Article

Rates and Predictors of Nonadherence to Postophthalmic Screening Tertiary Referrals in Patients with Type 2 Diabetes

Josh Tjunrong Sia[1], Alfred Tau Liang Gan[2], BaoLin Pauline Soh[2], Eva Fenwick[2,3], Joanne Quah[4,5], Thakur Sahil[2], Yijin Tao[2,6], Ngiap Chuan Tan[4,5], Charumathi Sabanayagam[2,3], Ecosse L. Lamoureux[2,3,7], and Ryan Eyn Kidd Man[2,3]

[1] Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[2] Singapore Eye Research Institute and Singapore National Eye Centre, Singapore
[3] Duke National University of Singapore Medical School, Singapore
[4] SingHealth Polyclinics, Singapore
[5] SingHealth Duke National University of Singapore, Family Medicine Academic Clinical Program, Singapore
[6] Department of Ophthalmology, First Affiliated Hospital of Kunming Medical University, Kunming, Yunnan, China
[7] Department of Ophthalmology, National University of Singapore, Singapore

Purpose: To determine the rates and develop an initial risk prediction model for nonadherence to post screening ophthalmic referral (PSOR) in type 2 diabetes mellitus (T2DM) patients attending a national diabetic retinopathy screening program in Singapore.

Methods: Data from 2387 patients with T2DM (mean [standard deviation] age: 66.5 [11] years; 52.5% female patients) who underwent teleophthalmic screening between 2010 and 2014 under the Singapore Integrated Diabetic Retinopathy Program were extracted from electronic medical records. All were referred for tertiary ophthalmic management at the Singapore National Eye Centre (SNEC). Nonadherence was defined as not attending the SNEC appointment within 6 months of the assigned appointment date. Regression analysis using traditional modified Poisson and conditional inference models was used to construct and evaluate the discriminative ability of the preliminary risk prediction model to identify nonadherent individuals.

Results: Nonadherence rates to PSOR was 12.7% (95% confidence interval, 11.4%–14.1%). In traditional multivariable models adjusted for sociodemographic, lifestyle, and ocular factors, nonadherent individuals had higher triglyceride levels and were less likely to have a referable eye condition ($P < 0.05$). This model was able to identify nonadherent individuals with an accuracy (area under the curve) of 84%. In contrast, the conditional inference model was able to achieve similar discriminative ability using only participants' ocular health characteristics.

Conclusions: The rates of nonadherence to PSOR in Singaporean individuals with T2DM is low, with better ocular health being strongly predictive of nonadherence in our Asian population.

Translational Relevance: Our results may inform interventions to decrease nonadherence to PSOR.

Introduction

Singapore has the second highest rate of diabetes mellitus (DM) in developed nations, with a national prevalence of 13.7%.[1] DM can have severe consequences on vision and quality of life if left uncontrolled.[2,3] Apart from diabetic retinopathy (DR), which is the most common visual complication of DM and the leading cause of vision impairment and

1

blindness among working adults globally,[1,4] DM is also a risk factor for other causes of vision loss, such as glaucoma, age-related macular degeneration (AMD), and cataracts.[2,5]

Early detection and intervention can, however, reduce the impact of diabetic eye diseases. Although studies have demonstrated that a 47% decrease in the average annual incidence of diabetes-related blindness over 5 years is possible with the implementation of eye screening services, these efforts have been hampered by the high rates of nonadherence to post screening ophthalmic referral (PSOR), ranging from 30% to 79%, in Western populations.[6–9] Several factors have been associated with nonadherence to PSOR, including low DM health literacy, lack of knowledge and awareness of eye disease, male sex, older age, depression, less severe eye disease, long commute distance to screening centers, low socioeconomic status, lack of time and shorter duration of diabetes.[6–8,10–13] However, there is scant information on both the rates of nonadherence to PSOR, as well as its associated determinants in Asia, which makes it challenging for health care practitioners to implement appropriate interventions to reduce nonadherence and improve the efficacy of diabetic eye screening programs.

