Hybrid Closed Loop (HCL) Systems: Will the drop in HbA1c be important?

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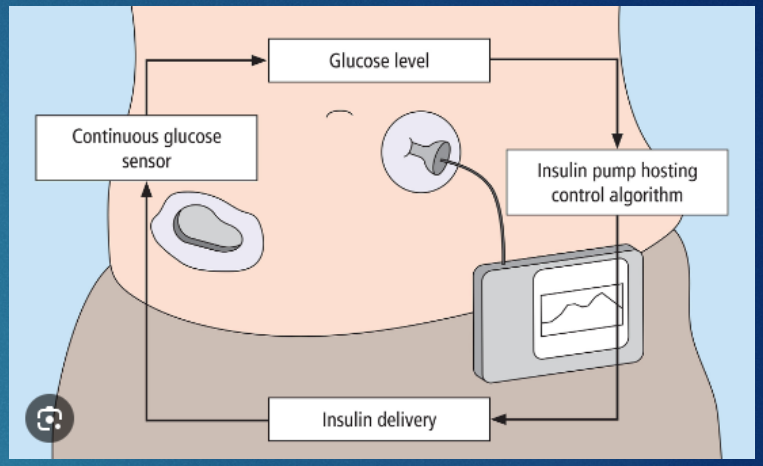
Hybrid Closed-Loop Systems and Retinopathy in Type 1 Diabetics

BRITISH ASSOCIATION OF RETINAL SCREENING

- Overview:
- 1. Overview of Hybrid Closed-Loop (HCL) Systems
- 2. Risk factors for progression of retinopathy in Diabetes
- 3. Rapid Glucose Drop: A Double-Edged Sword
- 4. Clinical Implications for Screening and Monitoring
- 5. Case Study
- 6. Summary

What is a Hybrid Closed Loop System?

- Glucose sensor and pump that uses an automated insulin delivery system which adjusts the insulin dose based on continuous glucose monitoring (CGM) measurements.
- Better glycemic control compared to traditional methods.
- Reduces long-term diabetes complications like neuropathy, nephropathy, and retinopathy.



2 Information about hybrid closed loop systems | Hybrid closed loop systems for managing blood glucose levels in type 1 diabetes | Guidance | NICE

NICE Guidance

- Hybrid closed loop (HCL) systems are now recommended as an option for managing blood glucose levels in type 1 diabetes for:
  - Adults who have an HbA1c of >= 58 mmol/mol (7.5%) or have or have disabling hypoglycaemia
  - Children or young people
  - Pregnant or those planning a pregnancy
- 5 yr implementation plan by NHS England
- Need for specialist support, cost-effective price and adequately trained staff

Hybrid closed loop systems for managing blood glucose levels in type 1 diabetes
Technology appraisal guidance
Reference number:TA943 Published: 19 December 2023

Risk Factors for Retinopathy PROGRESSION

Modifiable

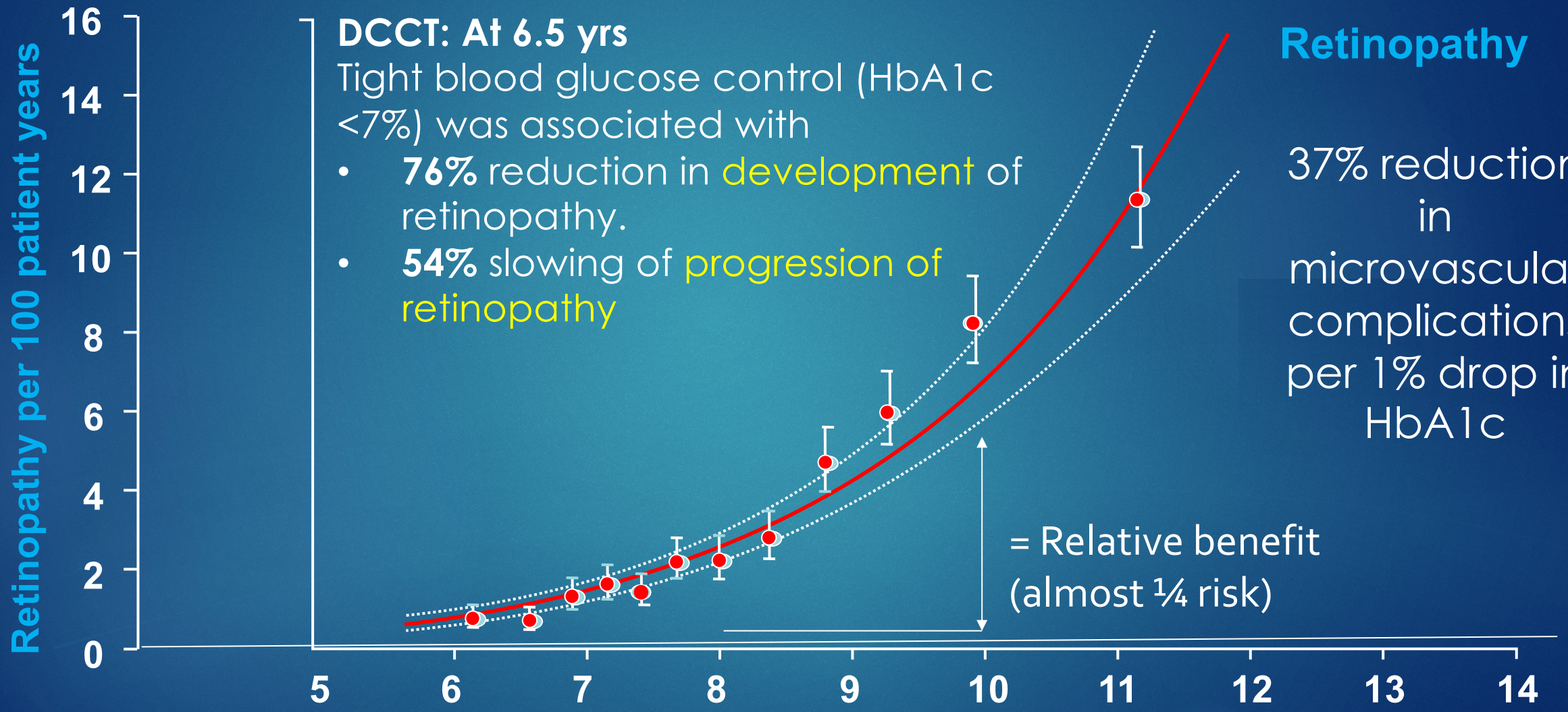
- Glycaemic control (HbA1c <7%)[1]
- Blood Pressure control (140/90mmHg) [1]
- Lipid control (ACCORD/FIELD)
- Drugs/ Devices (GLP-1/ HCL)
- Pregnancy (DIEP study[2])
- Renal disease (130/80mmHg)
- Non- attendance at screening [4]

