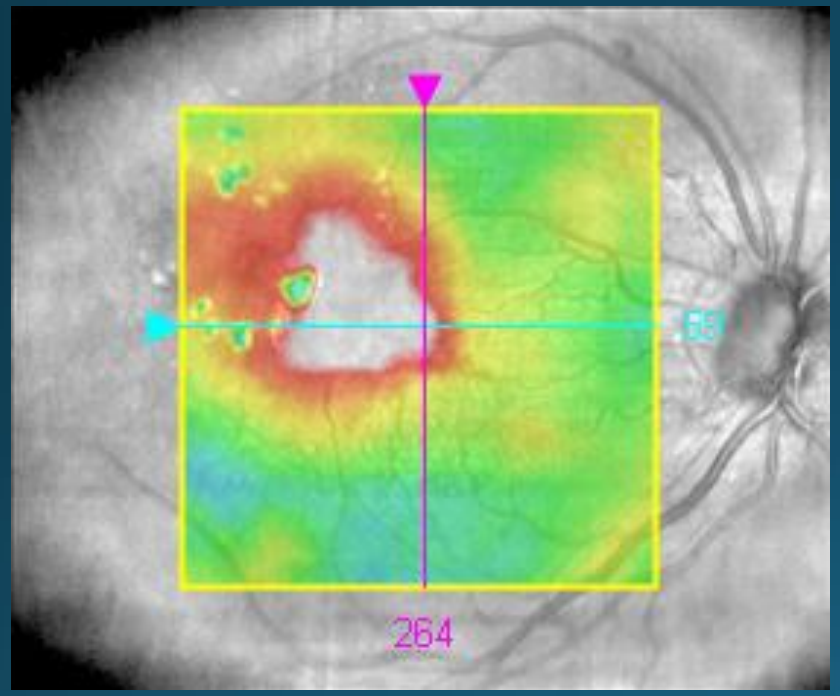
POST LASER

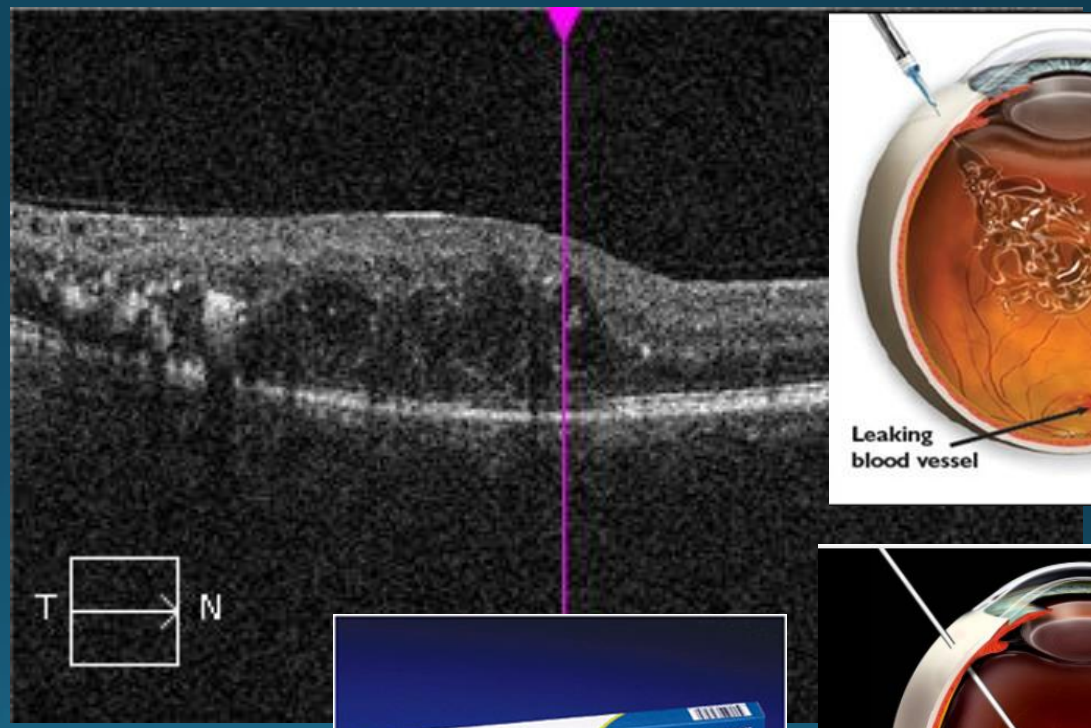
- Non-painful
- Straight-forward treatment
- Safe in pregancny

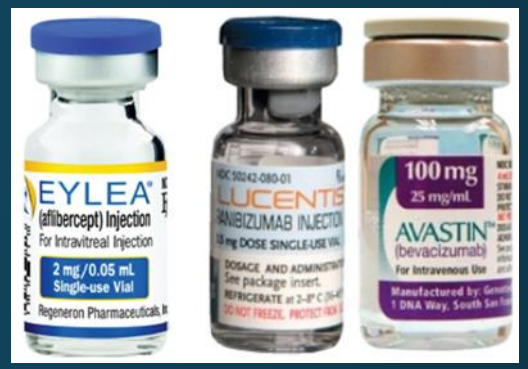
Treatment techniques and clinical guidelines for photocoagulation of diabetic macular edema. EarlyTreatment Diabetic Retinopathy Study Report Number 2. Early Treatment Diabetic Retinopathy Study Research Group. Ophthalmology 1987; 94(7): 761–774.

Centre-involving

Retinal thickening and oedema on OCT





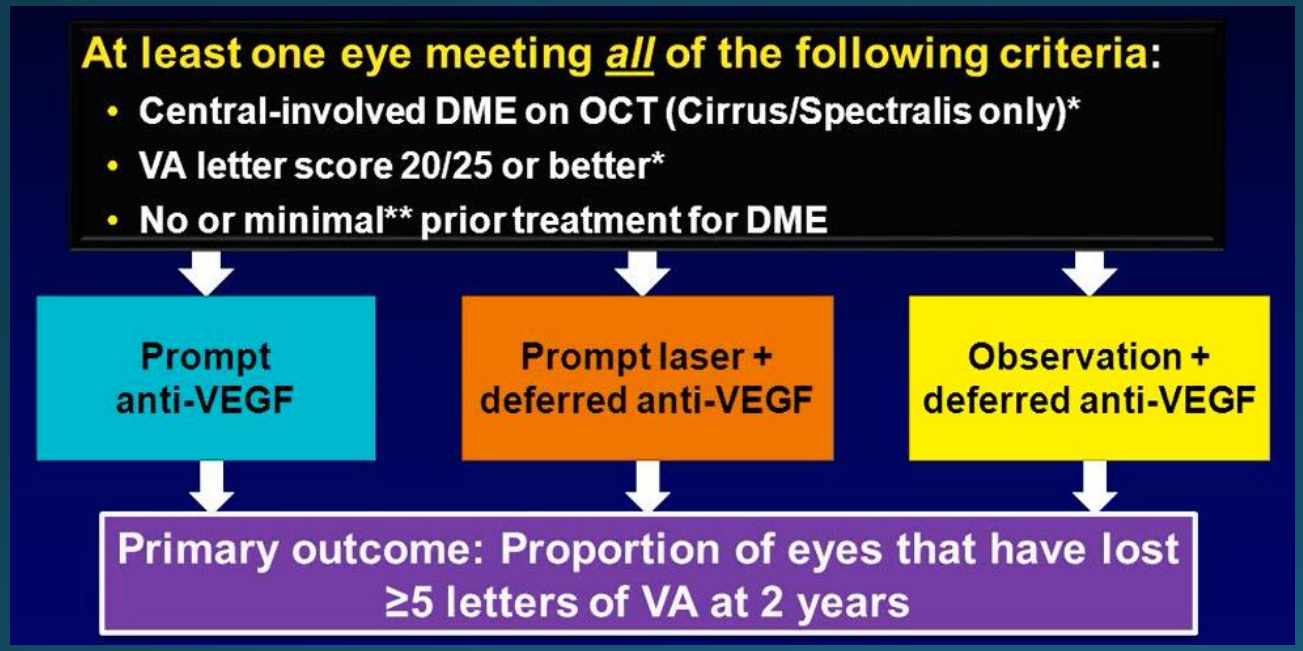


1) Observation
2) Anti-VEGF agents
3) Steroid implants
4) Vitrectomy surgery

Centre-involving with good vision

1. Observation
Systemic Control
HbA1c / BP/
cholesterol

- Is it better than 6/7.5? Protocol V study



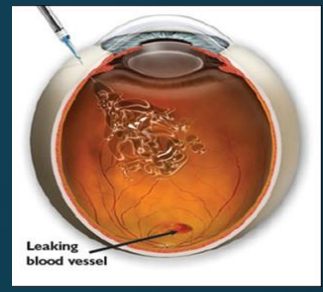
OBSERVATION recommended if vision good and only add in AntiVEGF when required

- **Aflibercept: 16%, Laser 17%, Observation 19%**
- **No difference between the groups at 2 years (p=0.79)**

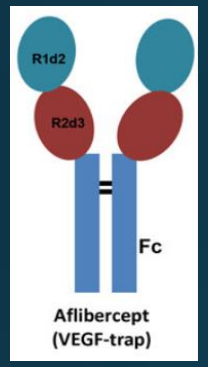
Baker CW, Glassman AR, Beaulieu WT et al. DRCRnet Protocol V. JAMA Apr 2019; 321 (19): 1880-1894

Centre-involving with impaired vision

Anti-VEGF injections



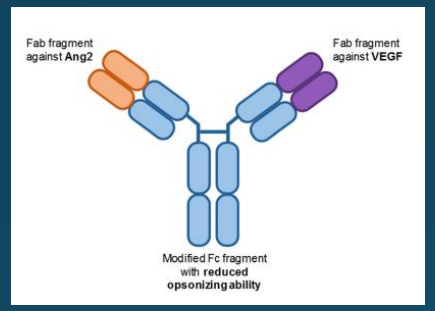
Aflibercept
2mg/ 8mg

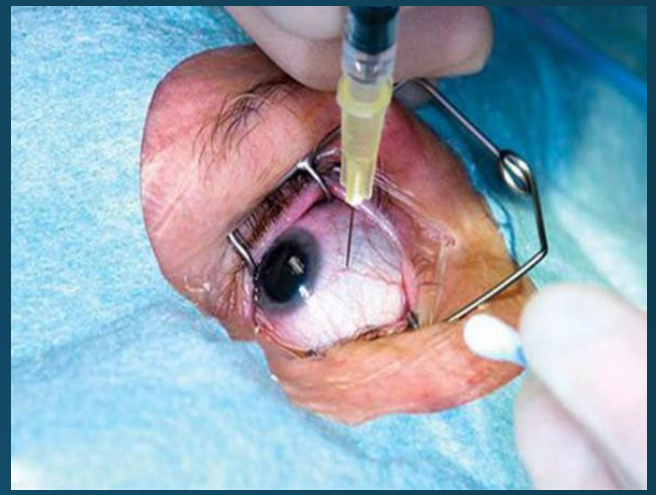


Ranibizumab
0.5 mg
& biosimilar

Brolucizumab
6mg (safety
concerns)