In this article, we aimed to address these knowledge gaps by estimating the rates of nonadherence to PSOR and determining its associated predictors in a large retrospective clinical cohort of Asian patients with type 2 DM (T2DM) who underwent a national teleophthalmic diabetic eye screening program: the Singapore Integrated Diabetic Retinopathy Program (SiDRP). Patients included in this study were referred for tertiary evaluation and management of their diabetes-related eye diseases. We hypothesize high rates of nonadherence to PSOR in this population, with factors such as DM severity and duration, younger age, less severe eye disease, and poorer systemic health being predictive of nonadherence. Using the above factors, we additionally aimed to construct and evaluate the accuracy of a preliminary risk prediction model to identify individuals who were nonadherent to PSOR.

Methods

In this retrospective clinical cohort study, electronic medical records (EMR) of a total of 4034 individuals who underwent teleophthalmic screening under the SiDRP between 2010 and 2014 were reviewed. All patients had ocular conditions necessitating ophthalmic referral to the Singapore National Eye Centre (SNEC). We excluded 1474 individuals who did not have complete data for all variables examined in this study, along with 173 individuals without gradable fundus images, leaving a total of 2387 individuals in the final analysis. This high proportion of missing data spanned the period when clinical-centric paper-based medical records were transitioning to medical cluster-centric EMR (between 2010 and 2012), with most of these missing data related to duration of diabetes (data not shown). The study followed the tenets of the Declaration of Helsinki, and ethics approval was obtained from the centralized institutional review board (reference # R1211/17/2015). All subjects consented to the use of their anonymized data for research prior to enrolling in the SiDRP program.

Overview of the SiDRP Program

The SiDRP is a nationwide teleophthalmic and primary care screening model that was set up in 2010. Since its inception, it encompasses all 18 government polyclinics islandwide in Singapore. When a patient with diabetes from the community visits any of these polyclinics for their annual eye screening, their visual acuity (VA) readings are taken and dilated fundus photographs captured using a nonmydriatic fundus camera (TRC NW8-NW200; Topcon, Tokyo, Japan) by trained nurses. The images are sent via high-speed internet to grading centers located at the SNEC and Tan Tock Seng Hospital (TTSH). Trained graders then grade these photographs for any lenticular or retinal abnormalities, with the report sent back to the polyclinic within the hour. These graders are subject to clinical audits every 6 months in which a random selection of their images are regraded by an ophthalmologist. All graders are expected to maintain a sensitivity and specificity ≥90% for ocular diagnoses from fundal images, compared with the ophthalmologist. Based on these grader reports, VA readings, and patients' ocular presentation, the primary care physician will then proceed to refer patients for a tertiary ophthalmic appointment within 3 months at a time and location of their choice (see Supplementary Table S1 for the SiDRP referral protocol). The appointments are made on the spot by trained clinic staff.

Nonadherence

Nonadherence was our main outcome and was defined as a patient not attending their SNEC

appointment within 6 months of their initial appointment date. Although all routine referrals are to be made within 3 months post screening, we allowed a grace period of 6 months to account for possible delay caused by lack of available appointment slots after rescheduling/postponement of existing appointments. This decision was based on consensus agreements from both primary and tertiary care physicians.

Predictors of Nonadherence

Referable conditions, such as DR, glaucoma, AMD, cataract, and other eye diseases, were detected through the analysis of an individual's two-field retinal photographs (centered on the optic disc and macula) by trained graders at reading centers located at SNEC and TTSH. The referral criteria for these conditions were defined as follows:

- DR: moderate nonproliferative DR or worse and/or presence of diabetic macular edema (DME).
- AMD: presence of geographic atrophy or neovascular AMD.
- Cataract: any media opacity with VA <6/12.
- Glaucoma: cup disc ratio ≥0.65 either eye, disc asymmetry ≥0.2, disc hemorrhage, notching, or rim thinning.
- Other conditions: presence of macular hemorrhage, retinal vessel occlusion, retinal detachment, and papilloedema