Non-modifiable

- Ethnicity (African Caribbean[3])
- Duration of diabetes
- Type of Diabetes (type 1>type 2)

1) UKPDS and DCCT studies, NICE Guidance Aug 2024)
2) Diabetes in early pregnancy (1995) Metabolic control and progression of retinopathy. Diabetes Care 18:631-637
3) Mangelis A, Wijewickrama P, Nirmalakumaran A, et al. People with type 1 diabetes of african caribbean ethnicity are at increased risk of developing sight-threatening diabetic retinopathy. *Diabetes Care*. Published online: April 26, 2023.
4) Forster A.S., Forbes A., Dodhia H., Connor C., Du Chemin A., Sivaprasad S., Mann S., Gulliford M.C. Non-attendance at diabetic eye screening and risk of sight-threatening diabetic retinopathy: A population-based cohort study. *Diabetologia*. 2013;**56**:2187–2193

Glycaemic Control (DCCT & UKPDS)



DCCT: At 6.5 yrs

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

- **76%** reduction in development of retinopathy.
- **54%** slowing of progression of retinopathy

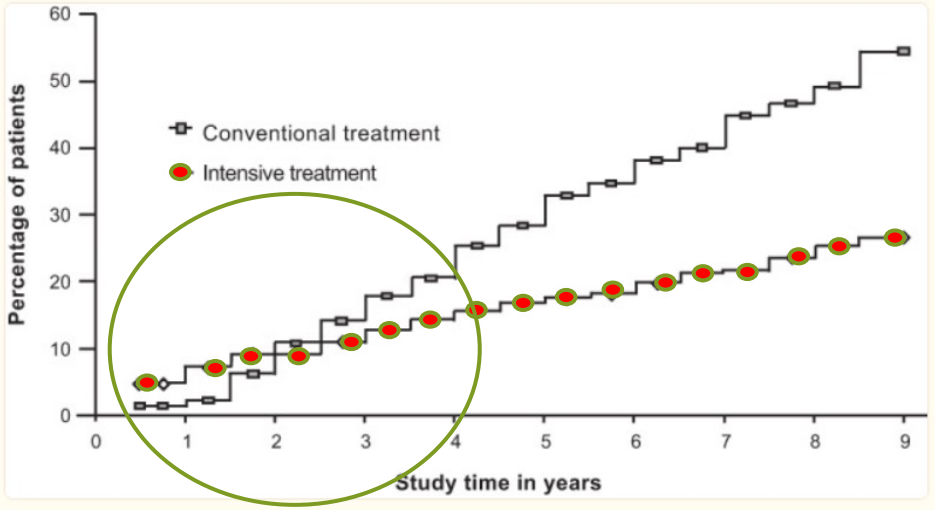
= Relative benefit (almost ¼ risk)

Retinopathy

37% reduction in microvascular complications per 1% drop in HbA1c

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

Paradoxical worsening of DR with sudden drop in glucose level : A Double-Edged Sword



Cumulative incidence of DR progression in the secondary intervention group (those with mild DR at baseline).

- The DCCT trial showed early worsening of retinopathy in some patients after sudden drop in HbA1c in type 1 patients.
- Early worsening of DR was found in 13.1% of people on intensive insulin therapy and 7.6% of those on conventional insulin therapy.
- A drop in HbA1c of 1.5% over 3 months or 2% over 6 months) can be associated with early progression of pre-existing DR.
- Still did better in the long term (up to 18 yrs) [1,3]
- Worse if baseline HbA1c higher, greater drop, duration of diabetes higher, baseline level of DR[1].
- May occur in pregnancy/ post bariatric surgery [2,3]
- Stabilised after 18 months [1,3]

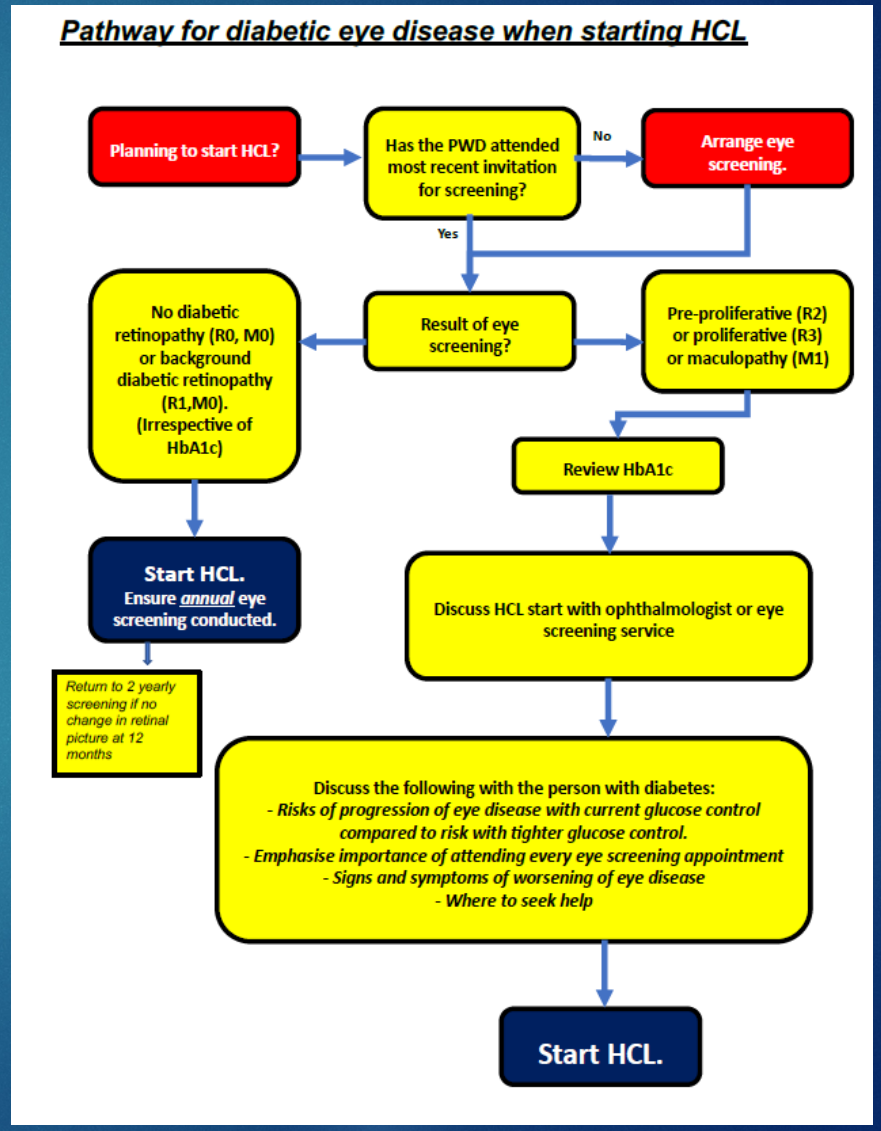
References 1) Aiello LP. Diabetic retinopathy and other ocular findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study. *Diabetes Care*. 2014;37:17-23 2) Bain SC, Klufas MA, Ho A, Matthews DR. Worsening of diabetic retinopathy with rapid improvement in systemic glucose control: A review. Diabetes Obes Metab. 2019 Mar;21(3):454-466 3) Akil H et al. Diabetes Ther (2022) 13:1–23 Early Worsening of Retinopathy in Type 1 and Type 2 Diabetes After Rapid Improvement in Glycaemic Control: A Systematic Review

