Risk of Blindness Among Patients With Diabetes and Newly Diagnosed Diabetic Retinopathy

Charles C. Wykoff,[1] Rahul N. Khurana,[2] Quan Dong Nguyen,[3] Scott P. Kelly,[4] Flora Lum,[4] Rebecca Hall,[4] Ibrahim M. Abbass,[5] Anna M. Abolian,[5] Ivaylo Stoilov,[5] Tu My To,[5] and Vincent Garmo[5]

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EPIDEMIOLOGY/HEALTH SERVICES RESEARCH

OBJECTIVE

To evaluate the association between initial diabetic retinopathy (DR) severity/risk of blindness in patients with newly diagnosed DR/good vision in the U.S.

RESEARCH DESIGN AND METHODS

This retrospective cohort study evaluated adult patients with good vision (20/40 or better) and newly diagnosed DR between 1 January 2013 and 31 December 2017 (index date) in the American Academy of Ophthalmology's Intelligent Research in Sight (IRIS) Registry. The primary exposure of interest was DR severity at index: mild nonproliferative DR (NPDR), moderate NPDR, severe NPDR, and proliferative DR (PDR). The main outcome measure was development of sustained blindness (SB), defined as study eyes with Snellen visual acuity readings of 20/200 or worse at two separate visits ≥3 months apart that did not improve beyond 20/100.

RESULTS

Among 53,535 eligible eyes (mean follow-up 662.5 days), 678 (1.3%) eyes developed SB. Eyes with PDR at index represented 10.5% (5,629 of 53,535) of the analysis population but made up 26.5% (180 of 678) of eyes that developed SB. Kaplan-Meier analysis revealed that eyes with moderate NPDR, severe NPDR, and PDR at index were 2.6, 3.6, and 4.0 times more likely, respectively, to develop SB after 2 years of DR diagnosis versus eyes with mild DR at index. In a Cox proportional hazards model adjusted for index characteristics/development of ocular conditions during follow-up, eyes with PDR had an increased risk of developing SB versus eyes with mild NPDR at index (hazard ratio 2.26 [95% CI 2.09−2.45]).

CONCLUSIONS

In this longitudinal ophthalmologic registry population involving eyes with good vision, more advanced DR at first diagnosis was a significant risk factor for developing SB.

Diabetes is an ongoing and growing public health issue (1), and blindness that is due to diabetic retinopathy (DR) remains a leading cause of adult-onset blindness (2–4). More severe DR is associated with deterioration of retinal vascular homeostasis, with the potential for vitreous hemorrhage, tractional retinal detachment, and subsequent vision loss and reduced vison-related quality of life (5–8). Approaches to reduce the incidence and burden of DR-related blindness vary, ranging from the prevention and management of the underlying disease to ocular therapies to treat active and progressing DR (9).

In clinical practice, ophthalmologists are often presented with an incomplete picture: a patient with newly diagnosed DR but limited information on diabetes history

[1]Retina Consultants of Texas, Blanton Eye Institute, Houston Methodist Hospital and Weill Cornell Medical College, Houston, TX
[2]Northern California Retina Vitreous Associates, Mountain View, CA
[3]Byers Eye Institute, Stanford University School of Medicine, Palo Alto, CA
[4]American Academy of Ophthalmology, San Francisco, CA
[5]Genentech, Inc., South San Francisco, CA

Corresponding author: Charles C. Wykoff, charleswykoff@gmail.com

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or management. The question then becomes how to best assess and manage the risk of developing DR-related blindness in the newly diagnosed patient with the limited information available. As such, the objective of the current study was to examine whether a common assessment performed by an ocular specialist, the severity of DR at first diagnosis, could provide relevant insights into the risk of developing sustained blindness (SB) in a real-world setting.

As the largest ophthalmology-focused registry in the world (10), the American Academy of Ophthalmology's Intelligent Research in Sight (IRIS) Registry (https://www.aao.org/iris-registry/about) is uniquely poised to meaningfully investigate DR-associated blindness in patients in the U.S. (11). With information collected from the electronic health records (EHRs) of ~66% of all practicing U.S. ophthalmologists and data captured from ~250 million visits from 60 million unique patients, the IRIS Registry enables empirical, practice-oriented examination of practice patterns, treatment pathways, and patient outcomes. Since its creation in 2014, the IRIS Registry has contributed important insights into age-related macular degeneration, myopic choroidal neovascularization, and cataract surgery (8,12,13). Accordingly, the current retrospective cohort analysis using data from the IRIS Registry investigated the impact of DR severity at initial diagnosis on the probability of developing blindness and time to development of blindness in patients with newly diagnosed DR and good vision.