All clinical and sociodemographic data were retrieved from the EMR database. Variables included in the analyses were age, sex, ethnicity, body mass index (BMI; kg/m^2), systolic (SBP) and diastolic blood pressure (DBP) (mm Hg), hemoglobin A1c (%), total cholesterol, high-density lipoprotein (HDL) (mmol/L), low-density lipoprotein (LDL) (mmol/L), and creatinine (mmol/L). Blood biochemistry was assessed using blood samples taken after at least 8 hours of fasting at the Singapore General Hospital laboratory. Snellen Visual Acuity was performed with habitual correction by trained nurses at 6 m and converted to logarithm of the minimum angle of resolution (logMAR) values for analysis. Values for both the better and worse-eye VA were utilized in analyses.

Statistical Analyses

We summarized continuous variables using means and standard deviations (SD), and categorical variables with counts and percentages. Comparison between patients who adhered and did not adhere to their appointments was made using the Mann-Whitney *U* test for continuous variables, and the Fisher's exact test for categorical variables. All variables that were significantly different between the two groups examined were entered simultaneously into a multivariable modified Poisson model, to determine their independent associations with nonadherence to PSOR. Because there was a small proportion of individuals who attended and was referred for tertiary ophthalmic management more than once within the time period of the study (N = 34), we made the decision to retain these visits as unique visits. However, we attempted to account for possible interdependencies in analyses by utilizing general estimating equations to estimate the risk ratios (RRs) and their standard errors for each predictor. We further conducted supplementary sensitivity analyses excluding these 34 individuals. The results of the latter are similar to that of the main analyses and are shown in Supplementary Table S2 and Supplementary Figure S1.

The receiver operating characteristic curve (AUC) of the model was then assessed to estimate the performance of the model in discriminating between patients who adhered and did not adhere to their appointments. A *P* value of <0.05 was considered statistically significant. In addition, we used a tree-based conditional inference analysis, which recursively partitions study participants into mutually exclusive groups by selected variables found significantly predictive of nonadherence to PSOR.[14] The conditional inference analysis makes much fewer modeling assumptions, allows for nonlinear interactions involving multiple variables, and is clearly visualized and easily interpreted for the purpose of identifying complex relationships between these variables; leading to a more compact model that maintains similar predictive accuracy to traditional multivariable models. A *P* value of <0.05 with Bonferroni correction for cumulative multiple testing to decide if a split was to be made at each step of the tree construction process. Analyses were performed using Stata version 15 (StataCorp LLC, TX, USA) and R version 3.5.0 (R Foundation, Vienna, Austria). The R package partykit version 1.2-2 was used for regression tree analyses.

Results

A total of 2421 visits made by 2387 patients were included in this analysis. Of the 2387 patients, 1877 (78.6%) were Chinese, 278 (11.7%) were Indian, 174 (7.3%) were Malays, and 58 (2.4%) were of other ethnicities. The mean age of the sample was 66.5 (SD,

Table 1.   Patients' Sociodemographic and Clinical Characteristics Stratified by Adherence to PSOR (N = 2421)