How will this impact Diabetic Eye Screening?

- 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."



Recommended pathway:

- Before starting HCL ensure that the person with diabetes has attended their most recent DESP appt. If not, then contact the screening programme for an appt as soon as possible.
- If the retinal screening examination shows no R0,M0 or R1, M0, continue with a 12 month screening interval (may need to use the CL override facility) and start HCL as planned.
- This will ensure that individual initiating HCL will receive a screen within 12 months to monitor any retinopathy.
- If no retinopathy is detected following this 12-month screen, the individual will automatically be put on the appropriate 2 yrly screening interval for their grading outcome.

Recommended pathway:

- If the result shows grade R2 (mod-severe NPDR) or proliferative diabetic retinopathy (grade R3A or R3S) or diabetic maculopathy (grade M1), or if the patient is already under HES, to discuss the decision to start HCL with ophthalmology teams.
- Ensure that the ophthalmology team are aware that these patients may need closer follow up within the local surveillance system so that treatment for diabetic eye disease can be started without delay if needed.
- Consider the stage of the eye disease and treatment plan and whether the HCL start should be delayed until after treatment is completed.

Hybrid Closed Loop SEL Diabetic Eye Pathway:

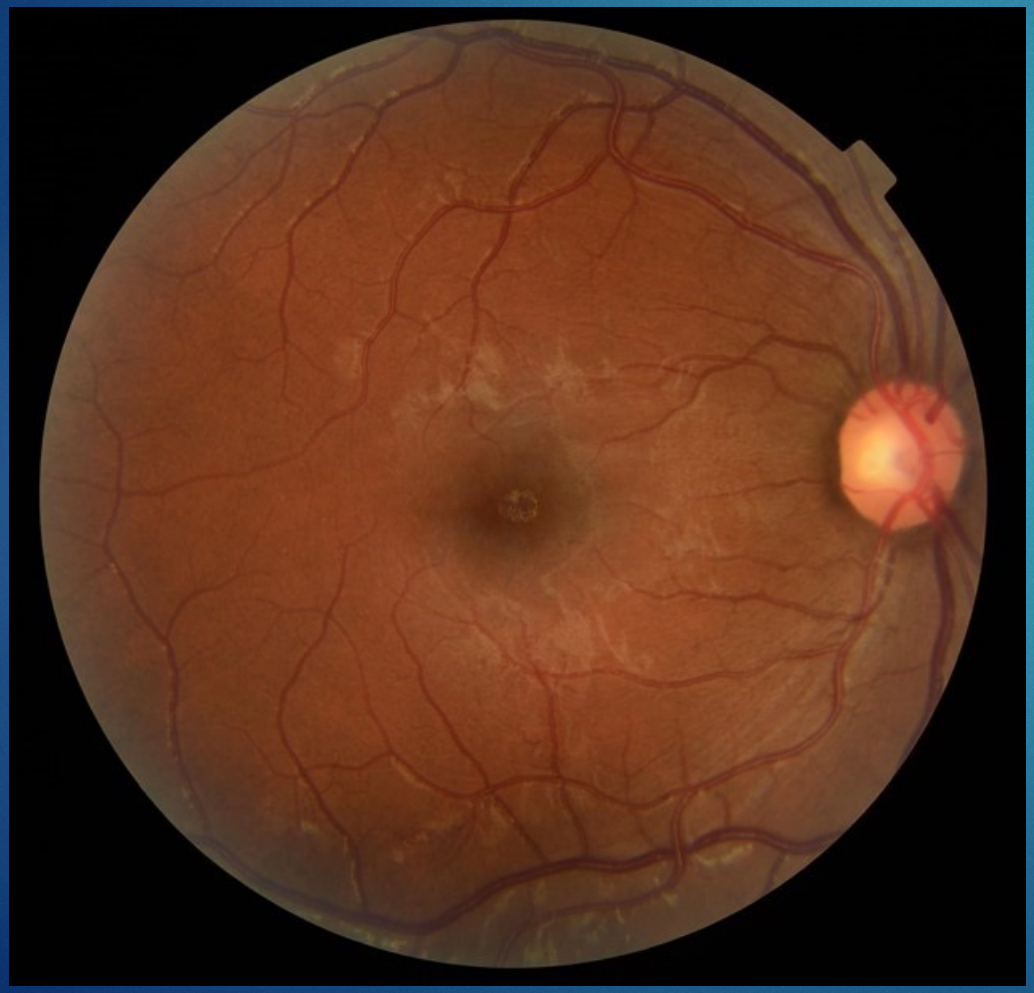
Retinal Grades	Diabetologist Actions	Diabetic Eye Screening Dept (DESP) Actions	Ophthalmologist Actions if care of HES
Low risk (in care DESP) R0M0- no retinopathy	Inform DESP that on HCL to ensure yearly/12 months screen rather than 2 yearly (for the first year on HCL) Ensure/check with patient that 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.