RESEARCH DESIGN AND METHODS

Study Design

This retrospective cohort analysis used data from the comprehensive national IRIS Registry that collects key information on the diagnosis, treatment, and outcomes of patients with eye disease from EHRs of participating ophthalmology practices. The IRIS Registry database consists of deidentified data; data collection methods have been described previously (11). As of 31 December 2017, the IRIS Registry included data from 46,645,106 patients from 12,275 ophthalmologists and other eligible clinicians from 2,673 practices. Institutional review board approval and written informed consent were not required for this analysis.

Study Population

The analysis population consisted of patients aged ≥18 years with good vision and newly diagnosed DR between 1 January 2013 and 31 December 2017.

Newly Diagnosed DR

Patients with newly diagnosed DR were identified using ICD-9 (1979–1998) and ICD-10 (1999–present) Clinical Modification (CM) codes (14,15). See Supplementary Table 1 for the full list of eligible diagnostic codes. To ensure that all DR cases were newly diagnosed, all patients were required to have ≥18 months of data in the IRIS Registry before onset of the incident DR diagnosis (preindex period) with no DR-related claims/visits. Only one eye per patient was included in the final analytic cohort (the eye that was first diagnosed with DR was chosen; if DR was diagnosed in both eyes on the same day, the study eye was randomly chosen).

Good Vision

Good vision was defined as patients having at least two visual acuity (VA) readings of 20/40 or better in the study eye before or up to 3 months after their incident DR diagnosis. VA readings recorded were based on Snellen VA (see Supplementary Appendix 1 for additional information).

Exclusion Criteria

Patients were excluded if they had any claims during the preindex period related to any of the prespecified retinal diseases (see Supplementary Appendix 1). All exclusion diagnostic (ICD-CM) codes and surgical procedure (Current Procedural Terminology) codes are provided in Supplementary Tables 1 and 2.

Exposure of Interest: DR Severity at Index

Eyes were classified on the basis of ICD-CM diagnosis codes for DR severity at index: *1*) mild nonproliferative DR (NPDR), *2*) moderate NPDR, *3*) severe NPDR, *4*) proliferative DR (PDR), or *5*) unspecified DR (see Supplementary Table 1 for additional details). If multiple DR records were present, the record with DR severity status specified closest to the incident DR index date was chosen. Patients with an unspecified DR severity status at index were assigned to a specific DR diagnosis if provided within 3 months of follow-up; otherwise, they remained classified as unspecified DR severity at index.

Event of Interest: SB

The primary event of interest, SB, was defined as patients with Snellen VA–corrected readings of 20/200 or worse at two separate visits ≥3 months apart in the study eye and who did not improve beyond 20/100 since the first reading of 20/200. Patients with only one VA reading of 20/200 or worse were excluded from the analytic cohort. The date of the first VA reading of 20/200 or worse was defined as the date of the event of interest (SB). All other patients in the analytic cohort were classified as nonblind, and their last date of follow-up in the study was defined as the date of their last Snellen VA reading.

Covariates

We examined whether demographic and clinical characteristics were associated with risk of developing SB. Among characteristics examined on or before index, we included demographic information on age, health plan insurance type, race, sex, smoking status, and practice size and setting; for clinical data, we included the VA measurement closest to index. Among time-varying clinical characteristics evaluated during follow-up (yes or no), we examined DR disease progression to PDR (among patients with DR severity status other than PDR at index); DR disease progression to severe NPDR (among patients with DR severity status other than severe NPDR or PDR at index, until PDR is reached); fellow eye DR status (ever diagnosed with DR, severe NPDR, or PDR); treatment with an insulin medication; and development of nonretinal diseases (cataracts, glaucoma, neovascular glaucoma), retinal diseases (age-related macular degeneration, retinal vein occlusion), and DR-related conditions (diabetic macular edema [DME], vitreous hemorrhage, retinal detachment). All covariates were selected a priori. Assessment of treatments for diabetes, DR, DME, and other ocular conditions and their potential impact on development of SB were beyond the scope of the analysis.

Statistical Analysis

Eyes were grouped according to whether they experienced the primary event of interest (development of SB). Frequencies,

means, and SDs were used to summarize variables of interest for both groups. Bivariate analyses (e.g., χ^2 test, Student *t* test) were used to examine the association between patients' covariates and SB. Because of the large sample size in this study, we considered the effect size (measured through the standardized difference) in addition to *P* values to examine differences across the groups. For characteristics with an effect size of <10% (i.e., standardized difference of 0.1), differences between groups were considered to be negligible (16,17).