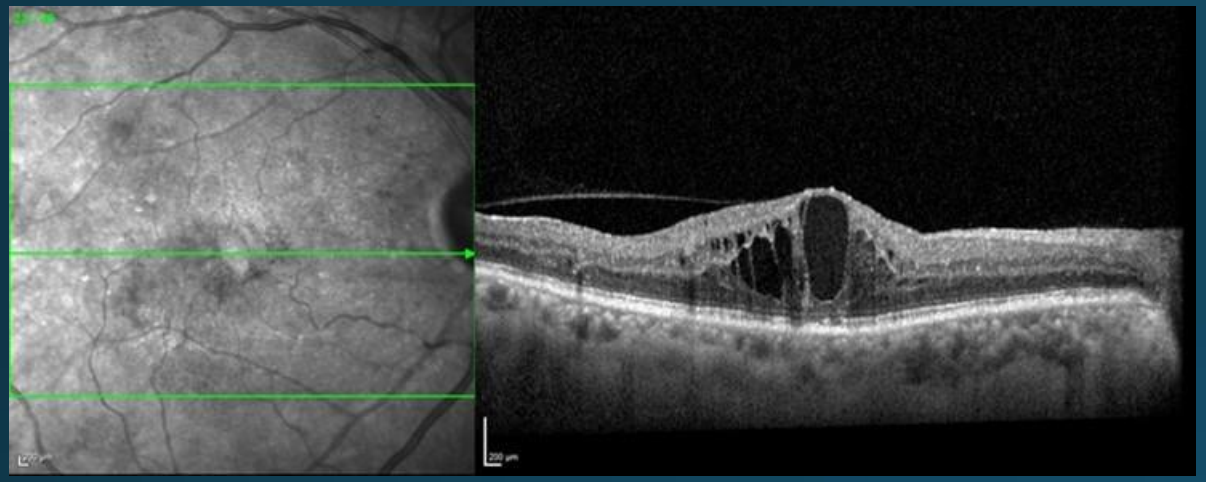
Faricimab is a bi-specific antibody against Ang-2 and VEGF (6mg)

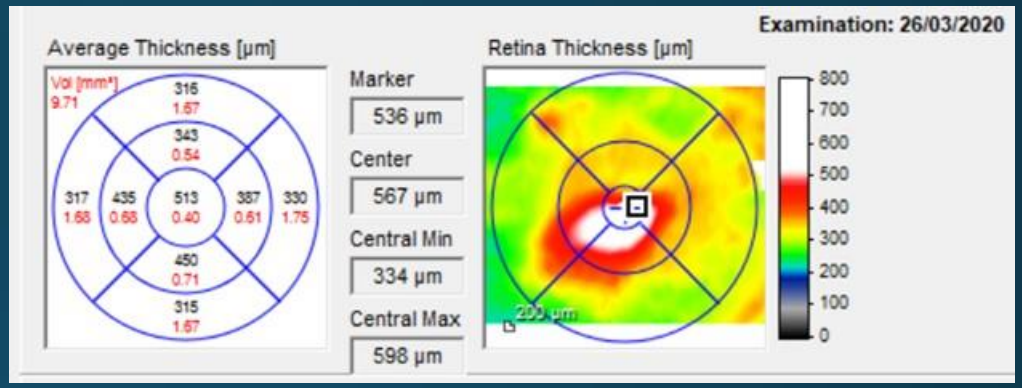


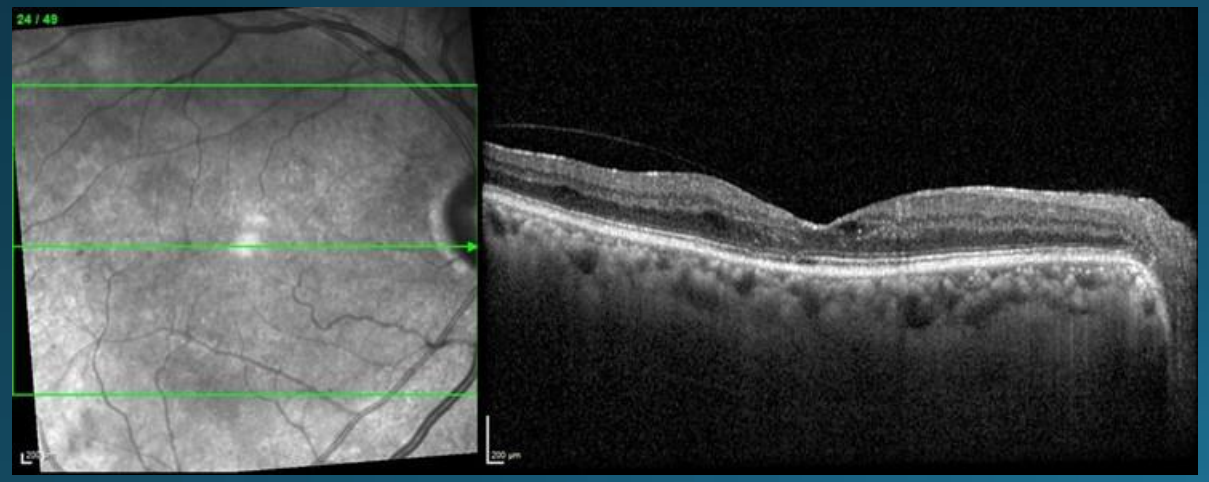


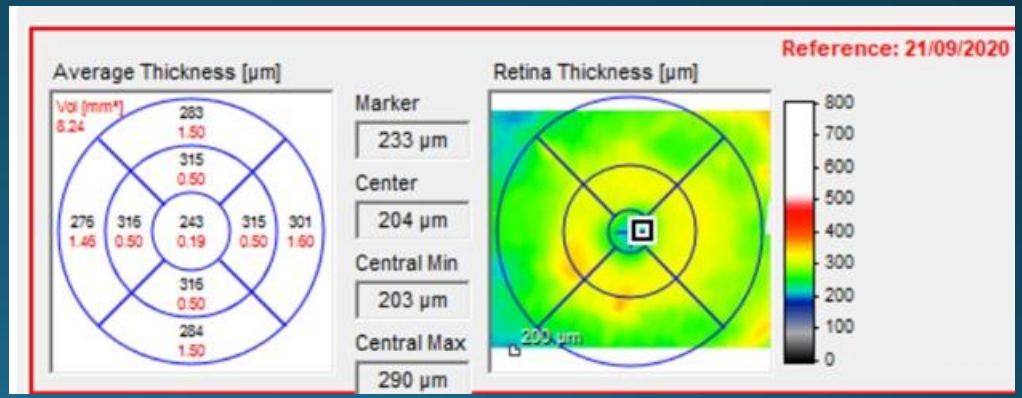
- 1st line treatment for central Diabetic Macular Oedema.
- Monoclonal antibody or recombinant fusion protein injections given monthly for the first few months (3-6m)
- Then start to extend intervals depending on response.
- Given as an outpatient and well tolerated
- 1:1500 risk of severe infection causing blindness.
- High burden of injections (usually 9 in first year).
- Faricimab & 8mg Aflibercept have a longer durability (fewer injections)- May last up to 12 weeks
- Can stop treatment once oedema resolves and monitor every 2-3 months

Highly effective Treatment: 71 yr old African male with DMO treated with 6 x injections of Aflibercept (Eylea), VA improved from 6/18- 6/7.5





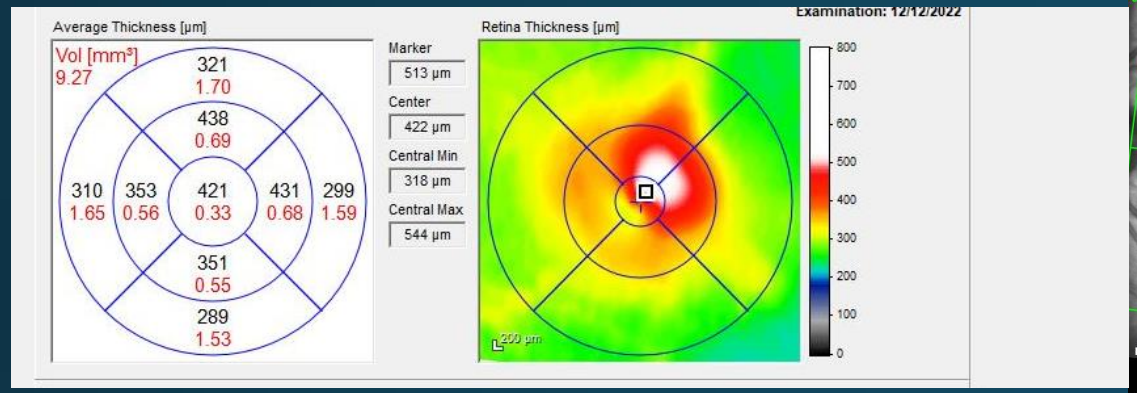




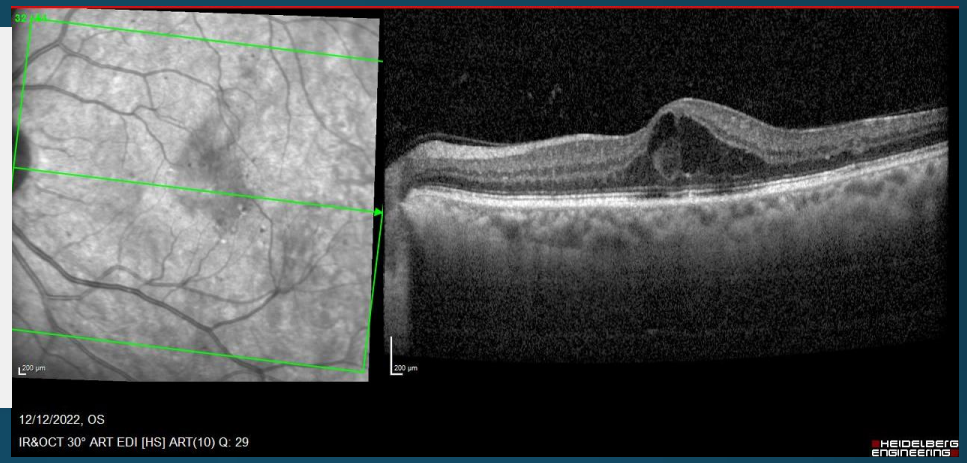
Will also improve retinopathy levels (2 step ETDRS levels)