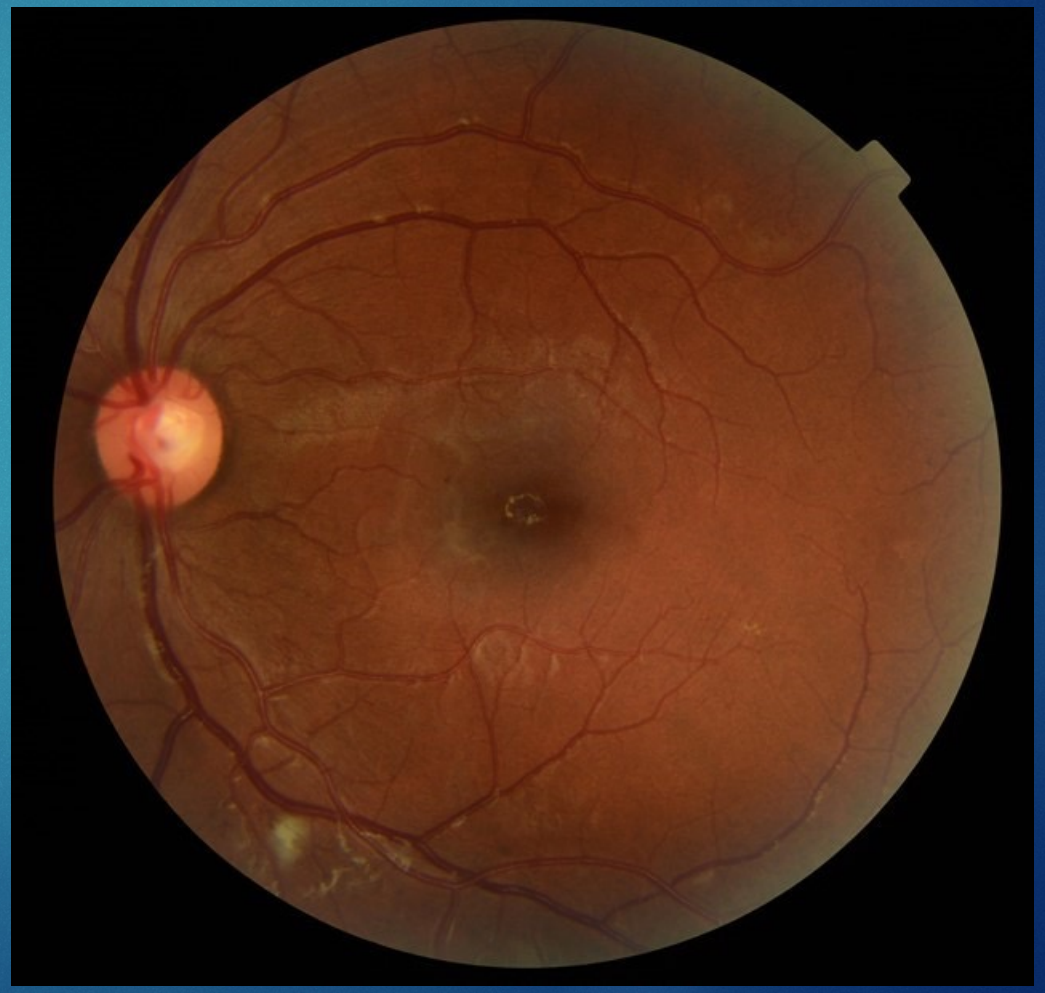
Case Study

Case AS

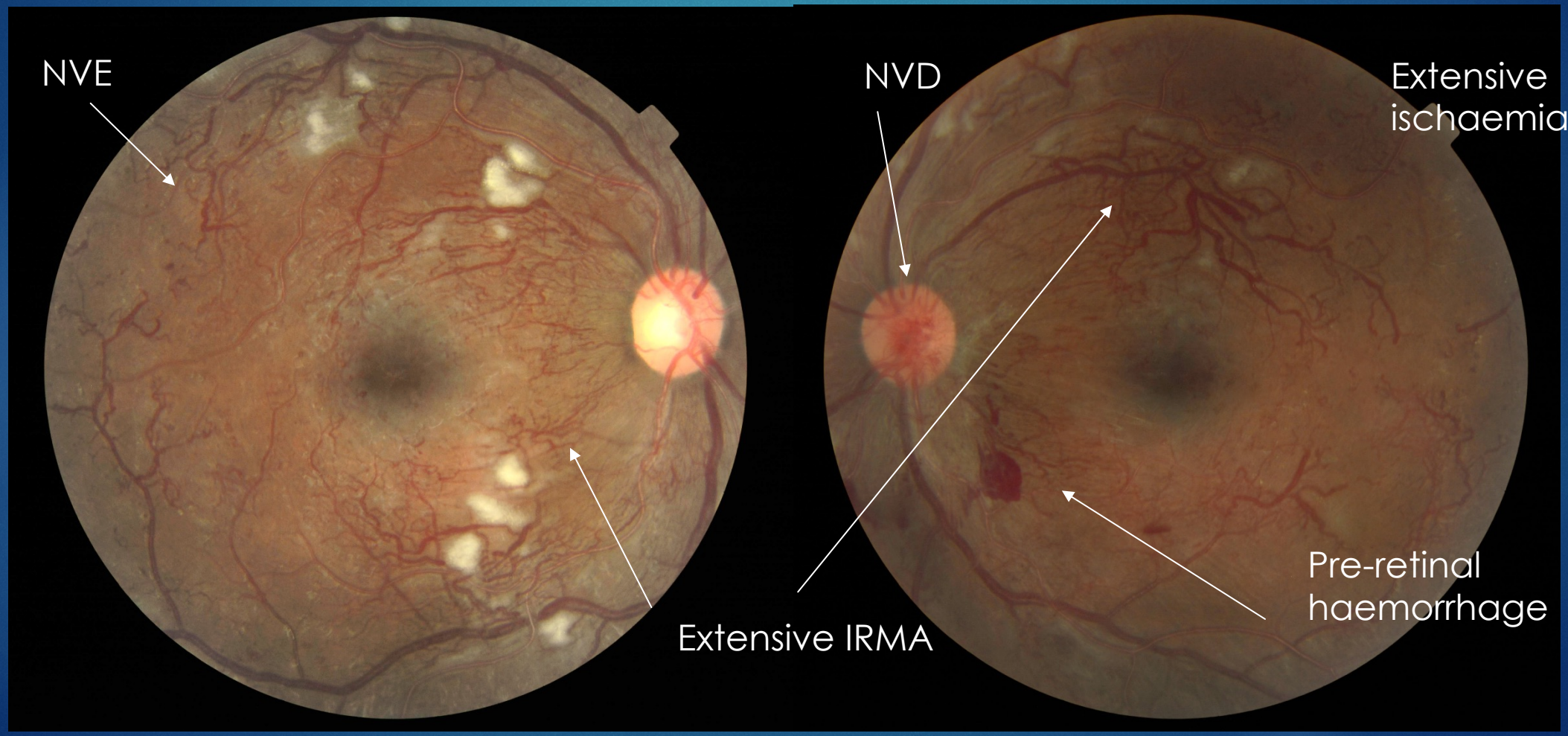
- 28 yr old with type 1 Diabetes for 5 years
- History of poor diabetic control and attendance
- HbA1c 16% (regularly above 145 mmol/mol) (NR 20-41)
- Attended DESP in May 2019- minimal DR
- Sudden onset of black floaters in her left eye for a few weeks (Sept 2020)
- Referred from Diabetic Eye Screening to the Eye Clinic
- VA 6/7.5 and 6/9.5