To evaluate the association between DR severity status at index and time to SB, patients were stratified according to DR severity at index, and a Kaplan-Meier survival curve was used to examine survival probability (i.e., probability of not developing SB). The probability of developing SB is 1 minus the probability of not developing SB. A discrete-time interval Cox proportional hazards regression model (18,19) with time-invariant and time-varying covariates was used to calculate adjusted hazard ratios (HRs) to assess the impact of DR severity at index on development of SB. Two models were developed that adjusted for *1*) index characteristics only and *2*) index characteristics as well as ocular conditions that developed during follow-up. Patients were followed from index date (DR diagnosis) until the date of the event (SB, date of first blind VA reading 20/200 or worse) or the date of the last VA reading (censoring event). A discrete-time interval approach allowed for a line of data for each discrete 3-month interval a patient contributed over the course of follow-up. Time-varying covariates were carried forward once the diagnosis code was identified during the follow-up period.

The models were examined for convergence, and the proportional hazards assumption was tested using likelihood ratio testing by comparing models with and without a log(time)-interaction term and visual inspection of log(−log) survival plots. No violations were detected. All analyses were performed using SAS 9.4 statistical software (SAS Institute Inc., Cary, NC).

RESULTS

Study Population

In total, 53,535 eyes from adult patients in the IRIS Registry had good vision (20/40 or better) and newly diagnosed (incident) DR between 1 January 2013 and 31 December 2017 and met the eligibility criteria for inclusion (Fig. 1). Because DR severity at index was the key exposure of interest, patients with other potentially vision-threatening retinal diseases at index, including DME, were excluded from the analysis population to avoid confounding the results. Sociodemographic and clinical characteristics at index are presented in Table 1. The majority of patients were female (28,687; 53.6%) and White (36,858; 68.8%) and had Medicare insurance at index (32,178; 60.1%). The mean (SD) age was 67.6 (11.2) years at index, with the highest percentages of eyes from patients in the age ranges of 60–69 years (16,871; 31.5%) and 70–79 years (17,968; 33.6%). At index, the majority of eyes had mild NPDR (26,387; 49.3%) or unspecified DR (15,797; 29.5%).

A total of 678 (1.3%) eyes developed SB during a mean (SD) follow-up time of 662.5 (421.7) days (Table 1). The most common ocular conditions that developed during follow-up were cataracts (33,026; 61.7%), glaucoma (18,960; 35.4%), and DME (6,064; 11.3%). The characteristics with the largest standardized difference between eyes that developed SB and those that did not were VA and DR severity at index and development of new PDR during follow-up. Eyes with worse vision at index (20/40) made up 39.5% (268 of 678) of eyes that developed SB, despite being 18.0% (9,659 of 53,535) of the overall analysis population. Similarly, eyes with PDR at index made up 26.5% (180 of 678) of eyes that developed SB, while being just 10.5% (5,629 of 53,535) of the overall analysis population. Of eyes that did not have PDR at index, a substantially greater proportion that developed SB developed PDR during follow-up compared with eyes that did not (24.5% vs. 2.5%, respectively; standard difference 0.61). Among nonblind eyes, 98.5% (52,064 of 52,857) met the criteria for good vision throughout follow-up.

Probability of Development of SB by DR Status at Index

The probability of developing SB increased with increased DR severity at index at both year 1 and year 2 (Fig. 2). The relative likelihood for developing SB was assessed by comparing the probability of developing SB in each DR severity group with mild NPDR at index. One year after DR diagnosis, eyes with moderate NPDR, severe NPDR, and PDR at index were 2.0, 2.7, and 3.8 times more likely, respectively, to develop SB than eyes with mild NPDR at index. Two years after DR diagnosis, eyes with moderate NPDR, severe NPDR, and PDR at index were 2.6, 3.6, and 4.0 times more likely, respectively, to develop SB compared with eyes with mild NPDR at index. Overall, eyes with unspecified DR at index showed similar results as eyes with mild NPDR at index and had a lower probability of developing SB throughout the study period than eyes with moderate or severe NPDR or PDR at index.

Associations Among DR Severity at Index, Covariates, and Development of SB

The association between DR severity and SB was assessed using two models of covariate adjustment (Fig. 3 and Supplementary Table 3). Model 1 adjusted for index characteristics without consideration for events occurring after index (Fig. 3, gray symbols and text). In model 1, eyes with more advanced DR at index had an increased risk of developing SB compared with eyes with mild NPDR at index. The highest risk for the development of SB was in eyes with severe NPDR at index (HR 2.64 [95% CI 2.26–3.09]; $P < 0.0001$) and PDR at index (2.43 [2.26–2.63]; $P < 0.0001$) compared with mild NPDR at index. Eyes with unspecified DR at index had an increased risk of developing SB compared with eyes with mild NPDR at index, although the HR was close to 1.0 (1.19 [1.11–1.27]; $P < 0.0001$). Other index characteristics associated with increased risk of SB in model 1 included worse vision at index as well as sex, race, and smoking status. Age >50 years and insurance other than private insurance were associated with a decreased risk for developing SB.

