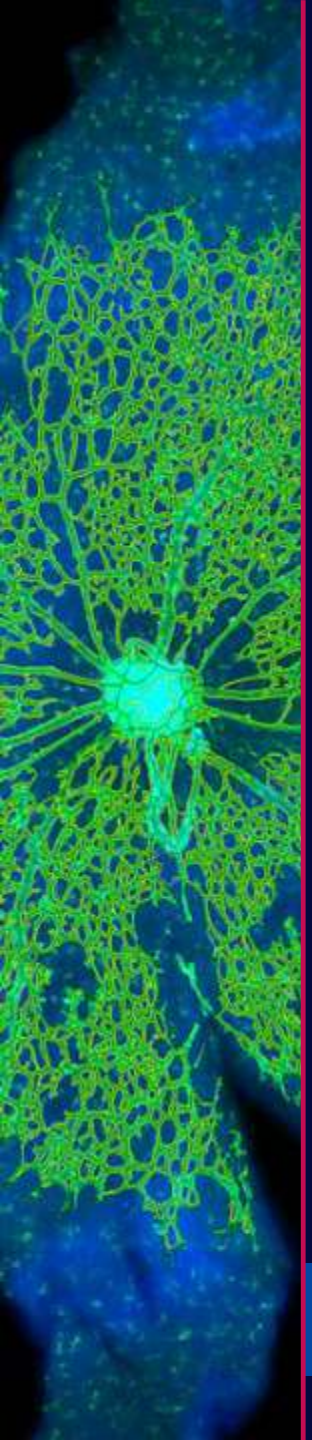
Disclosures

Financial Disclosures

- CW: Grant Support) Alcon, Allegro Ophthalmics, Allergan, Apellis, Bayer, Clearside Biomedical, DRCR Network, Genentech, Inc., Iconic Therapeutics, Ophthotech, Regeneron, ThromboGenics, Tyrogenex; Consultant) Alcon, Alimera, Allergan, Alnylam, Bayer, Clearside Biomedical, DORC International, Genentech, Inc., Iconic Therapeutics, ONL Therapeutics, Regeneron, ThromboGenics, Valeant; Recipient) Allergan, Genentech, Inc., Regeneron
- RCH, SPK, FL: Employee) American Academy of Ophthalmology
- IS, VG: Employee) Genentech, Inc.

Study Disclosures

- This study includes research conducted on human subjects
- The data used in this study are deidentified and exempt from Institutional Review Board approval or patient-level consent
- Funding was provided by Genentech, Inc., a member of the Roche Group, for the study and third-party writing assistance, which was provided by Betsy C. Taylor, PhD, CMPP, of Envision Pharma Group



Baseline Factors Influencing Time to Blindness in Patients With Diabetic Retinopathy: An AAO IRIS® Registry Analysis

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Key Clinical Question and Methods

Key Clinical Question

- In eyes with newly diagnosed DR and good vision, what demographic and clinical factors were associated with an increased risk of developing sustained blindness?