	Mean (SD)/N (%)		
Variable	Adherent (n = 2114)	Nonadherent (n = 307)	P^*
Age (years)	66.6 (11.1)	66.0 (9.8)	0.190
BMI (kg/m^2)	25.7 (4.5)	26.3 (4.7)	**0.036**
Diabetes duration (years)	7.5 (6.0)	7.3 (5.9)	0.639
SBP (mm Hg)	132.3 (18.2)	129.6 (17.7)	**0.007**
DBP (mm Hg)	69.9 (10.6)	69.4 (10.4)	0.530
HbA1c (%)	7.4 (1.6)	7.1 (1.3)	**0.001**
Total cholesterol (mmol/L)	4.5 (1.0)	4.5 (0.9)	0.948
HDL cholesterol (mmol/L)	1.4 (0.4)	1.4 (0.4)	0.058
LDL cholesterol (mmol/L)	2.5 (0.8)	2.4 (0.8)	0.152
Triglyceride (mmol/L)	1.5 (1.1)	1.5 (0.7)	0.163
Creatinine (mmol/L)	86.1 (38.4)	83.3 (39.2)	0.062
Presenting VA in better eye (logMAR)			
Presenting VA in worse eye (logMAR)	0.5 (0.5)	0.4 (0.3)	**0.001**
Female	1111 (52.6)	160 (52.1)	0.903
Race			
Malay	159 (7.5)	19 (6.2)	0.222
Indian	235 (11.1)	46 (15.0)	
Chinese	1670 (79.0)	234 (76.2)	
Others	50 (2.4)	8 (2.6)	
DR severity			
No DR	1362 (64.4)	258 (84.0)	**0.001**
Mild DR	376 (17.8)	30 (9.8)	
Moderate DR	245 (11.6)	9 (2.9)	
Severe DR	105 (5.0)	7 (2.3)	
Proliferative DR	26 (1.2)	3 (1.0)	
DME	345 (16.3)	13 (4.2)	**0.001**
Glaucoma	270 (12.8)	9 (2.9)	**0.001**
AMD	203 (9.6)	9 (2.9)	**0.001**
Cataract	608 (28.8)	35 (11.4)	**0.001**
Other eye condition	590 (27.9)	26 (8.5)	**0.001**
Two or more eye conditions	490 (23.2)	23 (7.5)	**0.001**
Antihypertensive medication use	1843 (87.3)	268 (87.6)	1.000
Anticholesterol medication use	1817 (86.1)	271 (88.6)	0.248
Antidiabetic medication use	1669 (79.1)	225 (73.5)	**0.031**

*Mann-Whitney U test or the Fisher's exact test. Bold indicates statistically significant results ($P < 0.05$).

11.0) years; duration of diabetes ranged from 1 to 39 years; and 52.5% were female patients. Out of 2421 visits, 307 visits did not result in attendance of tertiary referral within 6 months, which translates to a PSOR nonadherence rate of 12.7% (95% confidence interval [CI], 11.4%–14.1%). Nonadherent individuals had higher BMI, lower SBP, lower HbA$_{1c}$, better VA, were less likely to be using DM medication, have a referable eye condition, and have two or more concurrent condi-

tions, including DR, DME, glaucoma, AMD, cataract, and other eye conditions (Table 1).

Simultaneous inclusion of the above variables in a multivariable model showed that patients who had higher triglyceride levels at the time of their SiDRP visit were at greater risk of nonadherence to PSOR, with an adjusted RR of 1.07 (95% CI, 1.01–1.13) per mmol/L increase in triglyceride. Worse-eye VA was included instead of better-eye VA as univariable

Table 2.   Multivariable-Adjusted Predictors of Nonadherence to PSOR (N = 2421)

Variable	RR (95% CI)	*P*
Age (years)	0.99 (0.98–1.01)	0.320
Female	0.93 (0.76–1.15)	0.509
BMI (kg/m^2)	1.01 (0.99–1.03)	0.438
Race		
Chinese	Reference	
Indian	1.12 (0.87–1.44)	0.390
Malay	1.10 (0.72–1.68)	0.651
Others	1.12 (0.69–1.83)	0.639
SBP (mm Hg)	1.00 (0.99–1.00)	0.725
HbA1c (%)	0.94 (0.86–1.03)	0.179
HDL cholesterol (mmol/L)	1.27 (0.99–1.62)	0.058
LDL cholesterol (mmol/L)	0.97 (0.85–1.11)	0.667
Triglyceride (mmol/L)	1.07 (1.01–1.13)	**0.024**
Creatinine (mmol/L)	1.00 (1.00–1.01)	0.527
Presenting VA in worse eye (logMAR)	0.98 (0.92–1.03)	0.397
DR severity		
No DR	Reference	
Mild DR	0.58 (0.36–0.93)	**0.024**
Moderate DR	0.10 (0.05–0.20)	**<0.001**
Severe DR	0.27 (0.13–0.57)	**0.001**
Proliferative DR	0.43 (0.15–1.28)	0.131
DME	0.20 (0.09–0.43)	**<0.001**
Glaucoma	0.09 (0.04–0.17)	**<0.001**
AMD	0.12 (0.06–0.24)	**<0.001**
Cataract	0.16 (0.11–0.23)	**<0.001**
Other eye condition	0.15 (0.10–0.22)	**<0.001**
Two or more eye conditions[a]	0.28 (0.19–0.41)	**<0.001**
Antihypertensive medication use	1.11 (0.84–1.49)	0.462
Anticholesterol medication use	1.04 (0.76–1.44)	0.790
Antidiabetic medication use	0.86 (0.69–1.07)	0.187