Because other ocular diseases developed during follow-up could have contributed to the development of blindness, model 2 explored the effect of DR severity characteristics in the presence of the most common of these ocular conditions, adjusting for covariates included in model 1 (Fig. 3, black symbols and text). As an important cause of vision loss in patients with diabetes, newly developed DME was included as one of the DR-related conditions developed during follow-up. Index characteristic HRs were

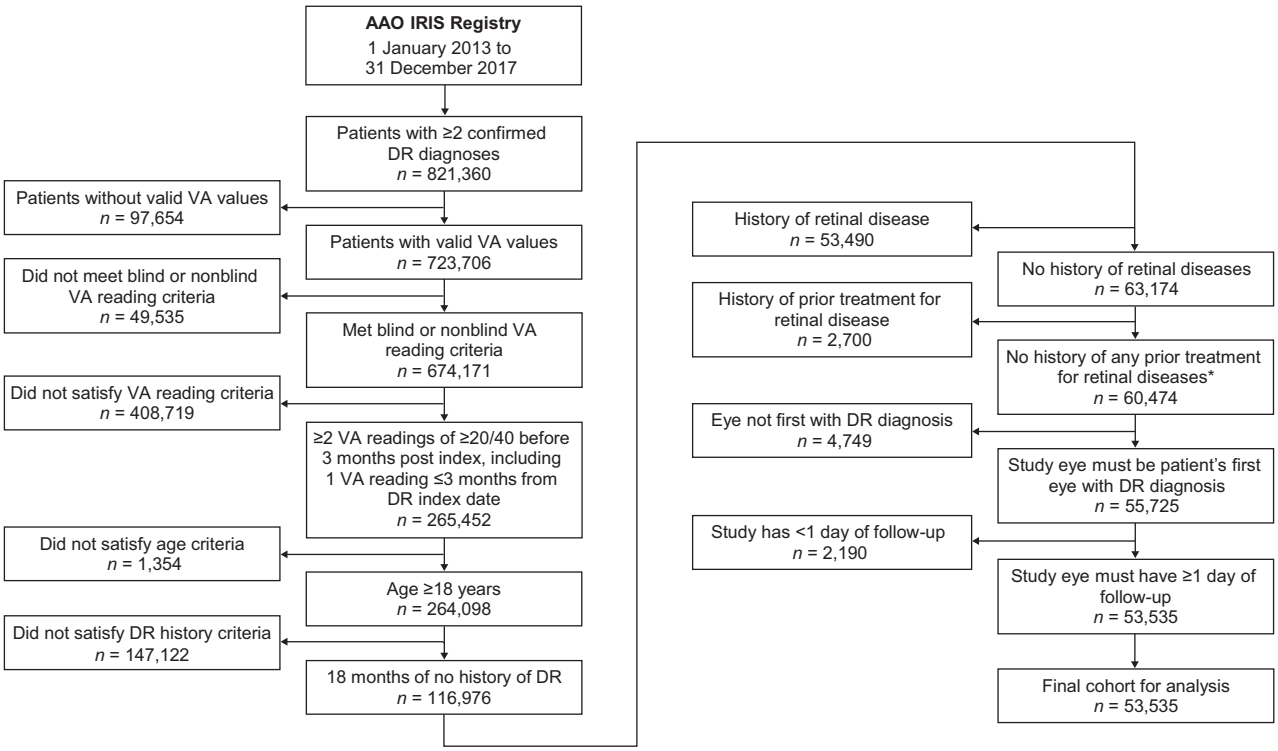

Figure 1—Patient attrition chart for the selection of IRIS Registry patients with newly diagnosed DR with good vision. *Retinal disease defined as wet or dry age-related macular degeneration, geographic atrophy, vitreous hemorrhage, retinal detachment, neovascular glaucoma, retinal vein occlusion, or DME. AAO, American Academy of Ophthalmology.

slightly attenuated overall when ocular conditions during follow-up were also considered. Nevertheless, overall results were generally comparable with model 1, with increased DR severity at index having an increased risk for development of SB compared with mild NPDR at index (PDR vs. mild NPDR at index: HR 2.26 [95% CI 2.09–2.45]; $P < 0.0001$). For the follow-up variables added in model 2, development of all conditions except neovascular glaucoma and new severe NPDR were associated with an increased risk of SB (Fig. 3 and Supplementary Table 3). Fellow eye DR status had a minimal impact on risk of SB. To account for any clustering of physicians, an additional multivariable Cox survival model that included a random effect for National Provider Identifier was performed to obtain the residual intraclass correlation. Because the residual intraclass correlation showed minimal variation with regard to the National Provider Identifier, interphysician variance did not affect the results, and no adjustments to the models were implemented.