DESP images- May 2019

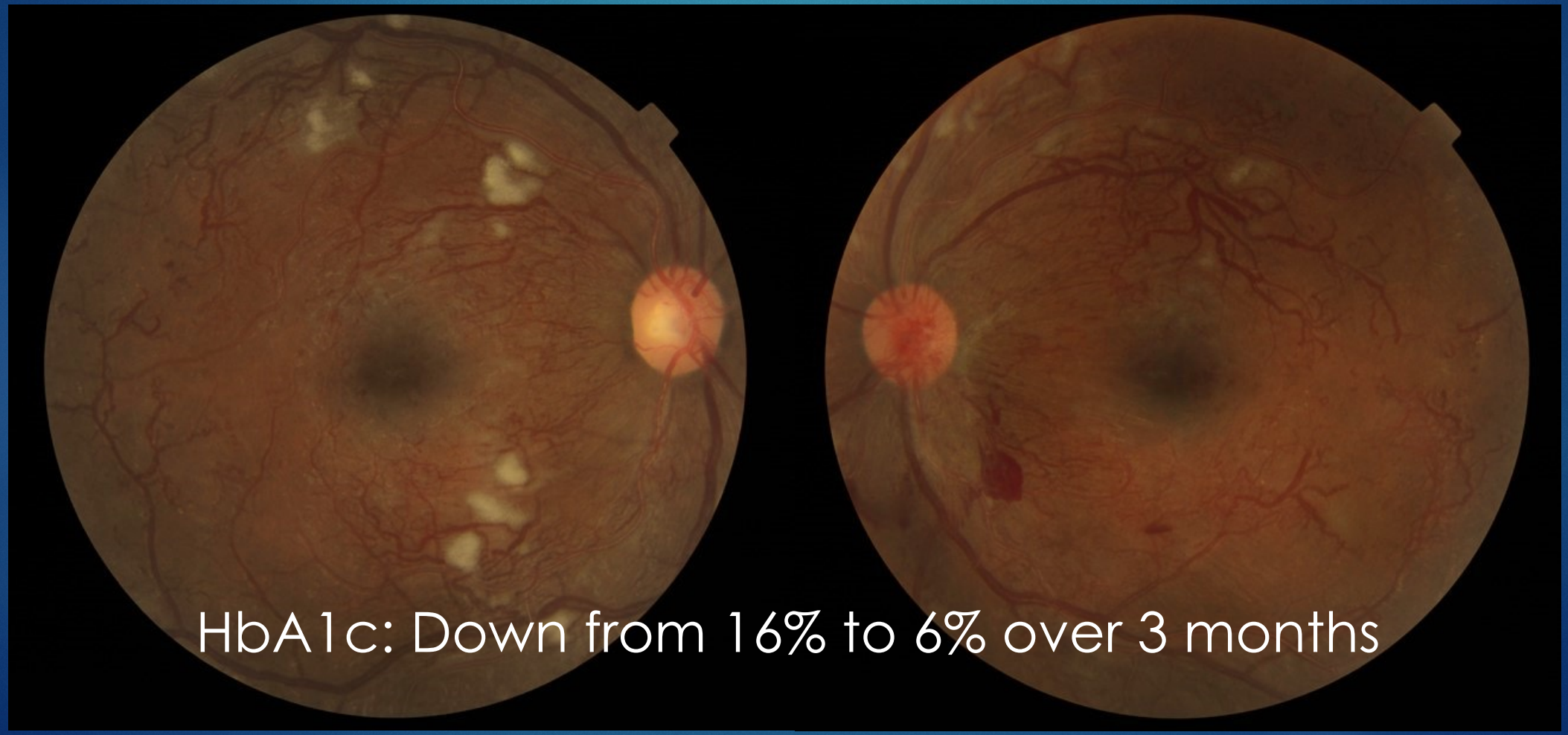




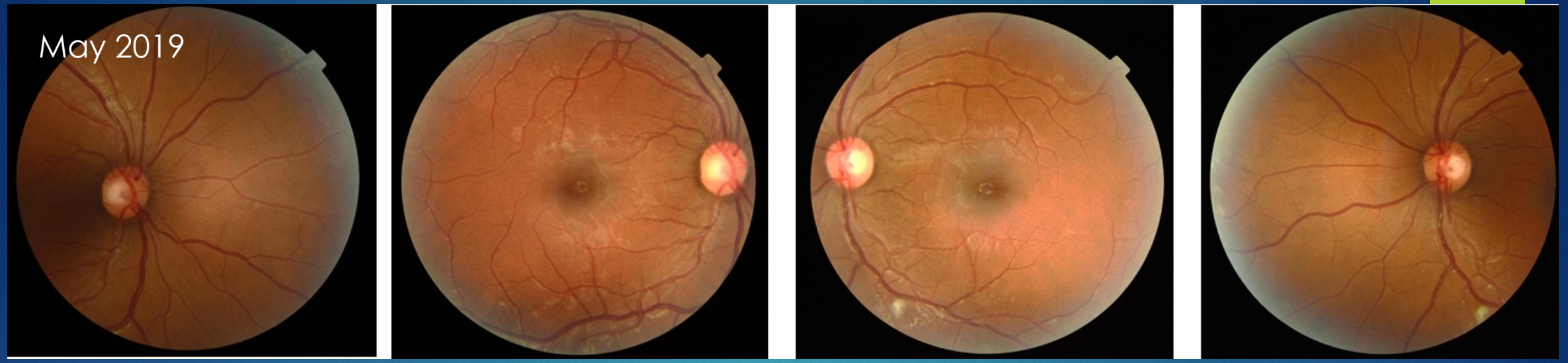
Seen in DESP Sept 2020- 16 months later post COVID, starting to get floaters in LEFT EYE