[a]Substitutes for the six individual eye conditions in the multivariable model. Bolded values indicate statistically significant results (*P* < 0.05).

analyses revealed worse-eye VA had a slightly stronger association with nonadherence to PSOR than better-eye VA (58% vs. 57%, data not shown). Presence of referable eye conditions was associated with a lower risk of nonadherence, with RRs ranging from 0.58 (for mild DR) to 0.09 (for glaucoma), with the presence of concomitant referable conditions being associated with a 72% lower risk of nonadherence compared with the presence of a single referable ocular condition (RR, 0.28; 95% CI, 0.19–0.40; Table 2). Adding each eye disease individually to a base model (AUC, 0.64) of sociodemographic and systemic risk factors significantly improved model prediction, with improved AUCs ranging from 0.67 (for AMD) to 0.69 (for DR severity). The full multivariable model with all six eye conditions included was able to discriminate between adherent and nonadherent individuals with an estimated predictive accuracy of 84% (AUC, 0.80; 95% CI, 0.81–0.87; Table 3). The conditional inference regression tree had similar predictive accuracy to the multivariable modified Poisson model. However, the regression tree only selected seven variables in the following order of statistical significance: more than one eye condition, the presence of cataract, other eye conditions, glaucoma, moderate and worse DR, AMD DR severity, and mild DR (Figure). The regression tree further found that the subgroup of individuals who did not have any of the earlier mentioned eye

Table 3. The AUC for Various Models in Prediction of Nonadherence to PSOR

Model	Description	AUC (95% CI)
1	Base[a]	0.64 (0.61–0.67)
2	Plus DR severity	0.69 (0.66–0.72)
3	Plus DME	0.68 (0.64–0.71)
4	Plus glaucoma	0.68 (0.65–0.71)
5	Plus AMD	0.67 (0.63–0.70)
6	Plus cataract	0.68 (0.65–0.71)
7	Plus other eye condition	0.68 (0.65–0.71)
8	Plus all six eye conditions[b]	0.84 (0.81–0.87)
9	Plus two or more eye conditions	0.70 (0.67–0.73)
10	Plus all six eye conditions and two or more eye conditions	0.84 (0.81–0.87)
11	Conditional inference regression tree	0.84 (0.81–0.86)