CONCLUSIONS

Using the world's largest ophthalmology registry, the current study investigated risk factors of SB in >53,000 patients with newly diagnosed DR and good vision, focusing on DR severity at index as the key exposure of interest. Notably, 678 eyes developed SB over an average follow-up time of 510.3 days (~1.4 years) from initial DR diagnosis, despite the availability of effective treatment options (20,21). Eyes with severe NPDR and PDR at the time of DR diagnosis were at a markedly greater risk of developing SB compared with eyes with mild or moderate NPDR at DR diagnosis; furthermore, this remained the case when controlling for demographics and clinical characteristics at index and during follow-up. In addition, the overall size and scope of the data set from the IRIS Registry lend validation to our finding that DR severity at the time of diagnosis is a critical, and potentially modifiable, risk factor for development of SB in patients with diabetes.

The global increase in DR-related vision impairment and blindness (22) underscores the importance of actively addressing vision loss in patients with diabetes. Multiple strategies exist to reduce DR-related blindness, varying from prevention to early detection to active treatment. Efforts to prevent DR development are generally focused on diabetes and hypertension management because poor glycemic control and elevated blood pressure have consistently been shown to exacerbate DR development and progression (9). Early detection and management of DR are also widely recognized as being key to reducing diabetes-associated vision loss (21,23). For example, blindness from DR was reduced significantly in Iceland, England, and Wales after introduction of and widespread adherence to national screening programs focused on identifying vision-threatening DR (24–27).

In this analysis, 6,450 eyes, or 12.0% of the analysis population, had severe NPDR or PDR at first DR diagnosis, highlighting gaps in the recommended DR screening process in the U.S. Consistent with our findings, recent retrospective U.S. health care claims analyses documented low rates of yearly eye examinations in patients with diabetes (28), with one-half of patients with type 2 diabetes and one-third of patients with type 1 diabetes having no eye examinations within a 5-year period in one analysis (29). Barriers to effective DR screening are

Table 1—Sociodemographic and clinical characteristics at index date and development of ocular conditions during follow-up

	Sustained blindness* (n = 678)		Nonblind (n = 52,857)			
Variable	n	%	n	%	P value	Standardized difference
Characteristics at index date						
Age (years)					<0.0001	0.29
<50	81	11.9	3,577	6.8		
50–59	127	18.7	7,585	14.4		
60–69	196	28.9	16,675	31.5		
70–79	188	27.7	17,780	33.6		
≥80	86	12.7	7,240	13.7		
Sex					0.0924	−0.06
Male	293	43.2	24,555	46.5		
Female	385	56.8	28,302	53.5		
Race					0.0042	0.11
White	441	65.0	36,417	68.9		
Black	140	20.6	8,276	15.7		
Asian	21	3.1	1,511	2.9		
Unknown/multinational/other	76	11.2	6,653	12.6		
Practice setting					0.0976	0.00
Urban	616	90.9	46,940	88.8		
Rural	62	9.1	5,917	11.2		
Practice size					0.4979	0.07
Small (<2,000 patients)	28	4.1	1,922	3.6		
Medium (2,000–2,999 patients)	32	4.7	2,965	5.6		
Large (≥3,000 patients)	618	91.2	47,970	90.8		
Insurance					0.0035	0.16
Private	227	33.5	15,088	28.5		
Medicare	361	53.2	31,817	60.2		
Medicaid	25	3.7	1,745	3.3		
Other/unknown/no insurance	65	9.6	4,207	8.0		
Smoking status					0.0656	0.02
Ever smoker	210	31.0	15,888	30.1		
VA					<0.0001	0.61
20/20 or better	79	11.7	10,881	20.6		
Worse than 20/20, better than 20/40	331	48.8	32,585	61.6		
20/40	268	39.5	9,391	17.8		
Conditions						
Cataracts†	379	55.9	28,872	54.6	0.5101	0.06
Glaucoma†	243	35.8	963	1.8	<0.0001	0.18
DR severity status					<0.0001	0.60
Unspecified DR	218	32.2	15,579	29.5		
Mild NPDR	182	26.8	26,205	49.6		
Moderate NPDR	79	11.7	4,822	9.1		
Severe NPDR	19	2.8	802	1.5		
PDR	180	26.5	5,449	10.3		
Medications					<0.0001	0.30
Insulin	332	49.0	18,115	34.3		
Ocular conditions developed during follow-up						
Study eye						
Cataracts‡	446	65.8	32,580	61.6	0.0375	0.06
Glaucoma‡	303	44.7	18,657	35.3	<0.0001	0.18
Neovascular glaucoma	19	2.8	240	0.5	0.3468	0.19
AMD	46	6.8	2,161	4.1	0.0024	0.12
RVO	61	9.0	551	1.0	<0.0001	0.33
DME	149	22.0	5,915	11.2	<0.0001	0.20
Vitreous hemorrhage	43	6.3	182	0.3	<0.0001	0.31
Retinal detachment	52	7.7	521	1.0	<0.0001	0.30
New severe NPDR§	22	4.6	584	1.1	0.0039	0.21
New PDR§	122	24.5	1,173	2.5	<0.0001	0.61