Methods

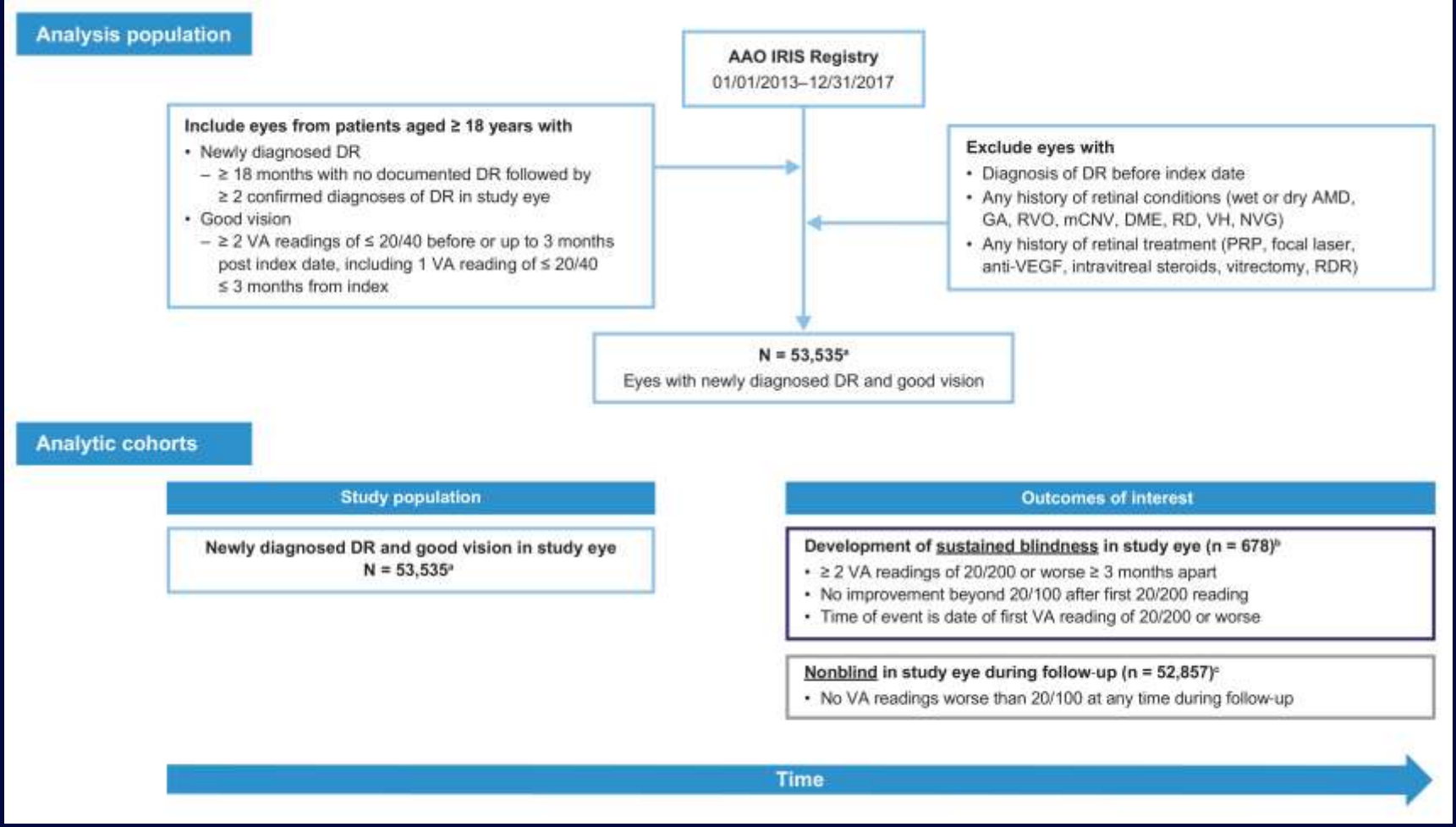
- The American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight) is a comprehensive national eye disease clinical registry that collects key information on the diagnosis, treatment, and outcomes for patients with DR
- Using IRIS Registry records from January 1, 2013 to December 31, 2017, we conducted a retrospective analysis of baseline demographic and clinical characteristics of patients with newly diagnosed DR
- Data were analyzed for time to the development of sustained blindness, and for baseline differences between patients who remained nonblind during the study period and those who developed sustained blindness
- Baseline factors and the occurrence of ocular conditions during follow-up were also assessed for their impact on the risk of developing sustained blindness

Limitations

- Electronic health records are not collected for research purposes, and are subject to data entry and coding errors
- Fundus photos were not available to verify patients' DR severity status
- VA was assessed using Snellen VA, and may not represent the patients' best-corrected VA
- Study did not control for severity of patients' underlying diabetes

DR, diabetic retinopathy; VA, visual acuity.

Causes of Sustained Blindness: Analysis Population and Analytic Cohorts



[a] 53,262 total patients. Analysis population only included eyes that met both inclusion and exclusion criteria and fell into 1 of the 2 cohorts. Only 1 eye per patient was included in each cohort, but 273 patients had 2 eyes included in study with 1 eye in each cohort (sustained blindness/nonblind). [b] 31 patients had DR on the same date in both eyes and met all criteria for the development of sustained blindness in both eyes; for these patients, 1 eye was chosen randomly based on whichever was present first in the dataset. [c] 50,648 of 52,857 (95.8%) patients in the nonblind cohort met criteria for good vision throughout follow-up (≥ 2 VA readings of ≤ 20/40 ≤ 3 months from index, never any VA readings of 20/60 or worse at 2 visits ≥ 3 months apart). AAO, American Academy of Ophthalmology; AMD, age-related macular degeneration; DME, diabetic macular edema; DR, diabetic retinopathy; GA, geographic atrophy; mCNV, myopic choroidal neovascularization; NVG, neovascular glaucoma; PRP, panretinal photocoagulation; RD, retinal detachment; RDR, retinal detachment repair; RVO, retinal vein occlusion; VA, visual acuity; VEGF, vascular endothelial growth factor; VH, vitreous hemorrhage.