CMT- 513 to 243 microns

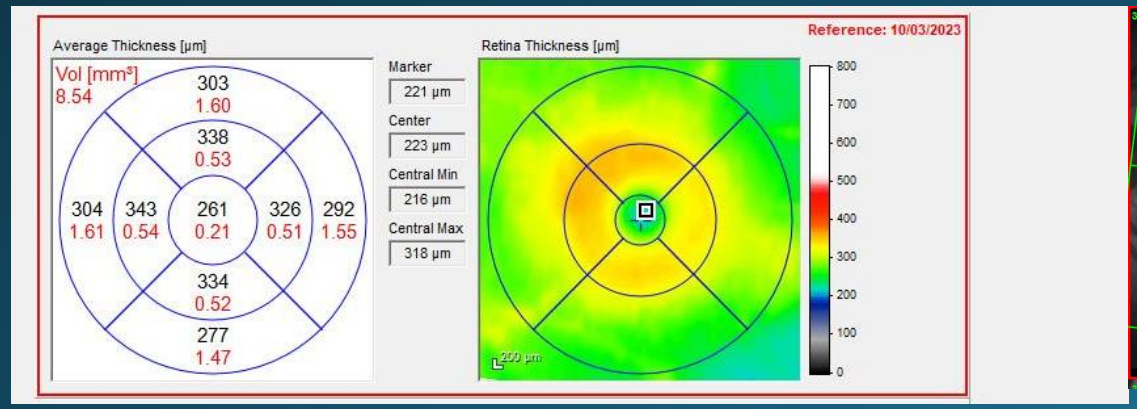
50 yr old African female with DMO treated with 3 x injections of Faricimab (Vabysmo), VA improved 6/18-6/9.5



PRE



PRE



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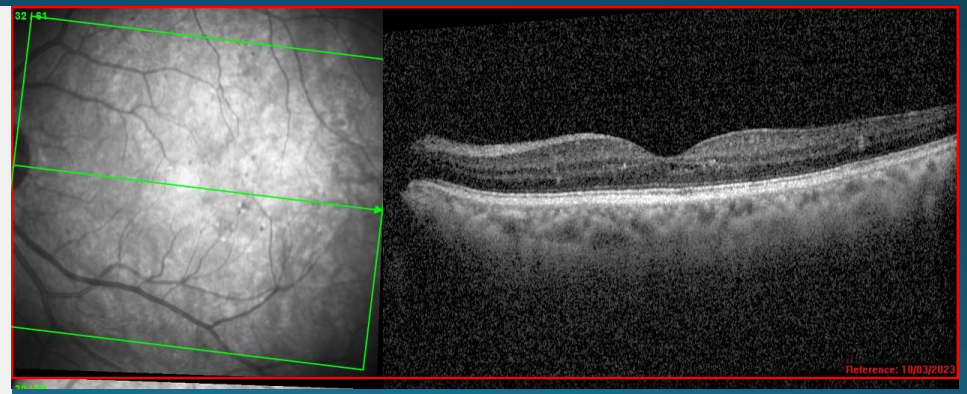
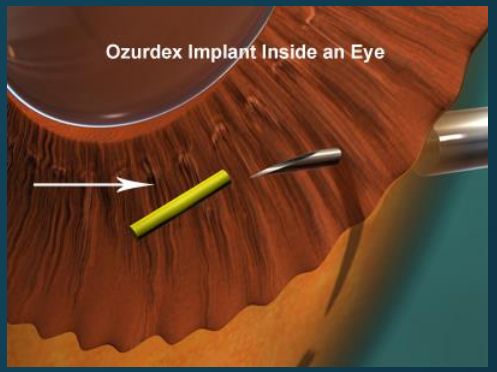


POST

Centre-involving with impaired vision

Steroid implant injections



Role of steroids in maculopathy

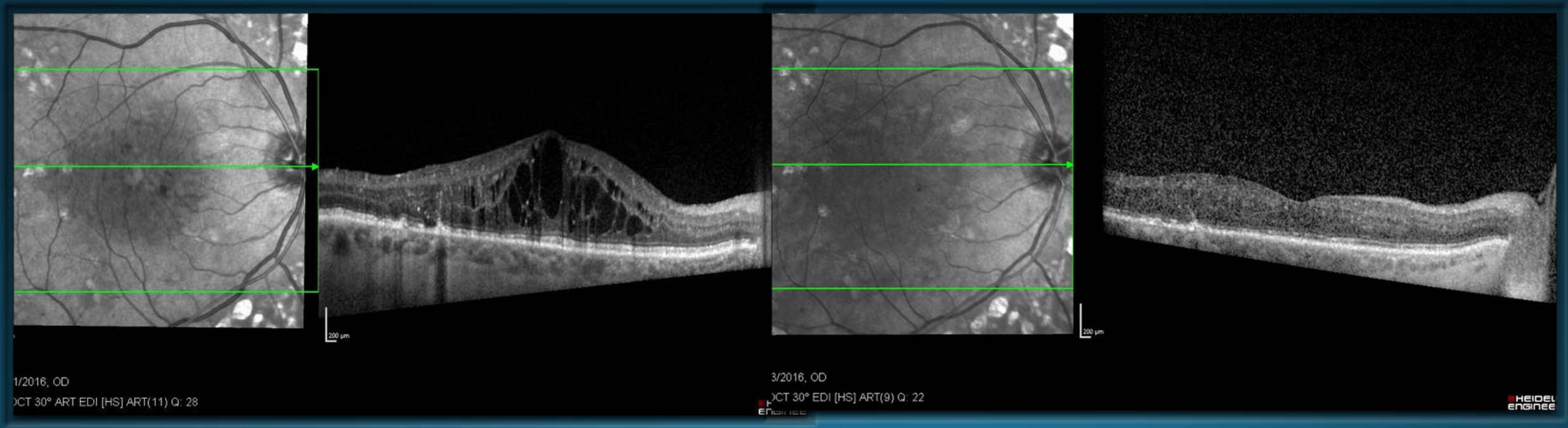
- 2nd line treatment
- Steroid therapy is most often considered for patients with:[2]
  - **Non responsive to Anti-VEGF**
  - **Pseudophakic eyes (have had cataract surgery)**
  - **Those not able to have anti-VEGF (pregnant)**
  - **Patients travelling/ unable to have regular injections**
  - **Patients with recent MI/ CVA**
- Reduced treatment frequency/lower cost [2,3]
- Side effects of raised IOP/ cataract formation may limit use

1. Schwartz SG, et al. *Curr Ophthalmol Rep*. 2013;1(3):144–149; 2. The Royal College of Ophthalmologists. Diabetic Retinopathy Guidelines. 2012; 3. Smiddy WE. *Ophthalmology.* 2011;118(9):1827-1833.

Pre-Dexamethasone (Ozurdex), VA 6/36, 574µm, intra-ocular pressure- 16

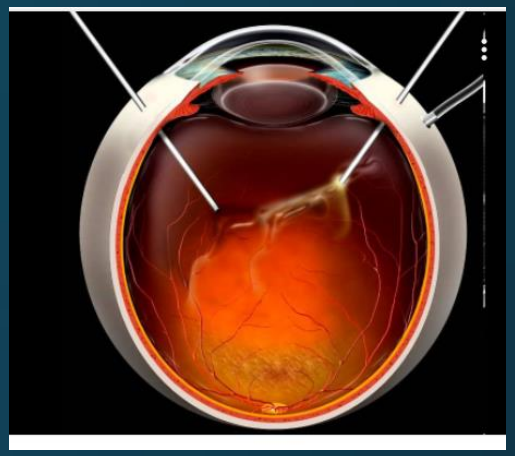
Post - Dexamethasone (Ozurdex), VA 6/12, 183µm, intra-ocular pressure- 26

Controlled on Xalatan - IOP 17, effect lasted 4 months

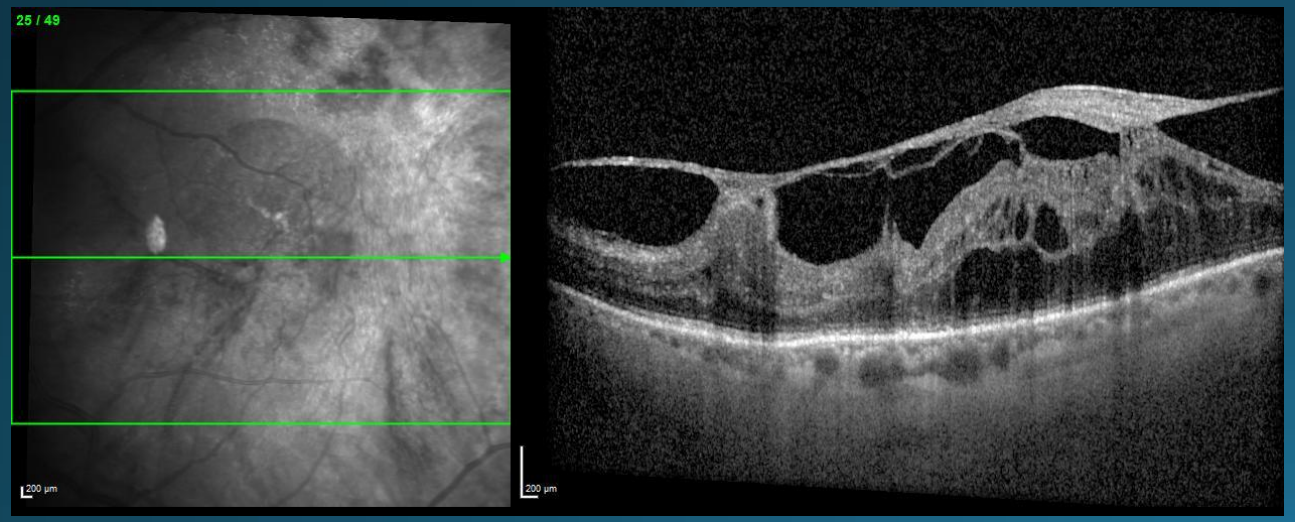


Centre-involving with impaired vision and traction

Vitrectomy Surgery



- Vitrectomy Surgery can be helpful in eyes where there is traction and thickening/ fibrosis of the retina.