Continued on p. 753

Table 1—Continued

Variable	Sustained blindness* (n = 678) n	%	Nonblind (n = 52,857) n	%	P value	Standardized difference
Fellow eye						
DR	43	6.3	1,997	3.8	0.3468	0.26
PDR	20	2.9	348	0.7	<0.0001	0.07
Severe NPDR	3	0.4	85	0.2	<0.0001	0.16
Follow-up time (days), mean (SD)	510.3 (367.2)		664.5 (422)			

For time-dependent variables, eyes were included in the count if the event occurred at any time during the follow-up period, with the exception of cataracts and glaucoma, which may have developed during baseline. Sustained blindness defined as VA readings of 20/200 or worse at two visits at least 3 months apart, with no improvement beyond 20/100 after first VA reading of 20/200 or worse. Nonblind defined as at least two VA readings of ≤20/40 at least 3 months from index and at most one VA reading of up to 20/100 during follow-up. *Thirty-one patients had DR on the same date in both eyes and went blind in both eyes. One eye was chosen randomly on the basis of whichever was present first in the data set. †Includes eyes with ocular condition documented at index visit. As chronic conditions, the presence of cataract and glaucoma may not have been recorded at the index visit if previously diagnosed. ‡Includes eyes with ocular condition at index or any time during the follow-up period. §Results for eye that did not have specified condition at baseline. AMD, age-related macular degeneration; RVO, retinal vein occlusion.

numerous and include lack of awareness and education among patients and physicians, access to care, burden of concurrent management of comorbidities related to diabetes or other underlying conditions, and availability of diagnostic equipment and qualified personnel to interpret screening results (9). Multiple approaches are currently being investigated to address these obstacles, including telemedicine approaches with remote image analysis. In addition, recent technological advances in image analysis and artificial intelligence are also being applied to enable machine-based detection and diagnosis of DR (30–32). Understanding and addressing specific barriers to effective DR screening will be critical for reducing DR-associated blindness.

Once DR becomes advanced, active treatment becomes the best way to reduce DR-related blindness. Therapeutic options to prevent or reduce vision loss in patients with advanced DR include laser photocoagulation and intravitreal anti–vascular endothelial growth factor (VEGF) injection (20). Because increased vision loss is associated with increased DR severity (7), prevention of DR worsening may also represent an important strategy for reduction of DR-related blindness. In clinical trials, anti-VEGF therapy has been shown to prevent and reverse DR progression in patients with DR both with and without DME (33–37). Early treatment is also supported by findings that indicate that patients with moderately severe to severe NPDR experience the greatest improvements in DR severity after