Causes of Sustained Blindness: Analysis Plan

Analysis plan		Key clinical questions	Analysis details
1 Development of sustained blindness	Starting population new DR good vision → Sustained blindness	• How many eyes with newly diagnosed DR and good vision developed sustained blindness?	• Survival analysis for the probability of developing sustained blindness
2 Risk factor assessment			
Baseline factors associated with blindness	Sustained blindness vs Nonblind	• How much did baseline DR severity affect the probability of remaining nonblind? • What were the baseline demographic and clinical characteristics associated with an increased or decreased risk for development of sustained blindness?	• Survival analysis for the probability of developing sustained blindness stratified by DR severity at index date • Quantification of the impact baseline covariates had on the risk of developing sustained blindness (HR)
Ocular diseases in follow-up associated with blindness	Sustained blindness vs Nonblind	• By how much did development of other ocular conditions associated with vision loss during follow-up increase risk for the development of sustained blindness?	• Quantification of the increased in risk of blindness (HR) with the occurrence during follow-up of – Progression to a more severe DR stage (severe: NPDR or PDR) – Development of a DR-related event (DME, VH, RD) – Development of other retinal diseases (AMD, RVO) – Development of nonretinal diseases (cataracts, glaucoma, NVG)

AMD, age-related macular degeneration; DME, diabetic macular edema; DR, diabetic retinopathy; HR, hazard ratio; NPDR, nonproliferative diabetic retinopathy; NVG, neovascular glaucoma; PDR, proliferative diabetic retinopathy; RD, retinal detachment; RVO, retinal vein occlusion; VH, vitreous hemorrhage.

Select Baseline Characteristics for Full Cohort of Eyes With Newly Diagnosed DR and Good Vision at Baseline

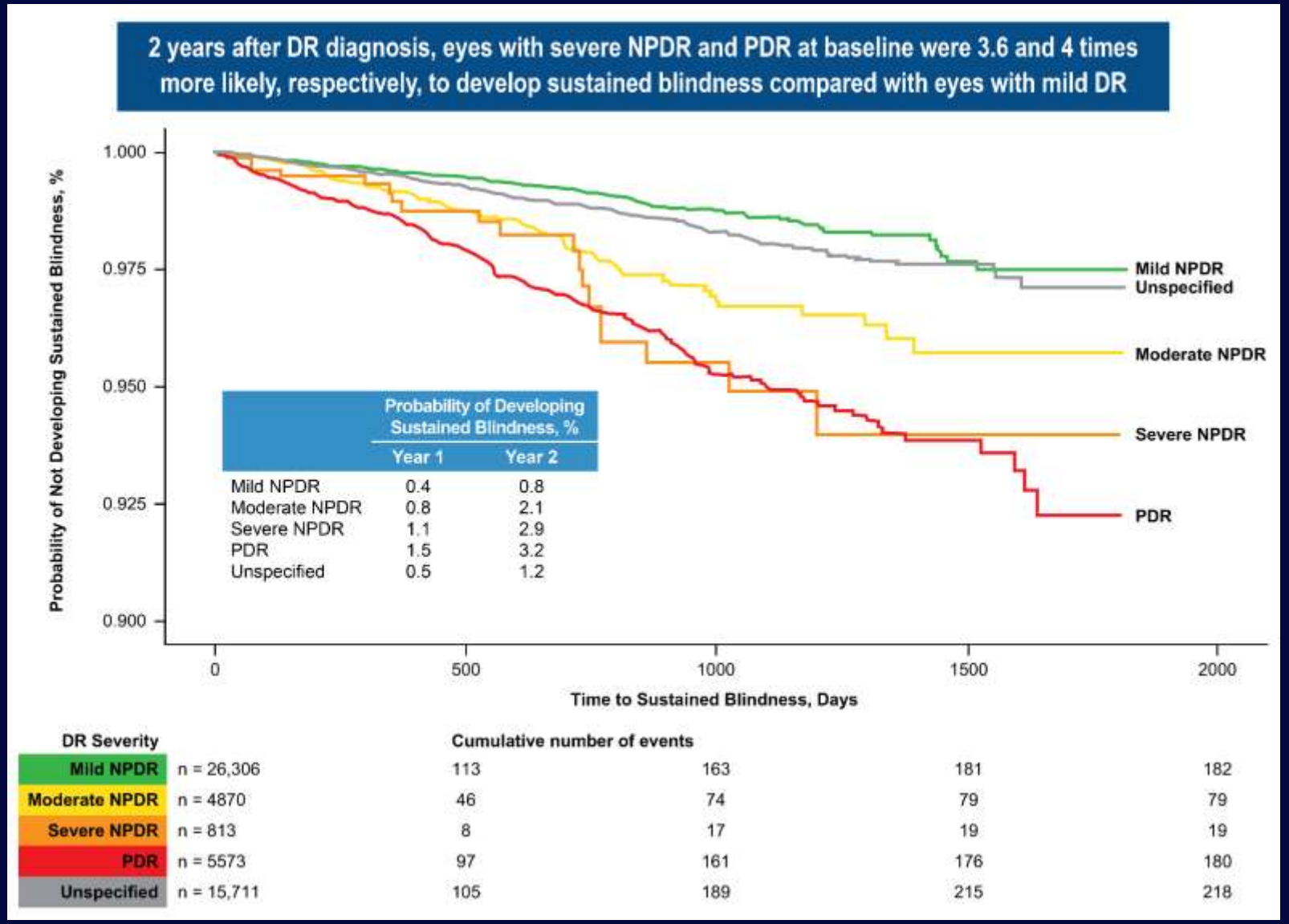
Demographic Characteristics	
Mean age, years (SD)	67.6 (11.2)
Female, n (%)	28,534 (53.6)
Race, n (%)	
White	36,681 (68.9)
Black	8357 (15.7)
Asian	1522 (2.9)
Native Hawaiian	250 (0.5)
American Indian	121 (0.2)
Unknown/multiracial	6331 (11.9)