Published in final edited form as:
Ophthalmology. 2010 June ; 117(6): 1087–1093.e3. doi:10.1016/j.ophtha.2009.10.040.

Vitrectomy Outcomes in Eyes with Diabetic Macular Edema and Vitreomacular Traction

Diabetic Retinopathy Clinical Research Network*

Abstract

Purpose—To evaluate vitrectomy for diabetic macular edema (DME) in eyes with at least moderate vision loss and vitreomacular traction.

Design—Prospective cohort study

Participants—The primary cohort included 87 eyes with DME and vitreomacular traction based on investigator's evaluation, visual acuity 20/63–20/400, optical coherence tomography (OCT) central subfield >300 microns and no concomitant cataract extraction at the time of vitrectomy.

Methods—Surgery was performed according to the investigator's usual routine. Follow-up visits were performed after 3 months, 6 months (primary endpoint) and 1 year.

Main Outcome Measures—Visual acuity, OCT retinal thickening and surgical complications.

Results—At baseline, median visual acuity in the 87 eyes was 20/100 and median OCT thickness was 491 microns. During vitrectomy, additional procedures included epiretinal membrane peeling in 61%, internal limiting membrane peeling in 54%, panretinal photocoagulation in 40% and injection of corticosteroids at the close of the procedure in 64%. At 6 months, median OCT central subfield thickness decreased by 160 microns, with 43% having central subfield thickness <250 microns and 68% having at least a 50% reduction in thickening. Visual acuity improved by 10 or more letters in 38% (95% confidence interval 28% – 49%) and deteriorated by 10 or more letters in 22% (95% confidence interval 13% – 31%). Postoperative surgical complications through 6 months included vitreous hemorrhage (5 eyes), elevated intraocular pressure requiring treatment (7 eyes), retinal detachment (3 eyes) and endophthalmitis (1 eye). Little changes in results were noted between 6 months and one year.

Conclusion—Following vitrectomy performed for DME and vitreomacular traction, retinal thickening was reduced in most eyes. Between 28% and 49% of eyes with characteristics similar

Ischaemic maculopathy

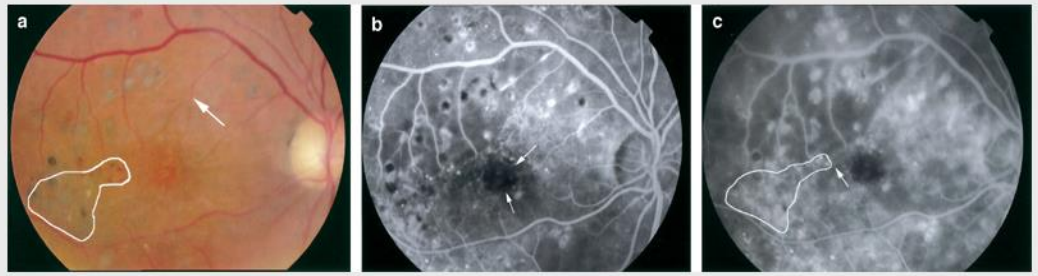
- Difficult to treat. Macular Laser can worsen ischaemic maculopthy- Check edge of peri-foveal network.
- Can treat with anti-VEGF therapy
- Can be associated with Chronic kidney disease*

FROM:
Reduced visual acuity following standard ETDRS macular laser for clinically significant macular oedema
E C Richardson, J Patel and P G Hykin

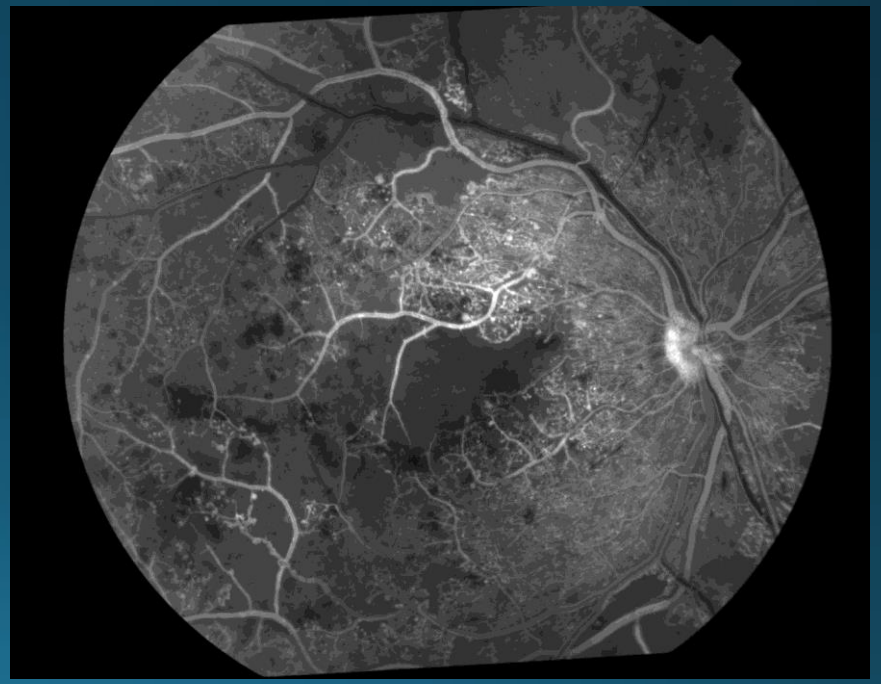
BACK TO ARTICLE

Figure 2.

Previous figure | Figure and tables index



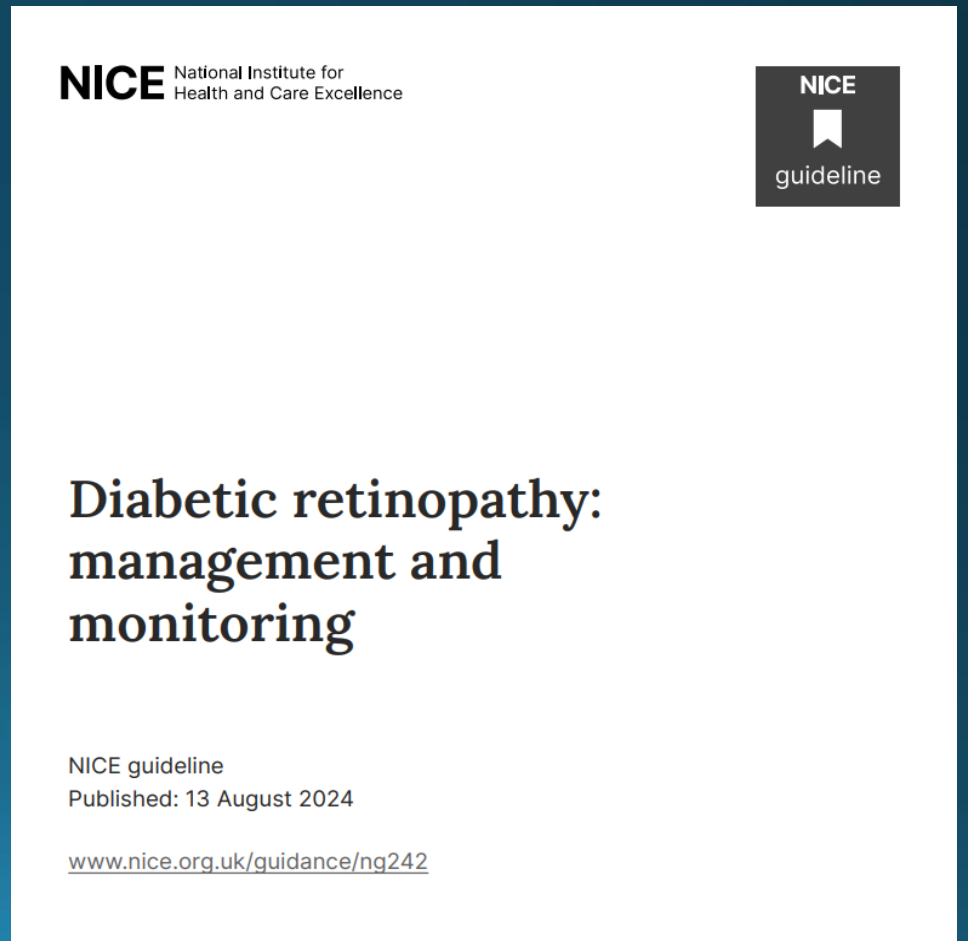
Photographs after temporal focal laser and visual deterioration. (a) Colour fundus photograph of the right macular region with the temporal area of retinal thickening (outlined) and the pre-existing area of superotemporal ischaemia (arrow). (b) Fluorescein angiogram of the right macular region showing an enlarged and irregular FAZ (arrows). (c) Fluorescein angiogram showing the treated area (outlined) and how this overlaps the temporal area of macular ischaemia (arrow).