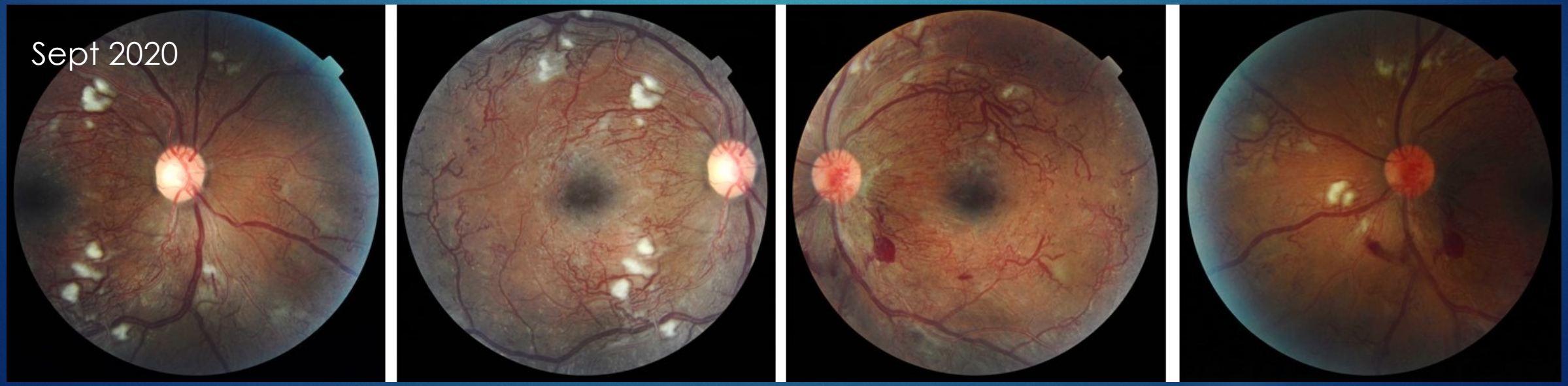


Referred to HES
Progression to advanced R3 (Proliferative)



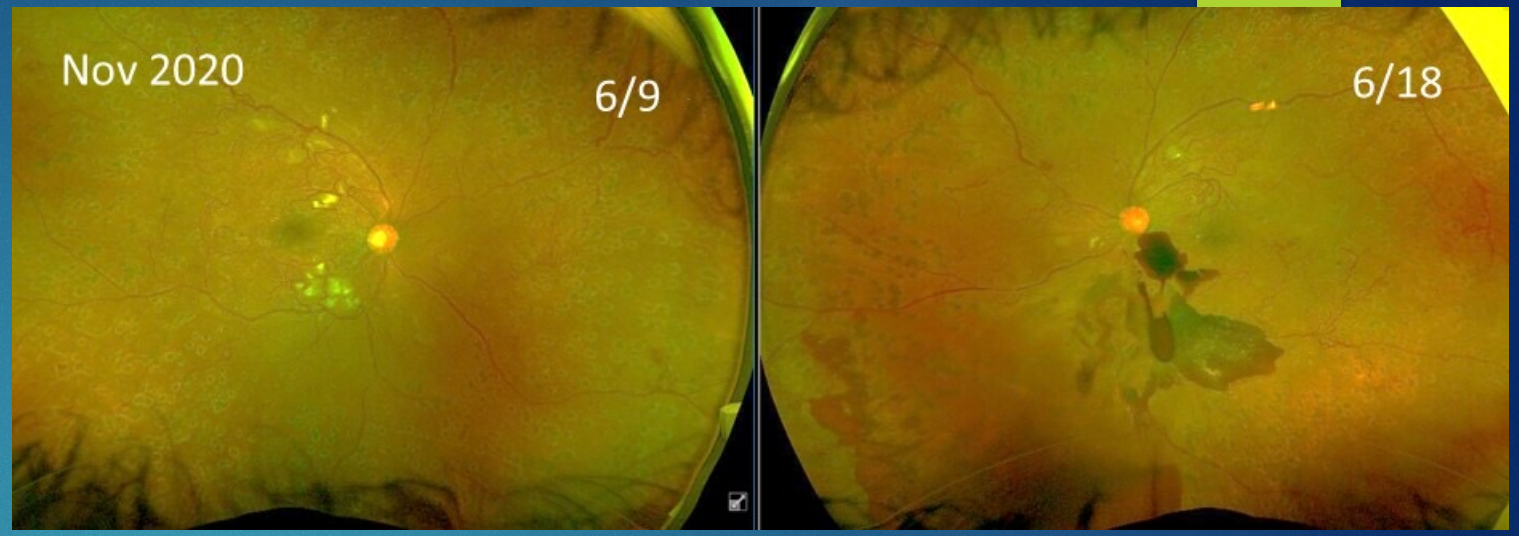
May 2019 to Sept 2020- HbA1c dropped from 16% to 6% in 3/12