Clinical Characteristics	
Visual acuity, mean (SD)[a,b]	
Corrected VA, LogMAR	0.14 (0.12)
DR severity, n (%)	
Mild NPDR	26,306 (49.4)
Moderate NPDR	4870 (9.1)
Severe NPDR	813 (1.5)
PDR	5573 (10.5)
Unspecified DR	15,711 (29.5)
Ocular conditions, n (%)	
Cataract	29,095 (54.6)
Glaucoma	1201 (2.3)

Outcomes were assessed for 53,535 eyes with newly diagnosed DR and good vision at baseline[c]

[a] Closest VA reading to index within 3 months pre index, or closest within 3 months post index if no VA readings on or before index date. [b] LogMAR 0 = 20/20; LogMAR 0.1 = 20/25. [c] 53,262 total patients; 273 patients had 2 eyes included in study, 1 eye in each cohort. DR, diabetic retinopathy; LogMAR, logarithm of the minimum angle of resolution; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; VA, visual acuity.

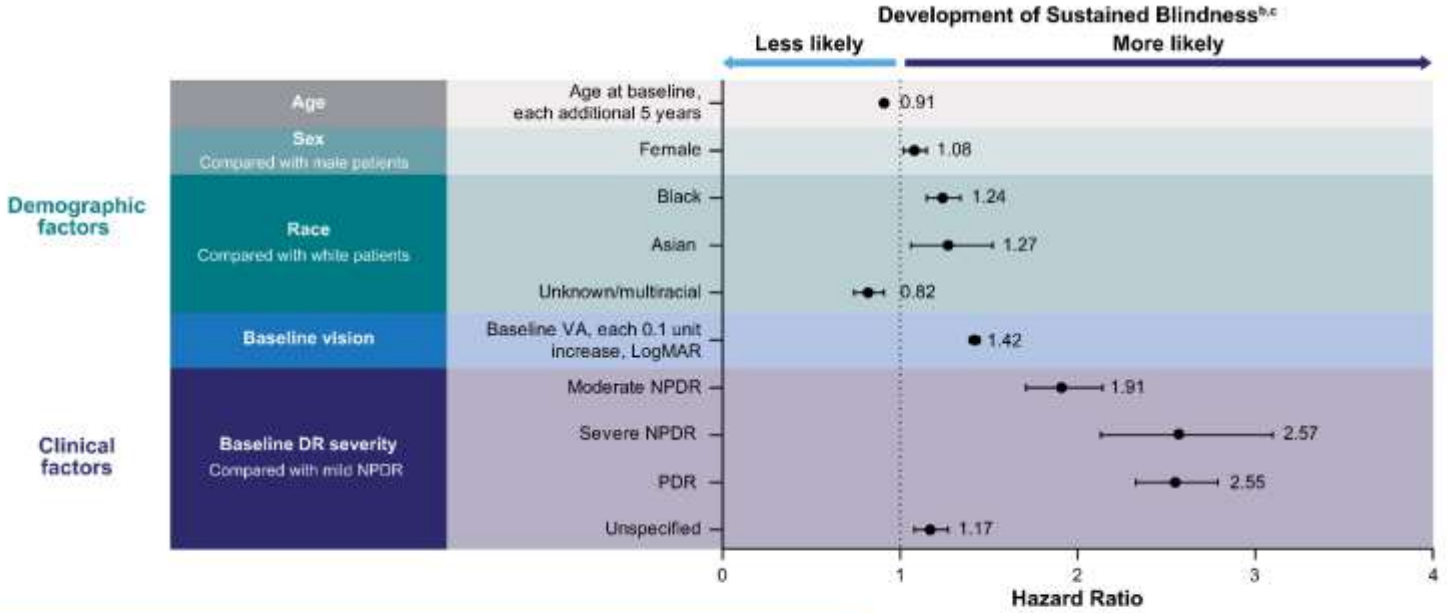
Probability of Not Developing Sustained Blindness by Baseline DR Severity