* D Shukla Et al. Macular ischaemia as a marker for nephropathy in diabetic retinopathy. Indian Journal of Ophthalmology 52(3):p 205-10. 2004

NICE Guidance- Aug 2024

- Important Risk Factors for Diabetic Retinopathy Progression.
- Need access to:
- Stage of diabetic Retinopathy
- HbA1c
- Renal Function
- BP
- Lipid Management
- Pregnancy status
- Ethnicity



BP in those with Diabetes (< >80 years)

Table 1: Clinic blood pressure targets for people aged under 80

Person under 80 with:	Clinic blood pressure target
• hypertension (with or without type 2 diabetes) **or** • type 1 diabetes plus albumin to creatinine ratio less than 70 mg/mmol **or** • chronic kidney disease plus albumin to creatinine ratio less than 70 mg/mmol	Below 140/90
• type 1 diabetes plus albumin to creatinine ratio of 70 mg/mmol or more **or** • chronic kidney disease plus albumin to creatinine ratio of 70 mg/mmol or more	Below 130/80

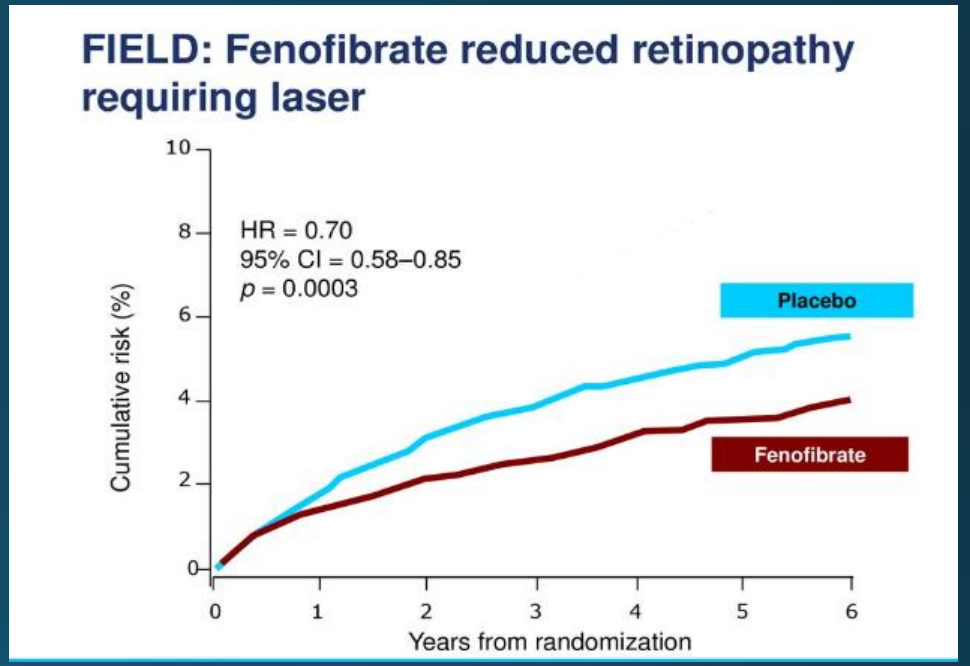
Table 2: Clinic blood pressure targets for people aged 80 and over

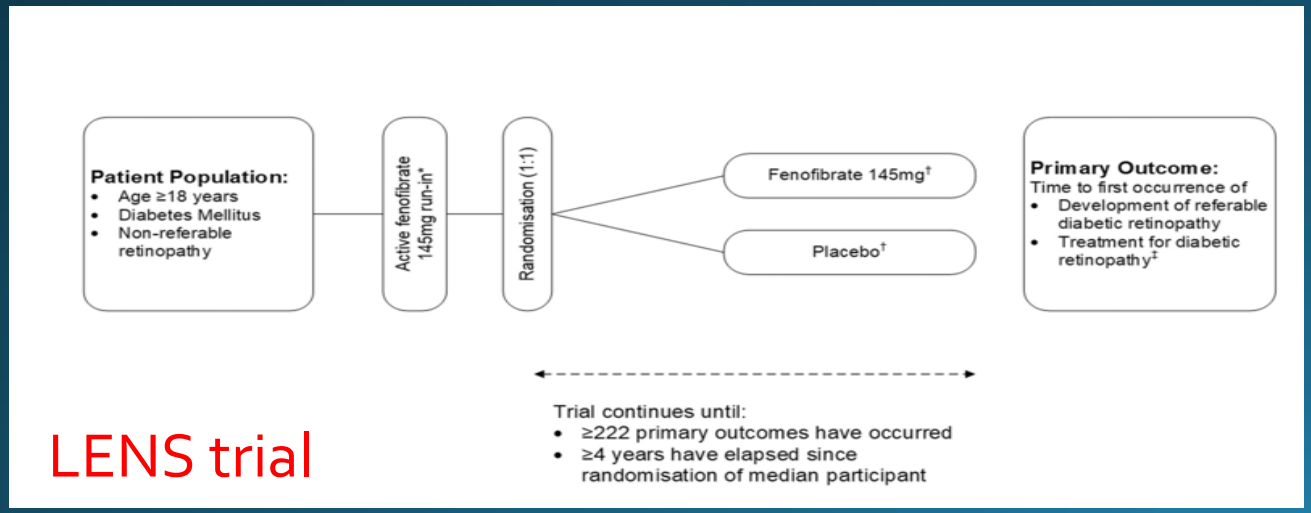
Person aged 80 and over with:	Clinic blood pressure target
• hypertension (with or without type 2 diabetes) **or** • type 1 diabetes (regardless of albumin to creatinine ratio)	Below 150/90
• chronic kidney disease plus albumin to creatinine ratio less than 70 mg/mmol	Below 140/90
• chronic kidney disease plus albumin to creatinine ratio of 70 mg/mmol or more	Below 130/80

Recommendations | Hypertension in adults: diagnosis and management | Guidance | NICE

Lipids in Diabetic Retinopathy

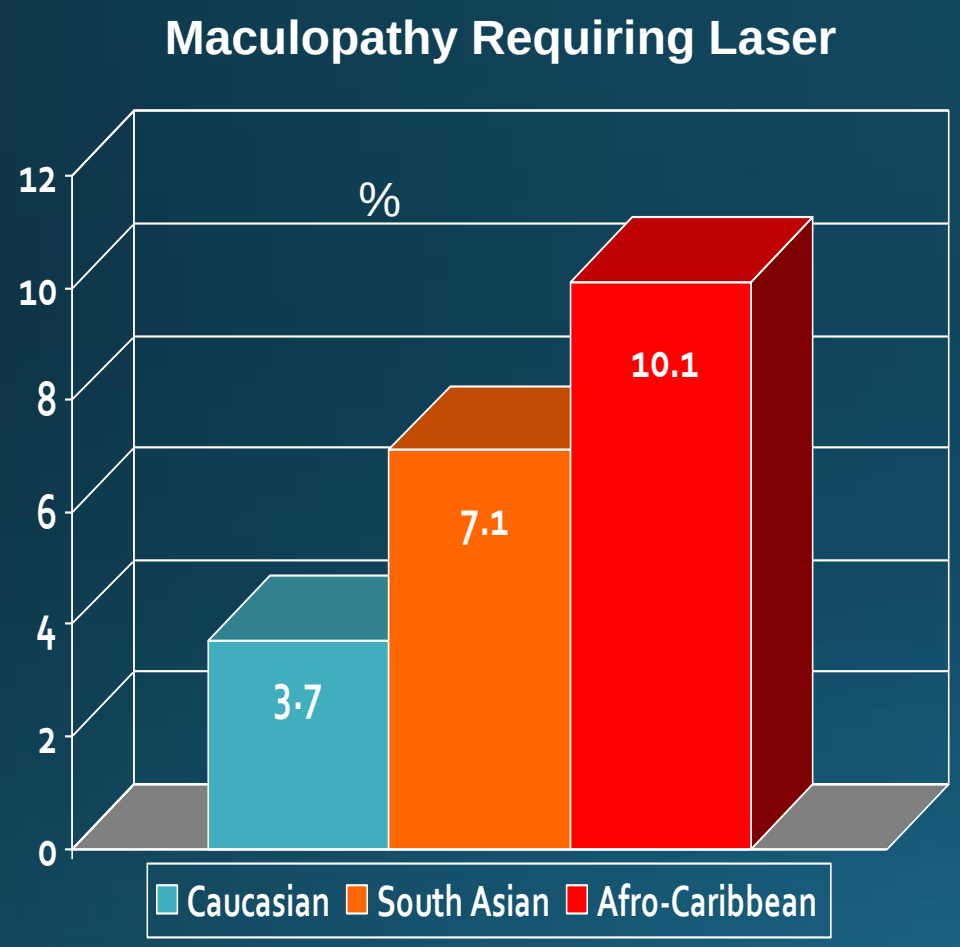
- No evidence that clearly showed that statins reduce progression of diabetic retinopathy.
- More evidence for Fenofibrate use (FIELD study)
- Recommended by NICE to start prescribing in DR in those with type 2 diabetes
- Concern about side effects/ pregnancy
- Await LENS trial results