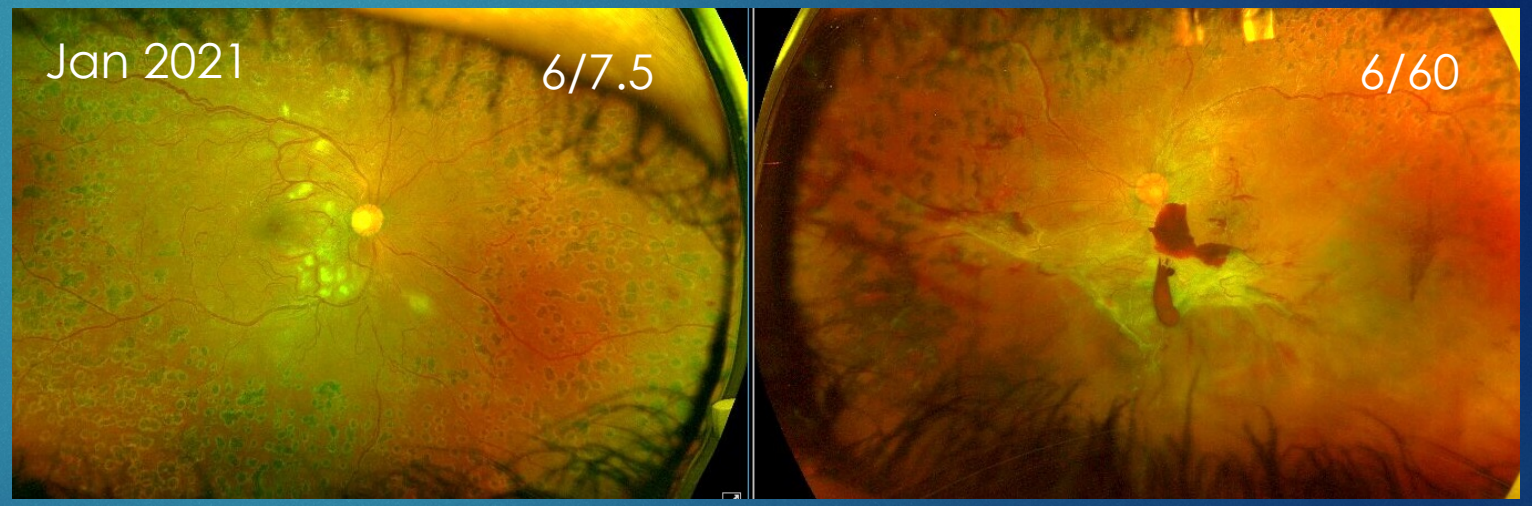


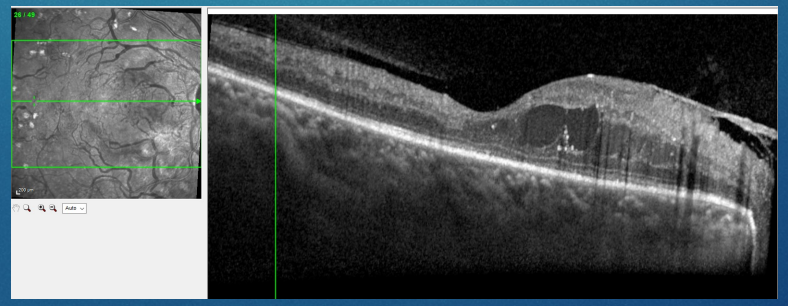


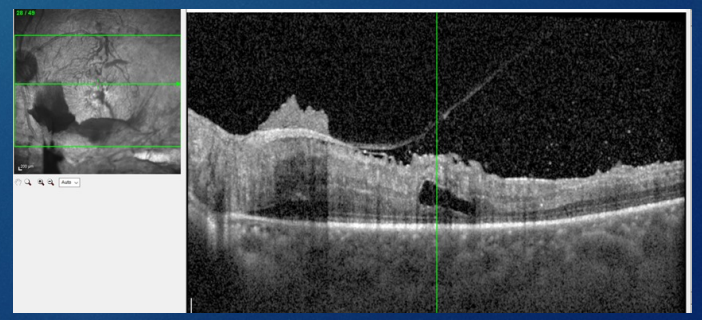
Continued to progress….

- VA 6/9 (0.16) and 6/18 (0.40)
- Despite PRP in both eyes
- Developed pre-retinal haem in the left eye with traction and fibrosis
- Referred for LEFT Vitrectomy in Jan 2021 & wash out in April 2021 due to vitreous haemorrhage with HM vision.
- After surgery LEFT eye recovered to 6/9.

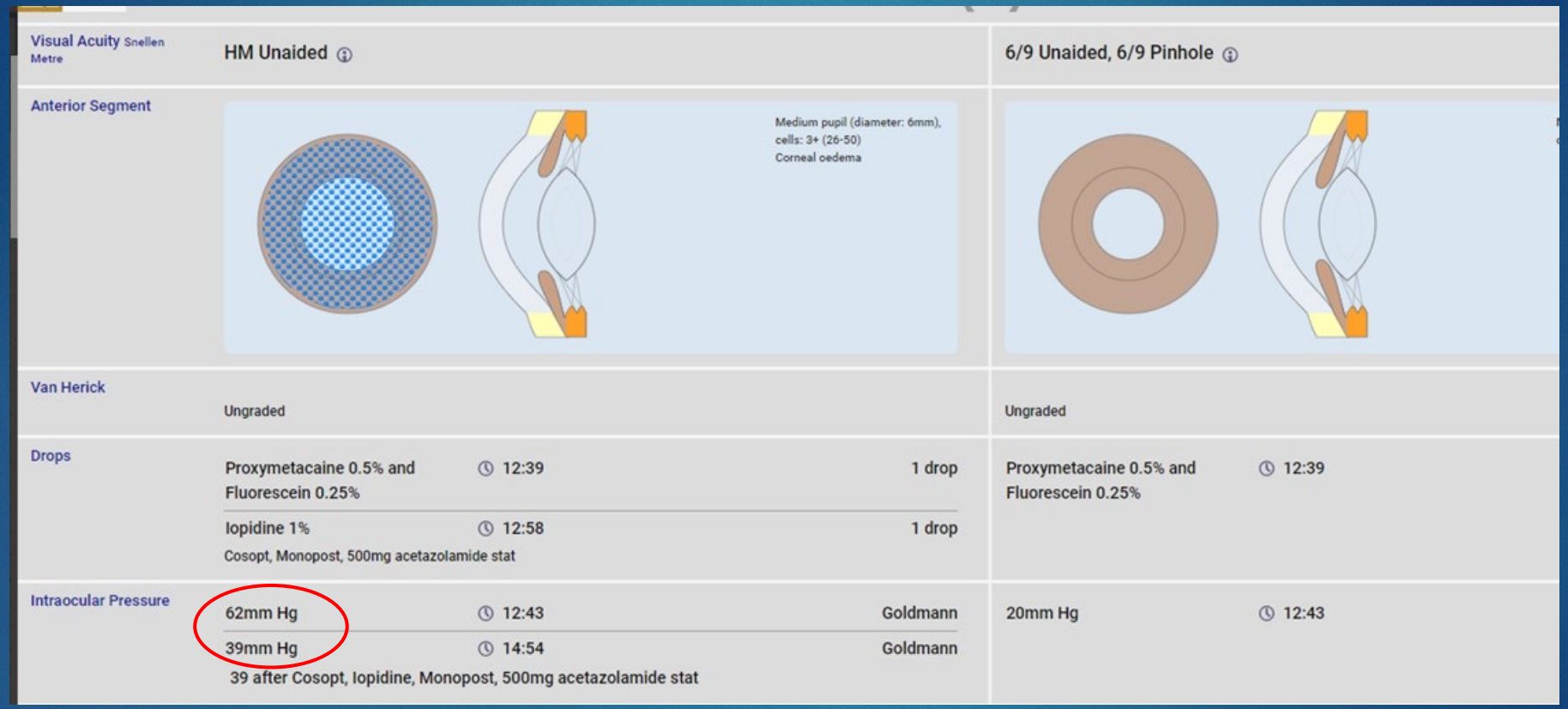








Oct 2021. Further PRP given, Right Eye became blurry and painful. Diabetic control remains poor.