Log-rank *P* < 0.0001. DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

Assessment of Key Baseline Characteristics Associated With an Increased Risk of Developing Sustained Blindness[a]

Demographic Characteristics	Nonblind n = 52,857	Sustained Blindness n = 678
Mean age, years (SD)	67.6	65.0
Female, n (%)	28,302 (53.5)	385 (56.8)
Race, n (%)		
White	36,417 (68.9)	441 (65.0)
Black	8276 (15.7)	140 (20.7)
Asian	1511 (2.9)	21 (3.1)
Native Hawaiian	248 (0.5)	4 (0.6)
American Indian	119 (0.2)	3 (0.4)
Unknown/multiracial	6286 (11.9)	69 (10.2)
Clinical Characteristics		
VA, mean (SD)		
Corrected VA, LogMAR	0.14 (0.12)	0.21 (0.14)
DR severity level, n (%)		
Mild NPDR	26,205 (49.6)	182 (26.8)
Moderate NPDR	4822 (9.1)	79 (11.7)
Severe NPDR	802 (1.5)	19 (2.8)
PDR	5449 (10.3)	180 (26.6)
Unspecified DR	15,579 (29.5)	218 (32.2)



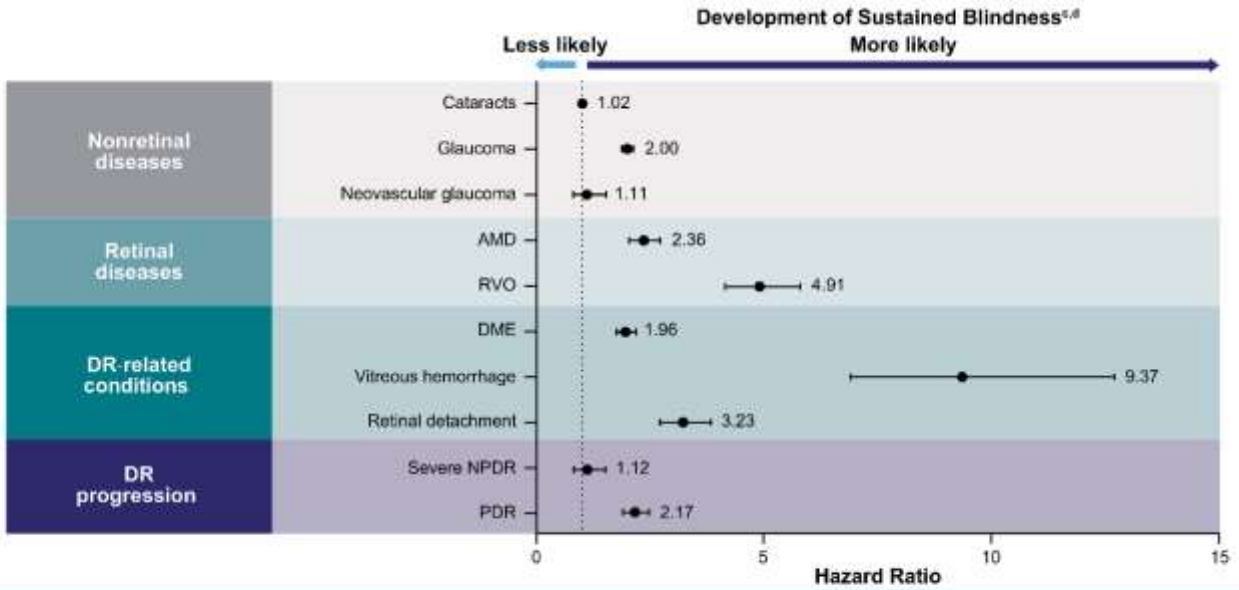
- More severe DR stage at baseline increased risk of developing sustained blindness
- Black and Asian race also increased risk of developing sustained blindness