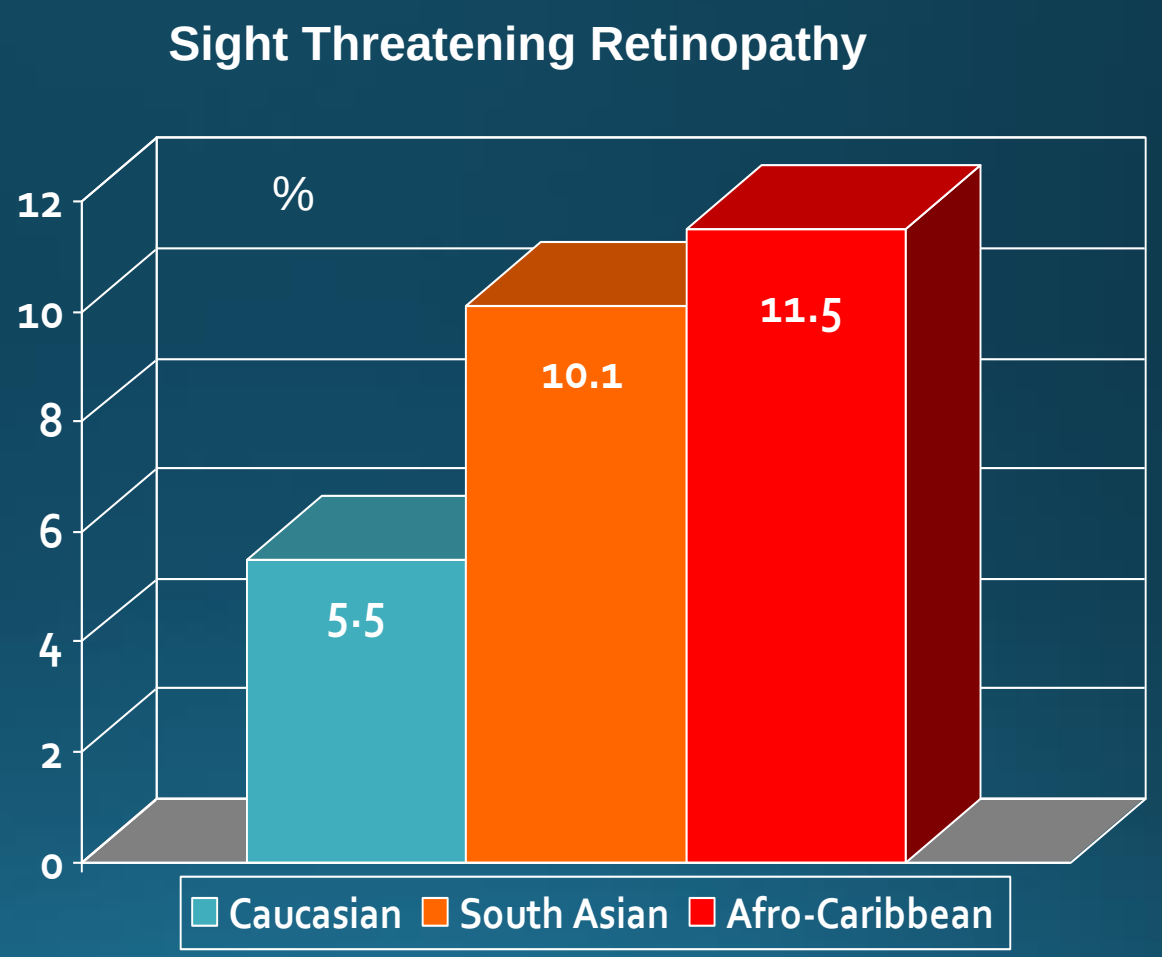




LENS trial

Ethnic variation

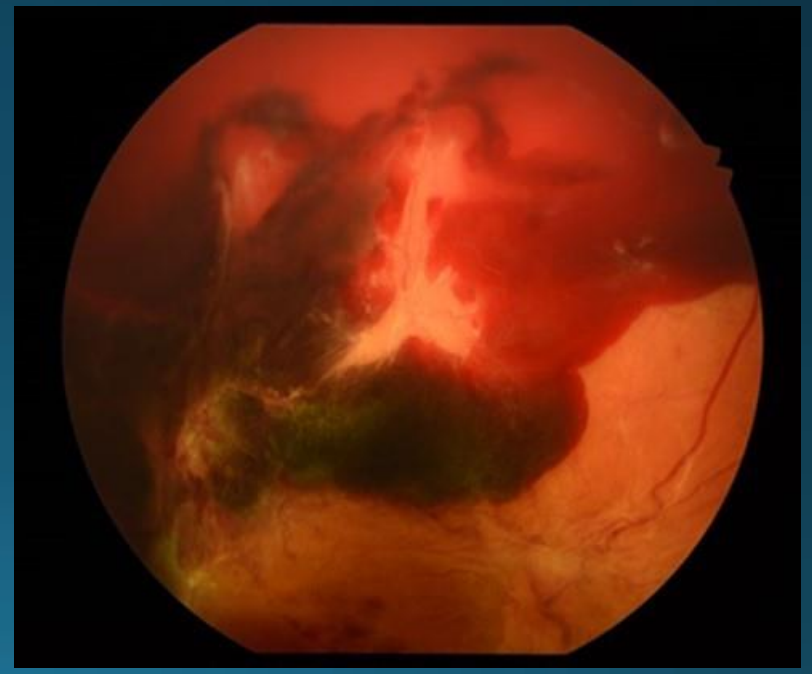




1) Gulliford et al (2010) Diabetic Medicine. 27(2):283/ 2) Mangelis et al (2023) Diabetes Care. May 1; 46 (5):1091-97 (African Caribbean x2 risk of ≥ R2 (9.7% vs 4,2%) and for M1 – risk 21% v 15%)

Pregnancy and Diabetes

- **Risk factors** include:
- Retinopathy levels at conception
  - Increased risk of R3a/PDR with R2 compared to R1 (1). Risk of obstretric complications increased.
  - Very low risk if RoMo at start of pregnancy (3).
- Duration of Diabetes prior to pregnancy
  - DIEP study (2) Risk greater in patients > 15 years of diabetes
- NICE recommends eye screening 2-3x in pregnancy
- Not able to have Anti-VEGF agents



(1) RM Best & U Chakravarthy. Diabetic retinopathy in pregnancy. BJO. 1997 Volume 81: 249-251

(2) Diabetes in early pregnancy (1995) Metabolic control and progressionof retinopathy. Diabetes Care 18:631-637

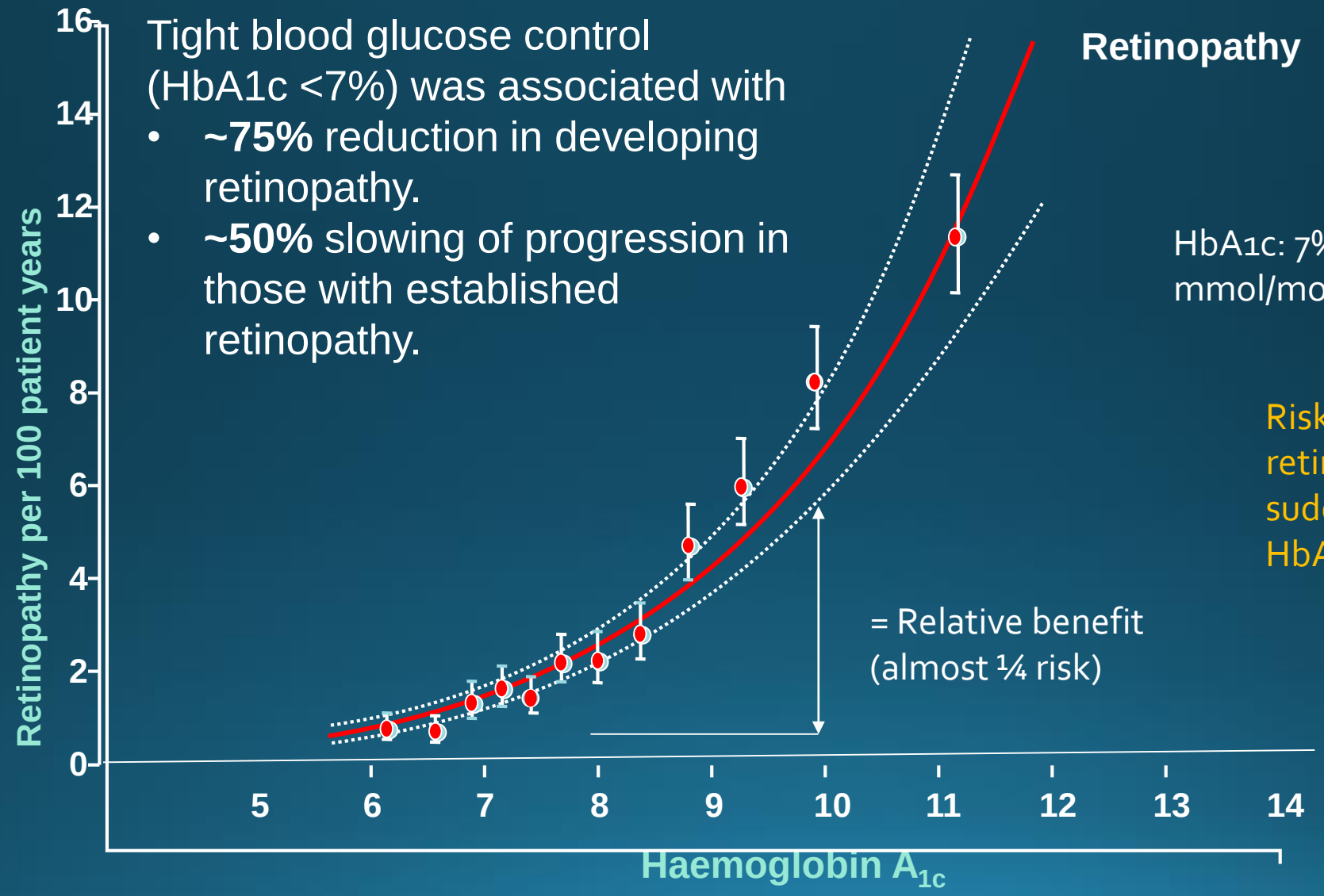
(3) Clarke, K., Webster, L., Althauser, S. *et al.* The risk of development and progression of diabetic retinopathy in a group of ethnically diverse pregnant women with diabetes attending three regional Diabetic Eye Screening Programs in the UK. *Eye* **38**, 179–184 (2024).

Glucose Control and HbA1c (DCCT & UKPDS)

DCCT

Tight blood glucose control (HbA1c <7%) was associated with

- **~75%** reduction in developing retinopathy.
- **~50%** slowing of progression in those with established retinopathy.