[a]Modified Poisson model adjusted for age, sex, BMI, SBP, triglycerides, and worse eye presenting VA.
[b]The AUC for model 8 was significantly higher than models 1–7, and 9.
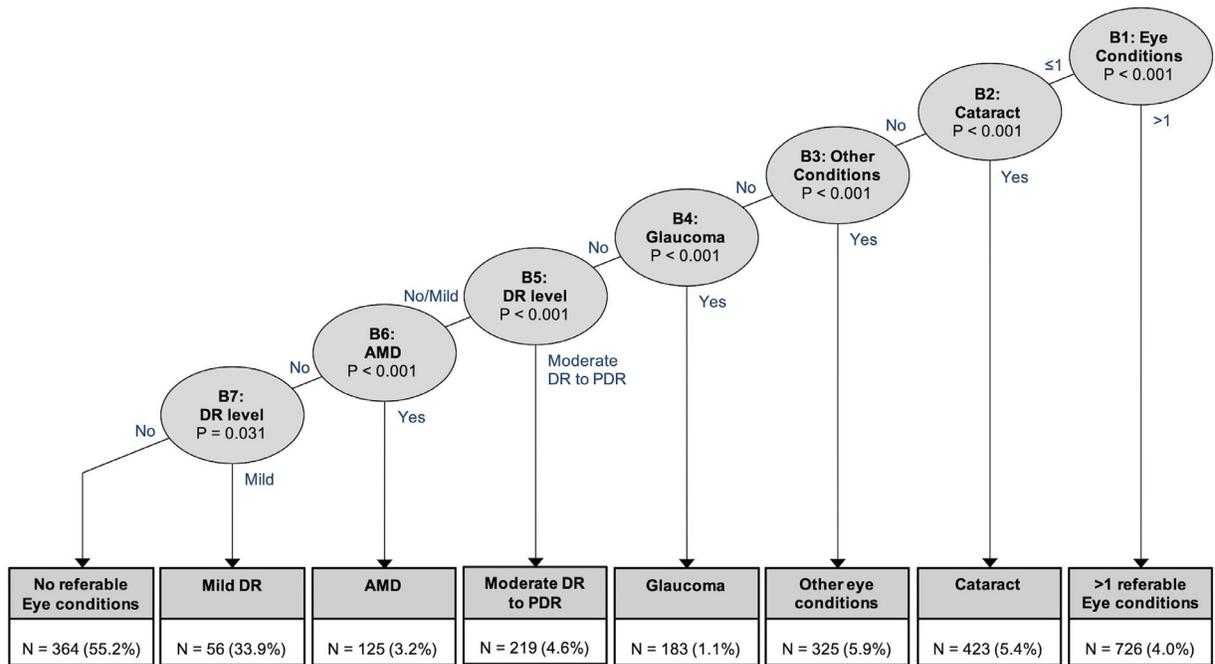AUCs for all models was significantly higher than the base model.

Figure. Conditional inference tree for the prediction of non-adherence to PSOR (N = 2421 visits). The dataset is successively split (from top right to bottom left) in order of the predictor variable that produces the largest significant difference in an asymptotic test statistic comparing non-adherence between the split groups. The tree has a total of 7 branches (B1 to B7) and ovals contain the splitting variable at each branch and the corresponding Bonferroni-corrected P-value for the split. Rectangular boxes are terminal nodes of the tree that patients are exclusively classified into. N refers to the number of patients in each node and the prevalence of non-adherence to PSOR is given adjacent within parentheses. For example, a patient with AMD and no other referable eye conditions would move downwards (southwesterly) the tree and be siphoned out at the sixth branch into the AMD node, with an estimated non-adherence probability of 3.2%.

conditions in retinal photos or only had mild DR were the most likely to miss attending their tertiary referrals, with estimated nonadherence probability percentages of 55.2% (95% CI, 49.9–60.4) and 33.9% (95% CI, 21.8–47.8), respectively.

Discussion

In this multiethnic, retrospective clinic-based study, we found a relatively low nonadherence to PSOR rate

of 12.7% in Asian patients with T2DM. Although traditional modified Poisson regression models identified several factors that were associated with nonadherence, namely having higher triglyceride levels, and having mild or no referable eye diseases in fundus images, conditional inference tree modeling allowed us to eliminate systemic factors while maintaining the model's AUC of 84%. Further prospective longitudinal, and qualitative studies are warranted to verify our findings, validate our preliminary risk prediction model, and explore the reasons underpinning nonadherence to PSOR.

To our knowledge, this is the first study in Asia to report the nonadherence rate to PSOR. Our rate of 12.7% is much lower than the 30% to 79% reported in previous Western studies.[6–8] We postulate that the lower levels of nonadherence might be because of the high literacy rates in Singapore ($\sim$88%),[15] as studies have shown a correlation between higher literacy rates with adherence to medical advice.[15,16] Another potential reason explaining our low nonadherence rate is the presence of a nationwide copayment scheme. The medical fees for Singaporeans are partially covered by the government (Medisave, Medishield Life, and Medifund), which may help to substantially alleviate the financial burden of health care, particularly for Singapore's elderly and underprivileged populations. Finally, Singapore is a small country, with an area of approximately 720 km^2. As such, the close proximity to health care services for residents may be a substantial contributory factor to the low nonadherence rate to PSOR observed in our study. Unfortunately, qualitative data to confirm these hypotheses, and information on whether individuals had private insurance plans to further mitigate costs, were not collected in this study. Future studies with the relevant data may be needed to verify and expand on our current findings.