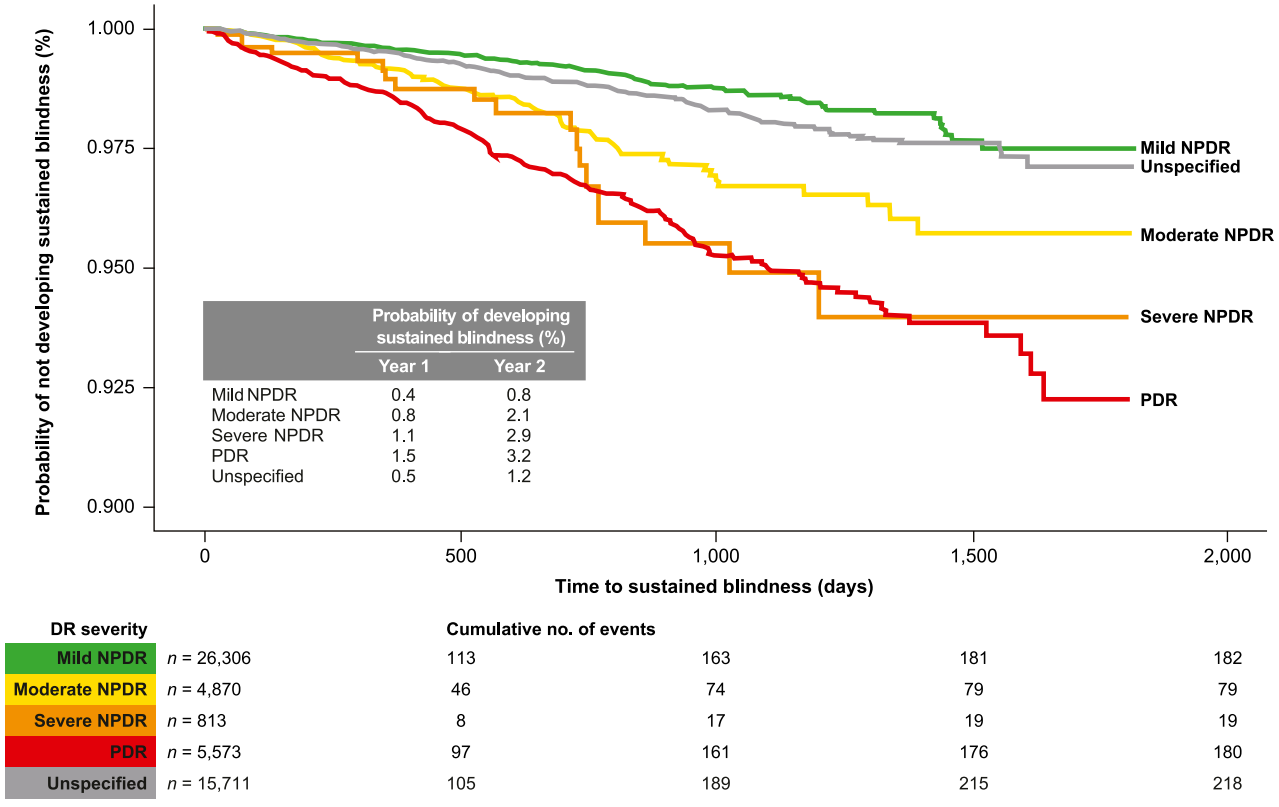

Figure 2—Kaplan-Meier survival analysis for the probability of not developing sustained blindness, assessed by DR severity at index. Log-rank $P < 0.0001$.