DCCT Group, NEJM, 1993;329(14):977-86

DR Progression with sudden drop in glucose level

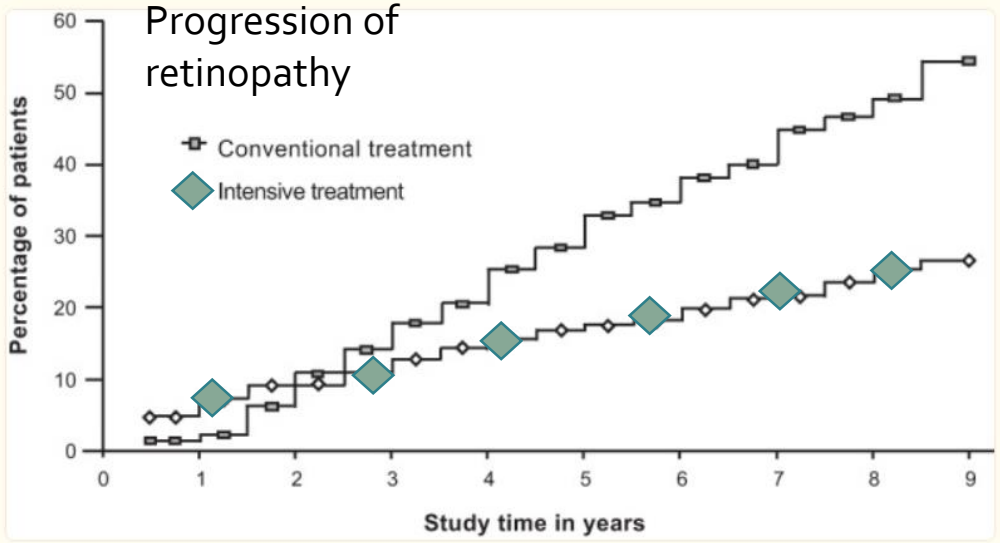


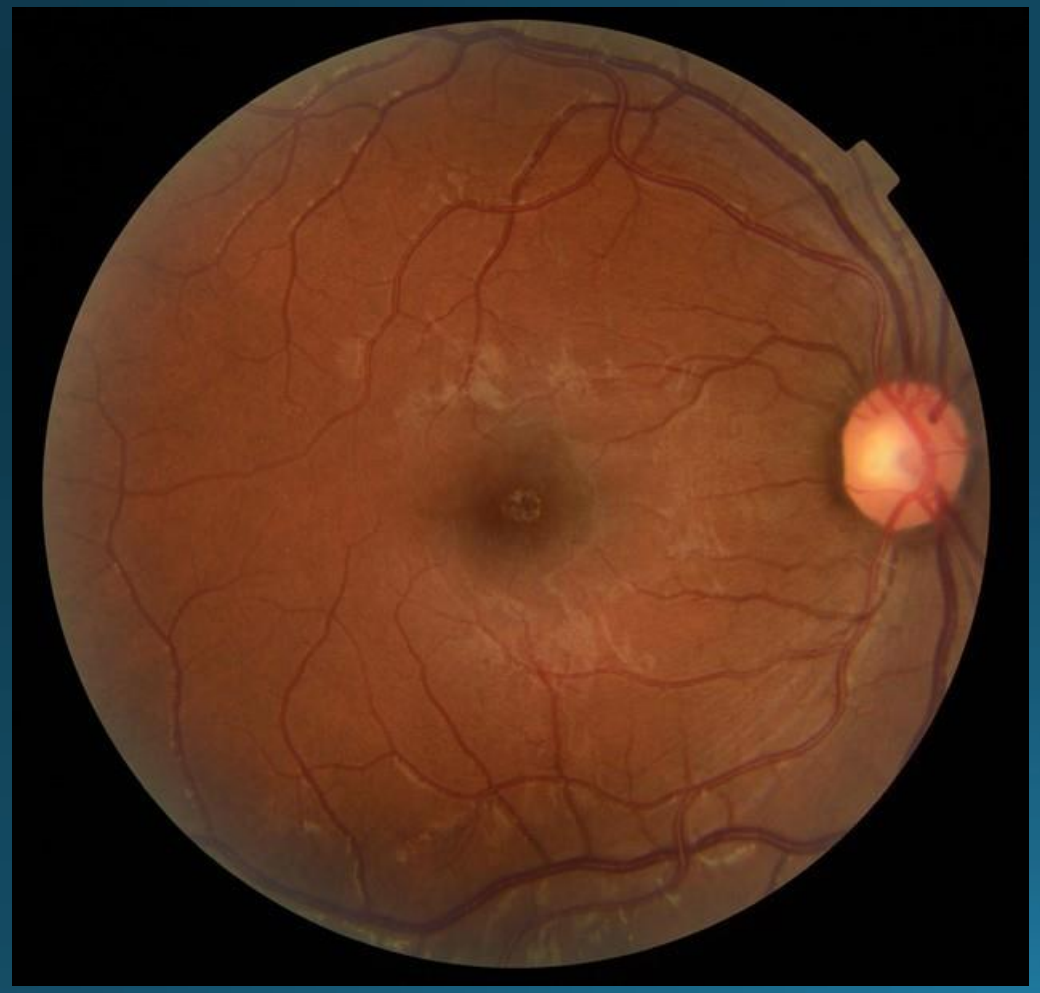
Figure 1

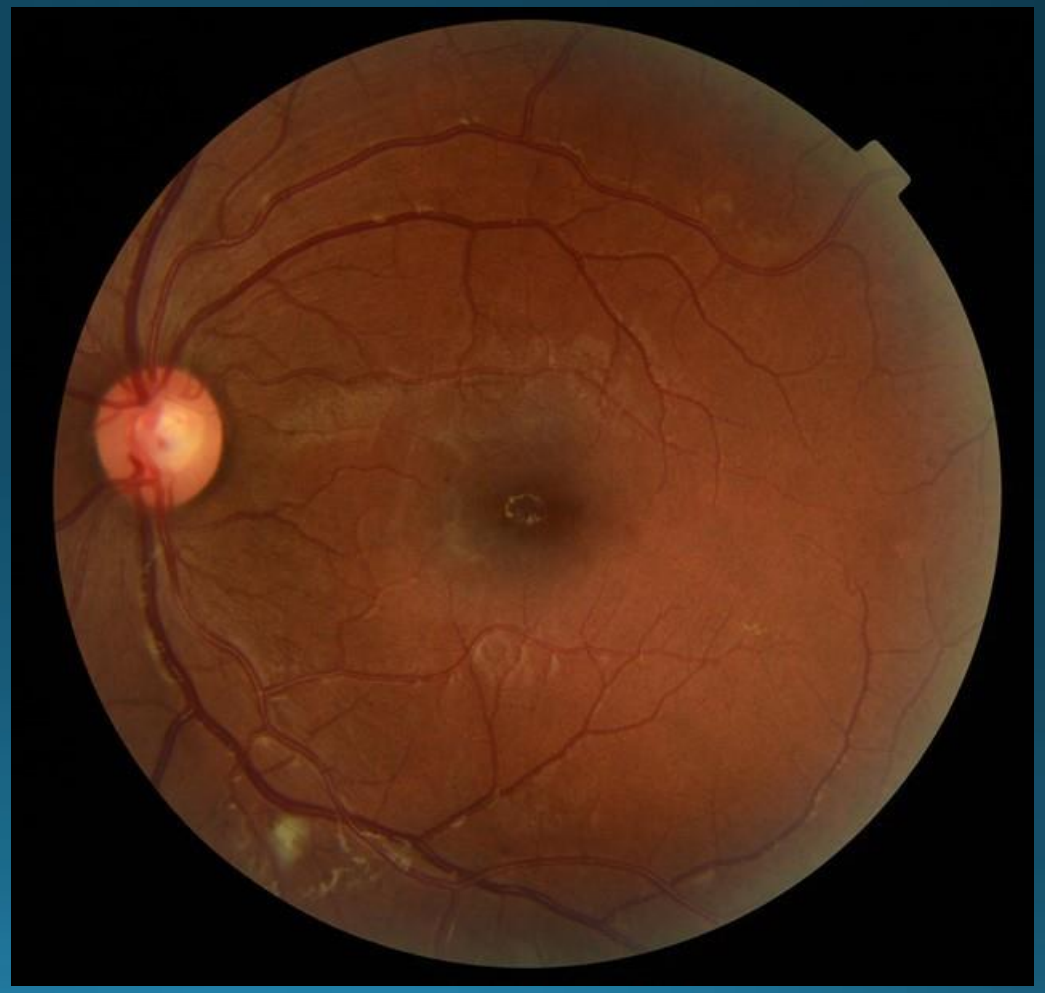
Cumulative incidence of DR progression (three-step or greater by ETDRS criteria) in the Diabetic Control and Complications Trial (DCCT) primary prevention cohort. There was little difference in percentage of patients with retinopathy progression between the Intensive and Conventional groups over the first 3 years; however, there was a 76% reduction in risk of DR progression evident at the conclusion of the DCCT after mean follow-up of 6.5 years.[28]

- The DCCT trial showed early worsening of retinopathy after sudden drop in HbA1c in type 1 patients. Still better in the long term (up to 18 yrs) (1)
- Relative risk of DR progression related to 1%, 2% or 3% decrease in HbA1c for approximately 6 months was 1.7, 2.8 and 4.7, respectively (3)
- Risk seems to reduce after 18 months
- May occur in pregnancy/ post bariatric surgery (4) and after pancreatic surgery.
- 10% to 20% of patients had worsening of DR within 3-6 months—2x risk for those with advanced DR at baseline (5).

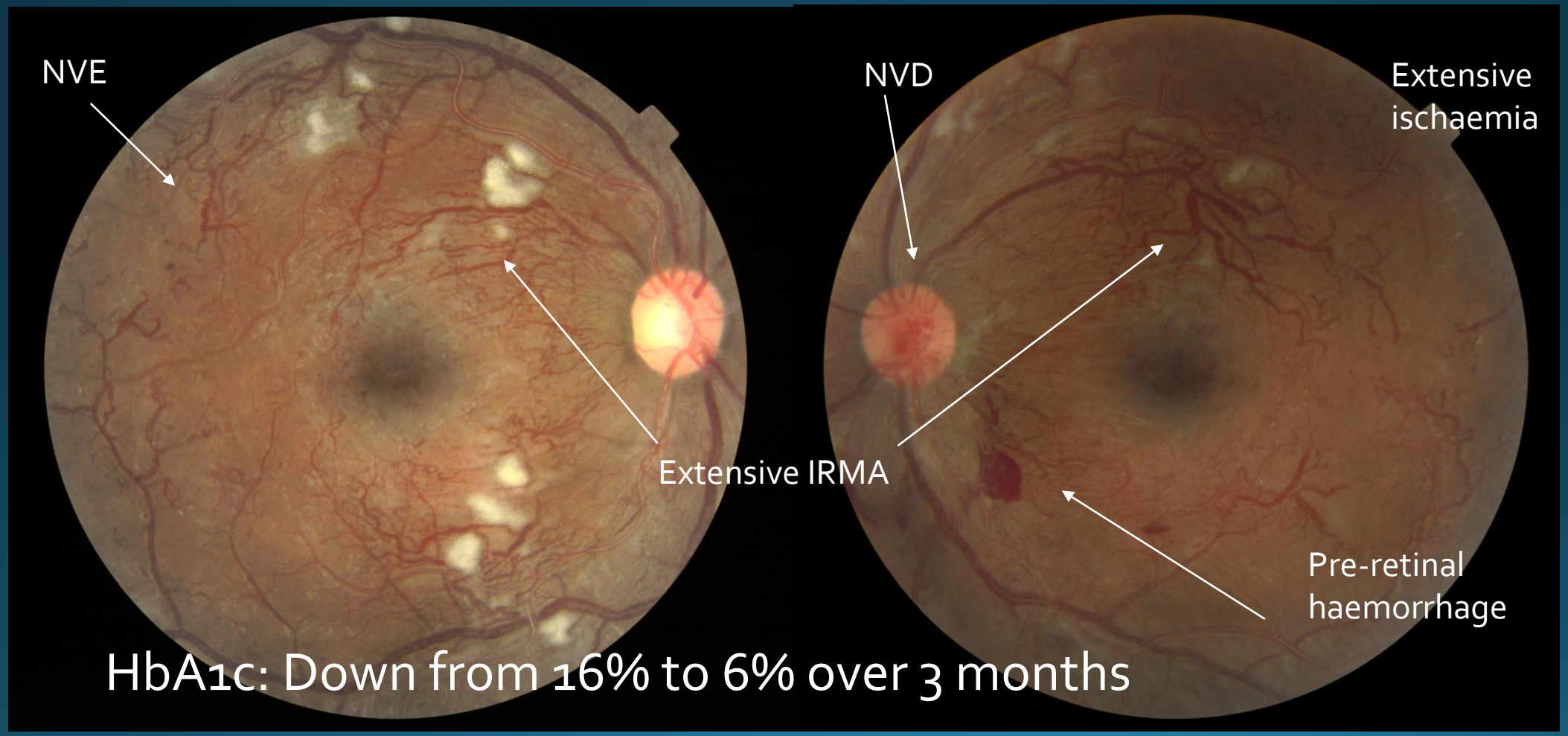
References 1) DCCT Group, NEJM, 1993;329(14):977-86. 2)) **Aiello LP. Diabetic retinopathy and other ocular findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study. *Diabetes Care*. 2014;37:17-23.** 3) Funatsu H, Yamashita H, Ohashi Y, Ishigaki T. Effect of rapid glycemic control on progression of diabetic retinopathy. *Jpn J Ophthalmol*. 1992;36:356-367 4) Bain SC, Klufas MA, Ho A, Matthews DR. Worsening of diabetic retinopathy with rapid improvement in systemic glucose control: A review. Diabetes Obes Metab. 2019 Mar;21(3):454-466.5
5) Feldman-Billard S et al. *Diabetes Metab.* 2018;44(1):4-14