[a] Data for key variables of interest are reported. The following additional baseline variables were assessed: insurance type, provider monitoring DR, provider practice size, urban or nonurban practice setting, diabetes mellitus type, presence of cataract, presence of glaucoma, insulin treatment status, and smoking history. [b] Multivariable Cox proportional hazards model using quarterly assessments (discrete interval approach) was used to estimate adjusted hazard ratios (95% CIs) for developing of sustained blindness. Model adjusted for additional factors, including diabetes mellitus type, smoking status, insurance type, and provider characteristics (practice size, type, and urban vs nonurban). [c] $P < 0.0001$ for age, black race, moderate NPDR, severe NPDR, and PDR comparisons; $P < 0.02$ for female, Asian race, unknown/multiracial, and unspecified DR severity comparisons. DR, diabetic retinopathy; LogMAR, logarithm of the minimum angle of resolution; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; VA, visual acuity.

Assessment of Key Ocular Conditions During Follow-up Associated With an Increased Risk of Developing Sustained Blindness[a]

Ocular Conditions Occurring During Follow-up	Nonblind n = 52,857	Sustained Blindness n = 678
Mean follow-up time, days	664.5	510.3
Nonretinal diseases, n (%)		
Cataracts	32,580 (61.6)	446 (65.8)
Glaucoma	18,657 (35.3)	303 (44.7)
Neovascular glaucoma	240 (0.5)	19 (2.8)
Retinal diseases, n (%)		
AMD	2161 (4.1)	46 (6.8)
RVO	551 (1.0)	61 (9.0)
DR-related conditions, n (%)		
DME	5915 (11.2)	149 (22.0)
Vitreous hemorrhage	182 (0.3)	43 (6.3)
Retinal detachment	521 (1.0)	52 (7.7)
DR status during follow-up, n (%)		
New severe NPDR[b]	584 (1.1)	22 (4.6)
New PDR[b]	1173 (2.5)	122 (25.5)

Mean follow-up time for all eyes: 662.5 days



Most frequently developed retinal conditions included DME and AMD

Patients who developed ocular conditions during follow-up, particularly glaucoma, AMD, RVO, DME, vitreous hemorrhage, retinal detachment, and progression to PDR, had an increased risk of developing sustained blindness

[a] Data for key variables of interest are reported. Fellow eye DR severity was also assessed. [b] Results for eyes that did not have specified condition at baseline. [c] Multivariable Cox proportional hazards model using quarterly assessments (discrete interval approach) was used to estimate adjusted hazard ratios (95% CIs) for developing of sustained blindness. Model adjusted for additional factors, including diabetes mellitus type, smoking status, insurance type, and provider characteristics (practice size, type, and urban vs nonurban). [d] $P < 0.0001$ for glaucoma, AMD, RVO, DME, vitreous hemorrhage, retinal detachment, and PDR; $P \geq 0.5$ for cataracts, neovascular glaucoma, and severe NPDR. AMD, age-related macular degeneration; DME, diabetic macular edema; DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; RVO, retinal vein occlusion.

Conclusions

- 2 years after DR diagnosis, eyes with severe NPDR and PDR at baseline were 3.6 and 4 times more likely, respectively, to develop sustained blindness compared with eyes with mild DR
- Risk factor assessment for baseline characteristics:
  - More severe DR stage at baseline increased risk of developing sustained blindness
  - Black and Asian race also increased risk of developing sustained blindness
- Risk factor assessment for ocular disease during follow-up:
  - Development of glaucoma, AMD, RVO, DME, VH, RD, and progression to PDR increased risk of developing sustained blindness
- These data highlight the need for closer monitoring or earlier intervention in these patients at higher risk for developing blindness

AMD, age-related macular degeneration; DME, diabetic macular edema; DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; RD, retinal detachment; RVO, retinal vein occlusion; VH, vitreous hemorrhage.