Various studies conducted in Western populations revealed factors associated with nonadherence that were similar to that elicited in our traditional multivariable analyses, specifically with regard to higher triglyceride levels and less severe DR.[8,12,17] Considering that DR has few visual symptoms until the disease becomes quite advanced,[18] it is not unusual for patients with mild disease to not realize the importance of early intervention, which likely explains our observation of the association between milder disease with higher rates of nonadherence rates to PSOR. In contrast, despite an established correlation between poor disease control and lack of adherence to various disease intervention strategies,[19] it is surprising that only higher triglyceride levels, and not other indicators of poor control, for example, raised HbA1c and blood pressure levels, were significantly associated with

increased risk of nonadherence to PSOR in our study. Moreover, removal of this variable in conditional inference models did not significantly affect discriminative accuracy, suggesting that higher triglyceride levels may not be an important overall contributor to nonadherence to PSOR.

Our study involved a large clinic-based sample attending government polyclinics in Singapore, which makes our results generalizable to the majority of Singaporean individuals who live with diabetes, as most of these patients visit the polyclinic for their chronic disease care. Furthermore, our study utilized a standardized grading system for diabetes-related eye diseases, and also drew from a wide selection of participant sociodemographic and clinical parameters allowing for a comprehensive characterization of factors predicting nonadherence to PSOR. In addition, aside from the traditional multivariable models utilized in previous studies, we also used regression tree modeling in our analyses to determine the sociodemographic and clinical risk factors associated with nonadherence to PSOR.[14]

However, it is important to note that our study was retrospective in nature, and as such we may not have collected all potential factors associated with nonadherence to PSOR, such as a patient's clarity with regard to the referral process; patients' perceptions on DR and their view on the importance of eye examinations; distance, travel time, and mode of transportation to the tertiary hospital; as well as whether these individuals were privately insured, all of which have been established to play a role in the uptake of tertiary eye referrals.[17,20,21] Furthermore, our participants were drawn from government polyclinic databases and may not reflect individuals who chose to follow-up with doctors from private practice. Finally, a limitation of our approach was that we utilized the same data to build and evaluate the model, which may have led to an overestimation of model performance. We chose not to conduct internal validation (e.g., by splitting the sample into separate training and validation sets) due to possible selection bias arising from the large volume of missing data (N = 1647). As such, further prospective quantitative, as well as qualitative work to elicit the reasons underpinning nonadherence to PSOR, are warranted to improve and validate the model's predictive accuracy.

Conclusions

Our study showed that the rate of nonadherence to PSOR was low in a multiethnic Asian

population with T2DM. Using traditional multivariable and conditional inference tree models, our study identified common key factors, such as more than one eye condition, the presence of cataract, other eye conditions, glaucoma, DR severity, and AMD, that can be used to characterize nonadherent individuals. The results of our study are the first steps toward allowing primary care practitioners to understand and design intervention strategies to target individuals who are likely to be nonadherent to PSOR, ultimately decreasing the burden of blindness and diabetic-related eye disease on Singapore's health care system. Future prospective studies that include both quantitative and qualitative data are needed to understand underpinning reasons for nonadherence to PSOR, as well as to refine the discriminant accuracy and validate the predictive model in clinical practice.