AS- type 1 - 28 year old (since age 22) poor control, HbA1c 16%, seen in DESP May 2019



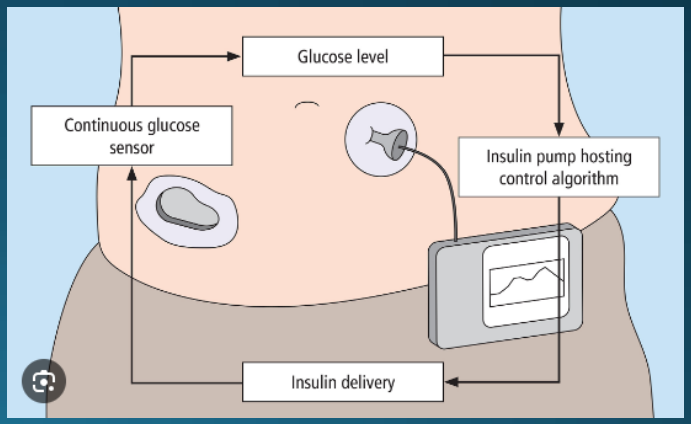


Seen in DESP Sept 2020- 16 months later post COVID, starting to get floaters in LEFT EYE with R3A



GLP-1 agonists (Semaglutide) & ?Hybrid Closed loop systems (OMNIPOD etc) & worsening DR

- May show early worsening of DR with drop in HbA1c.
- Should notify ophthalmologist to check eyes if large drop expected especially if have R2/R3A/M1 changes.
- The SUSTAIN 6 trial showed a higher risk of early worsening of DR. Stabilization after 12 to 18 months.
- Study from Stockholm of 370,000 pts disputes worsening with GLP-1 agonists (ASRS 2024)- Barkmeier et al.
- New FOCUS trial n=1,500 patients (placebo v semaglutide). The primary outcome is progression of DR; secondary outcomes: the incidence of anti-VEGF injections, laser photocoagulation & vitrectomy. (February 2027)
- HCL – may have a similar effect on worsening of DR- hence NSC call for screening yearly rather than 2 yearly in those with RoMo.



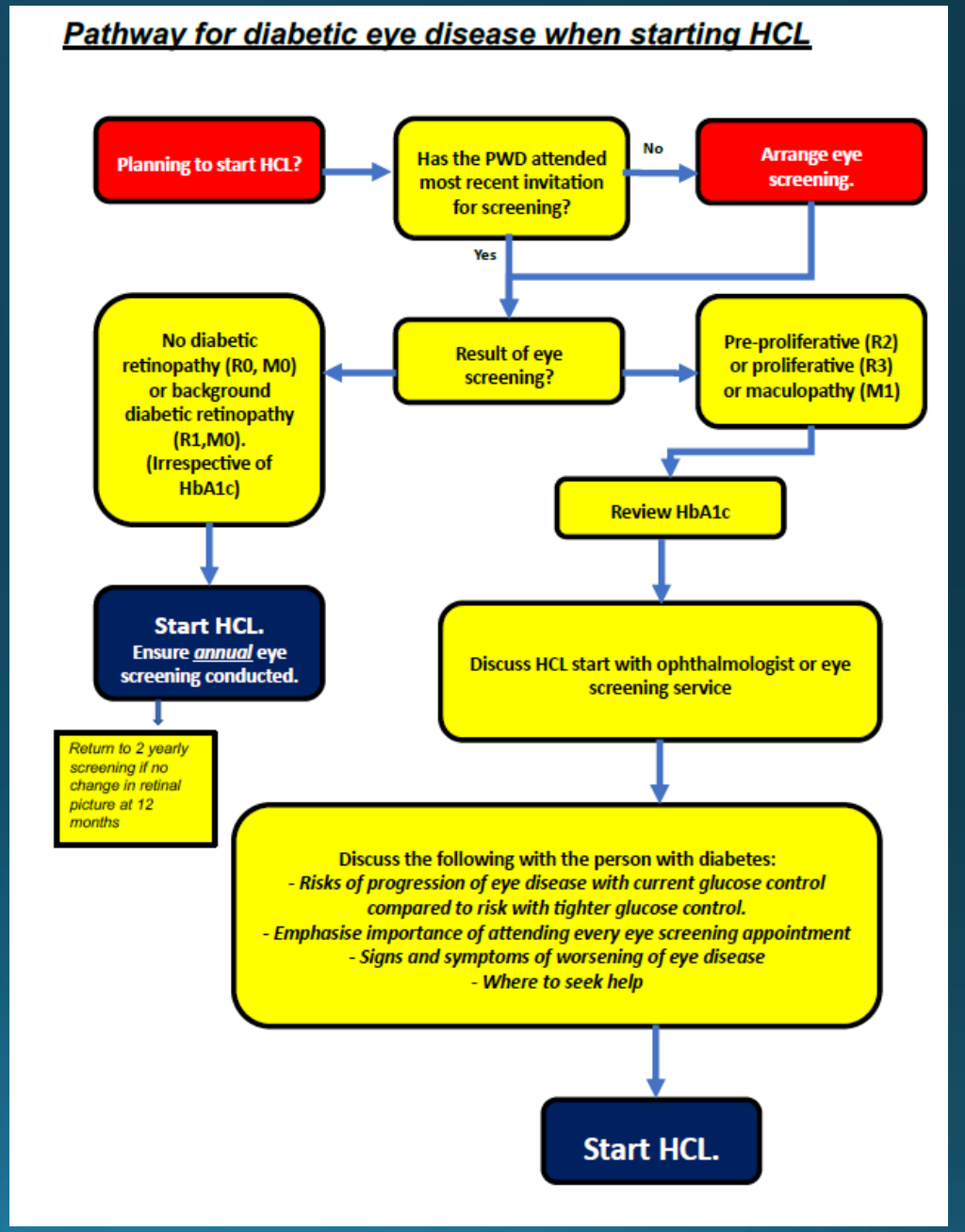
1 Saw M et al. *Eye (Lond).* 2019;33(12):1842-1851
3.Visbøll T et al. *Diabetes Obes Metab.* 2018;20(4):889-897.
4. Akil H, Burgess J, Nevitt S, Harding SP, Alam U, Burgess P. Early Worsening of Retinopathy in Type 1 and Type 2 Diabetes After Rapid Improvement in Glycaemic Control: A Systematic Review. Diabetes Ther. 2022 Jan;13(1):1-23.

HCL guidance

- No evidence currently exists about the effects of starting Hybrid Closed Loop systems on DR.
- In view of potential initial increased risk of DR progression New guidance and recommended pathway published regarding all those living with type 1 diabetes starting HCL systems. (Feb/March 2024).

- Overall risk:

"When high glucose concentrations are reduced over 6 months (or less) the risk that moderate/severe retinopathy worsens is increased from 8% to 13%. By 18 months, there is no difference in eye disease. After 6 years those with reduced glucose levels have halved the risk of developing sight threatening retinopathy."



Hybrid Closed Loop SEL Diabetic Eye Pathway:

KING'S HEALTH PARTNERS DIABETES ENDOCRINOLOGY OBESITY

Health Innovation Network South London

Contact DESP when patient starts HCL. DESP will ensure the correct action is taken for patient recall
For clinical questions/advice contact local DESP clinical lead

Retinal Grades	Diabetologist Actions	Diabetic Eye Screening Dept (DESP) Actions	Ophthalmologist Actions if care of HES
Low risk (in care DESP) R0M0- no retinopathy	Inform DESP that on HCL to ensure yearly/12 months screen rather than 2 yearly (for the first year on HCL) Ensure/check with patient that they attend 12 months screening for first year.	If patient screened >=6 months ago, to re-invite for a screen in 4-6 weeks and ensure recall period is not more than 12 months If patient screened<6 months ago, over-ride any 24-month outcome to 12 months.	N/A
R3(S)- stable treated	If symptoms of floaters (re-activation) - contact DESP or ophthalmology consultant	Should be on 1 yearly follow up in surveillance	Should be on 1 yearly follow up if in virtual clinics
Medium risk (in care DESP) R1M0	Ensure attendance at Screening 1 yearly or	Will remain on yearly screening	N/A
R1M1 (early) R2M0 (early)	Ensure attendance at OCT clinic/ DESP surveillance clinic (6 monthly)	Will be in OCT, surveillance clinics 6 monthly - to refer to HES if worsening	If in virtual clinics - ensure 3 monthly review
High risk (in care ophthalmology) R2M1, R3AM0, R3AM1 Advanced M1 (if attending HES for injections/laser/review)	Inform ophthalmology local lead of HCL. Ensure eye check within 3/12 of starting HCL. Check HbA1c if > 9% Use less aggressive HCL settings if HbA1c>9% and intensify gradually over 3 months. May need to delay HCL if active untreated R3A present	Likely to be DNA from ophthalmology due to non-attendance re-invite within 3 months for R3A pts and 6 months for other grades DESP failsafe check patients in care of HES to ensure they are not lost to follow up	Ensure HCL users stay on a 2-3 monthly review until treatment complete and stable.

Samantha Mann, Clare Connor, Sufyan Hussain 2024

Summary….

- Who is eligible and how Diabetic Eye Screening works?
- Stages of Diabetic Retinopathy and maculopathy
- Various treatment options for Retinopathy and Maculopathy
- Key risk factors and when to involve Ophthalmology in GLP1-RA and HCL treatment.
- Key points from the new NICE Guidance- Diabetic Retinopathy: Management and Monitoring

- Thank you
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