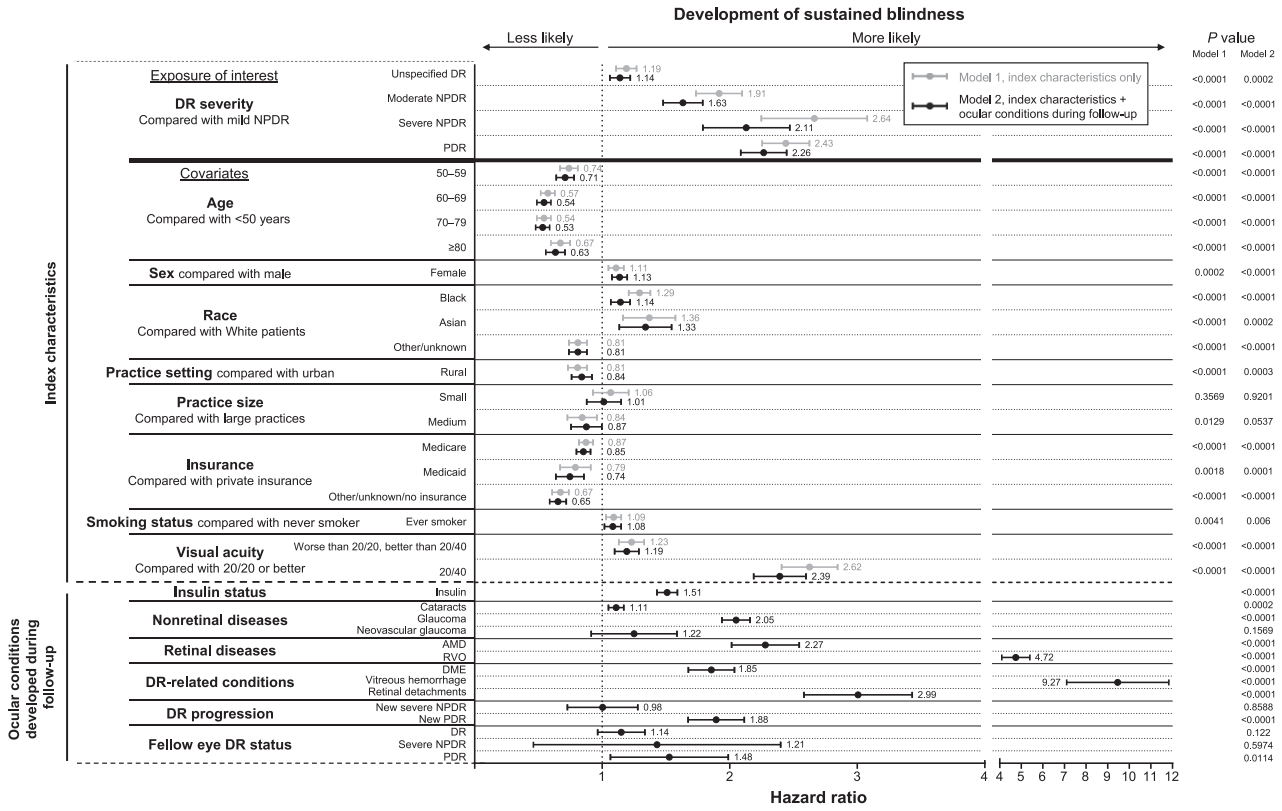

Figure 3—Risk factor assessment for sustained blindness, models 1 and 2. Adjusted HRs and 95% CIs assessing the impact of index characteristics and the development of ocular conditions during follow-up on development of sustained blindness. Values calculated using a discrete-time interval Cox proportional hazards regression model with time-invariant and time-varying covariates. Patients were followed from index date (DR diagnosis) until the date of the event (sustained blindness, date of first blind VA reading 20/200 or worse) or the date of the last VA reading (censoring event). Time-varying covariates were handled as carry-forward indicator variables (i.e., once patients became exposed, they were regarded as exposed from that point forward, regardless of actual exposure status at each quarterly assessment). AMD, age-related macular degeneration; RVO, retinal vein occlusion.

anti-VEGF treatment (37,38). When considering interventions and early treatment, retinopathy progression risk scores may also be useful to help identify patients at highest risk for vision loss (39).

Study limitations include both the retrospective nature of the analysis and the limitations associated with EHRs, which can be subject to data entry and coding errors. Specific EHR constraints relevant to this analysis were the ophthalmological focus of the registry, which did not consistently capture systemic parameters, such as glycated hemoglobin, that are standard for the assessment of diabetes management. The majority of common diabetes-associated systemic risk factors, such as elevated glycated hemoglobin, blood pressure, and lipid levels, are likely to have influenced the development of blindness through DR and DR progression and were thus accounted for, at least indirectly, in the current analysis. However, given the complexity of diabetes, there could have been systemic factors that acted independently of DR progression to influence the development of blindness. By acting outside of DR, the contribution of these factors would not have been captured as part of the current ophthalmology-focused analysis. The precise magnitude of factors acting outside of DR or DR progression in the current analysis could not be assessed. There was also a lack of fundus photographs available to confirm DR severity status, resulting in almost one-third of eyes not being assigned a specific DR severity category at index. Results for patients with unspecified DR severity at index were most similar to patients with mild NPDR at index in terms of both the probability of not developing SB (Fig. 2) and the risk of developing SB in both multivariable Cox models (Fig. 3). The similarity to patients with mild NPDR at index is consistent with patients with unspecified DR severity at index not having any features of more severe disease that would have resulted in classification of moderate or severe NPDR or PDR. Diabetes type at index was ultimately excluded from the predictive models because of the high number of patients whose diabetes type could not be classified as a result of missing data or conflicting diagnosis or treatment codes (type 1, type 2, and type unknown 77.5%, 9.2%, and 13.3%, respectively). Additional classification was attempted using a modified version of the Klompas algorithm (40), but the improvement in classification was minimal at best. Another potential limitation was that VA assessments were performed using Snellen approximation instead of the more precise Early Treatment Diabetic Retinopathy Study letter method used in clinical trials. In addition, the overall mean follow-up time for patients was ∼1.8 years. Given the chronic nature of diabetes and DR, these results may not be reflective of longer-term risk. Finally, this analysis did not account for any treatments for diabetes, DR, or other ocular conditions received during the follow-up period. The impact of treatment and its interaction with DR severity at index

in predicting development of blindness remains an important question to be explored in future analyses.

Among patients with diabetes and good vision (20/40 or better) in a real-world clinical setting, eyes with severe NPDR and PDR at the time of DR diagnosis were more than two times more likely to develop SB compared with eyes with mild NPDR at initial diagnosis. In addition, despite public health guidelines designed to increase eye screening in patients with diabetes, patients are still presenting with advanced DR. The current results support the continued need for improved DR screening, patient education, and care coordination to reduce the burden of diabetes-associated blindness in the U.S.

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Genentech, Inc. employees participated in the design and conduct of the study; analysis and interpretation of the data; preparation, review, and approval of the manuscript; and decision to submit the manuscript for publication.

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