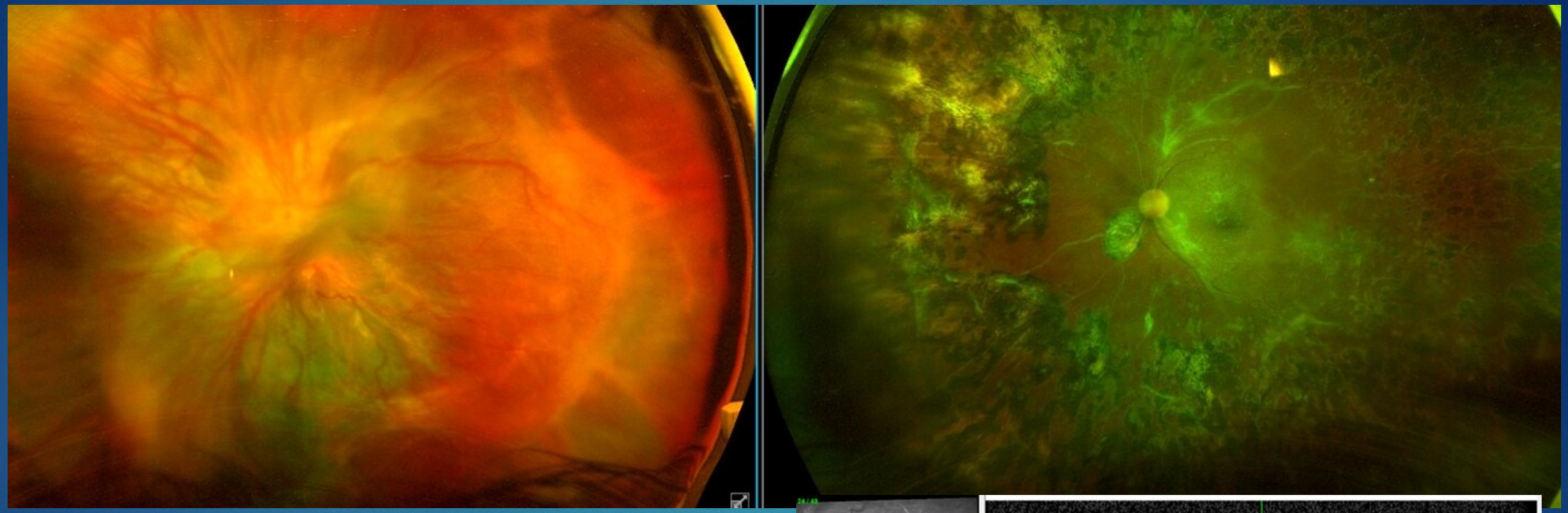
Visual Acuity Snellen Metre	HM Unaided	6/9 Unaided, 6/9 Pinhole
Anterior Segment	Medium pupil (diameter: 6mm), cells: 3+ (26-50) Corneal oedema	
Van Herick	Ungraded	Ungraded
Drops	Proxymetacaine 0.5% and Fluorescein 0.25% 12:39 1 drop Iopidine 1% 12:58 1 drop Cosopt, Monopost, 500mg acetazolamide stat	Proxymetacaine 0.5% and Fluorescein 0.25% 12:39
Intraocular Pressure	62mm Hg 12:43 Goldmann 39mm Hg 14:54 Goldmann 39 after Cosopt, Iopidine, Monopost, 500mg acetazolamide stat	20mm Hg 12:43

Diagnosed with rubeosis & NVG. Referred to Glaucoma for Surgery- Ahmed tube with MMC to control IOP (Nov 2021).

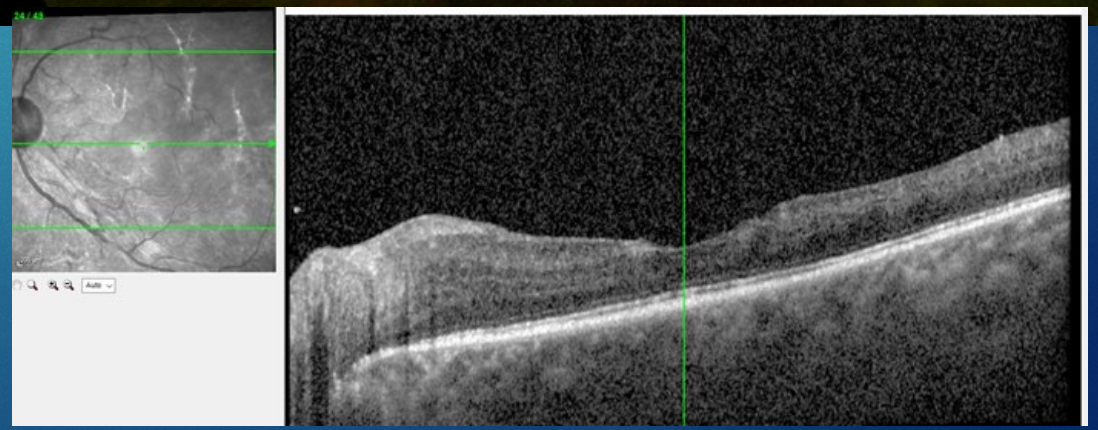
Right Eye progressed to NPL but thankfully LE remains stable

NPL

6/9



NO OCT possible



Vision now NPL in RE and 6/9 in LE

Case Study

- Young Type 1 with background of long term very poor control (HbA1c 16%/ TIR 19%)
- Sudden drop in HbA1c may have triggered worsening of retinopathy- Although COVID may have also played a role.
- High level of ischaemia in right eye- became rubeotic despite PRP
- Vitrectomy in left eye – stabilised the eye
- Need to watch out for these high risk patients that may progress to sight threatening disease if HbA1c drops too suddenly.

Summary

- HCL systems should overall be beneficial and improve glycaemic control.
- We don't currently know the impact of these devices on DR (need monitoring and research)
- Could lead to rapid glucose reductions that may worsen retinopathy in some patients.
- Understanding this interaction is key and adoption of the new recommendations and pathway should mitigate any increased risk.
- - Final Recommendations:
- - Educate patients/ health care professionals about the possibility of retinopathy progression when starting HCL therapy and where to get help
- - Ensure Screening for retinopathy more frequent in the early stages of HCL use, particularly in patients with prior poor control, worse baseline retinopathy and longer duration of diabetes.

Thank you

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