Acknowledgments

References

1. International Diabetes Federation. *IDF Diabetes Atlas*. 8th ed. 2017. Available at: http://fmdiabetes.org/wp-content/uploads/2018/03/IDF-2017.pdf. Accessed 5th November 2019.
2. Zheng Y, Lavanya R, Wu R, et al. Prevalence and causes of visual impairment and blindness in an urban Indian population: the Singapore Indian Eye Study. *Ophthalmology*. 2011;118:1798–1804.
3. Fenwick EK, Pesudovs K, Khadka J, et al. The impact of diabetic retinopathy on quality of life: qualitative findings from an item bank development project. *Qual Life Res*. 2012;21:1771–1782.
4. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. *Lancet*. 2010;376:124–136.
5. Nguyen TT, Wang JJ, Sharrett AR, et al. Relationship of retinal vascular caliber with diabetes and retinopathy: the Multi-Ethnic Study of Atherosclerosis (MESA). *Diabetes Care*. 2008;31:544–549.
6. Keenum Z, McGwin G, Jr., Witherspoon CD, Haller JA, Clark ME, Owsley C. Patients' adherence to recommended follow-up eye care after diabetic retinopathy screening in a publicly funded county clinic and factors associated with follow-up eye care use. *JAMA Ophthalmol*. 2016;134:1221–1228.
7. Lee SJ, Livingston PM, Harper CA, McCarty CA, Taylor HR, Keeffe JE. Compliance with recommendations from a screening programme for diabetic retinopathy. *Aust N Z J Ophthalmol*. 2008;27:187–189.
8. Newcomb PA, Klein R. Factors associated with compliance following diabetic eye screening. *J Diabet Complications*. 1990;4:8–14.
9. Bäcklund LB, Algvere PV, Rosenqvist U. New blindness in diabetes reduced by more than one-third in Stockholm County. *Diabet Med*. 1997;14:732–740.
10. Lewis K, Patel D, Yorston D, Charteris D. A qualitative study in the United Kingdom of factors influencing attendance by patients with diabetes at ophthalmic outpatient clinics. *Ophthalmic Epidemiol*. 2007;14:375–380.
11. Pun Sandra PY, Coates V, Benzie Iris FF. Barriers to the self-care of type 2 diabetes from both patients' and providers' perspectives: literature review. *J Nurs Healthc Chronic Illn*. 2009;1:4–19.
12. Will JC, German RR, Schuman E, Michael S, Kurth DM, Deeb L. Patient adherence to guidelines for diabetes eye care: results from the diabetic eye disease follow-up study. *Am J Public Health*. 1994;84:1669–1671.
13. Zgibor JC, Songer TJ. External barriers to diabetes care: addressing personal and health systems issues. *Diabetes Spectr*. 2001;14:23–28.
14. Hothorn T, Hornik K, Zeileis A. Unbiased recursive partitioning: a conditional inference framework. *J Comput Graph Stat*. 2006;15:651–674.
15. Ko Y, Lee JY, Toh MP, Tang WE, Tan AS. Development and validation of a general health literacy test in Singapore. *Health Promot Int*. 2012;27:45–51.
16. Miller TA. Health literacy and adherence to medical treatment in chronic and acute illness: a meta-analysis. *Patient Educ Couns*. 2016;99:1079–1086.
17. Murchison AP, Hark L, Pizzi LT, et al. Nonadherence to eye care in people with diabetes. *BMJ Open Diabetes Res Care*. 2017;5:e000333.
18. Fante RJ, Durairaj VD, Oliver SC. Diabetic retinopathy: an update on treatment. *Am J Med*. 2010;123:213–216.

19. Herttua K, Martikainen P, Batty GD, Kivimäki M. Poor adherence to statin and antihypertensive therapies as risk factors for fatal stroke. *J Am Coll Cardiol*. 2016;67:1507–1515.

20. Mtuya C, Cleland CR, Philippin H, et al. Reasons for poor follow-up of diabetic retinopathy patients after screening in Tanzania: a cross-sectional study. *BMC Ophthalmol*. 2016;16:115.

21. Fisher MD, Rajput Y, Gu T, et al. Evaluating adherence to dilated eye examination recommendations among patients with diabetes, combined with patient and provider perspectives. *Am Health Drug Benefits*. 2016;9:385.