Prevalence of Diabetic Retinopathy in the United States, 2005-2008

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Context The prevalence of diabetes in the United States has increased. People with diabetes are at risk for diabetic retinopathy. No recent national population-based estimate of the prevalence and severity of diabetic retinopathy exists.

Objectives To describe the prevalence and risk factors of diabetic retinopathy among US adults with diabetes aged 40 years and older.

Design, Setting, and Participants Analysis of a cross-sectional, nationally representative sample of the National Health and Nutrition Examination Survey 2005-2008 (N=1006). Diabetes was defined as a self-report of a previous diagnosis of the disease (excluding gestational diabetes mellitus) or glycated hemoglobin A_{1c} of 6.5% or greater. Two fundus photographs were taken of each eye with a digital nonmydriatic camera and were graded using the Airlie House classification scheme and the Early Treatment Diabetic Retinopathy Study severity scale. Prevalence estimates were weighted to represent the civilian, noninstitutionalized US population aged 40 years and older.

Main Outcome Measurements Diabetic retinopathy and vision-threatening diabetic retinopathy.

Results The estimated prevalence of diabetic retinopathy and vision-threatening diabetic retinopathy was 28.5% (95% confidence interval [CI], 24.9%-32.5%) and 4.4% (95% CI, 3.5%-5.7%) among US adults with diabetes, respectively. Diabetic retinopathy was slightly more prevalent among men than women with diabetes (31.6%; 95% CI, 26.8%-36.8%; vs 25.7%; 95% CI, 21.7%-30.1%; *P*=.04). Non-Hispanic black individuals had a higher crude prevalence than non-Hispanic white individuals of diabetic retinopathy (38.8%; 95% CI, 31.9%-46.1%; vs 26.4%; 95% CI, 21.4%-32.2%; *P*=.01) and vision-threatening diabetic retinopathy (9.3%; 95% CI, 5.9%-14.4%; vs 3.2%; 95% CI, 2.0%-5.1%; *P*=.01). Male sex was independently associated with the presence of diabetic retinopathy (odds ratio [OR], 2.07; 95% CI, 1.39-3.10), as well as higher hemoglobin A_{1c} level (OR, 1.45; 95% CI, 1.20-1.75), longer duration of diabetes (OR, 1.06 per year duration; 95% CI, 1.03-1.10), insulin use (OR, 3.23; 95% CI, 1.99-5.26), and higher systolic blood pressure (OR, 1.03 per mm Hg; 95% CI, 1.02-1.03).

Conclusion In a nationally representative sample of US adults with diabetes aged 40 years and older, the prevalence of diabetic retinopathy and vision-threatening diabetic retinopathy was high, especially among Non-Hispanic black individuals.

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DIABETIC RETINOPATHY IS THE leading cause of new cases of legal blindness among adults aged 20 to 74 years in the United States.[1] Vision loss due to diabetic retinopathy occurs through a variety of mechanisms, including retinal detachment, preretinal or vitreous hemorrhage, associated neovascular glaucoma, and macular edema or capillary nonperfusion.[2] The presence of diabetic retinopathy may indicate microcirculatory dysfunction in other organ systems.[3,4] Diabetes-related blindness is a personal catastrophe to the individual and costs the United States approximately $500 million annually.[5] However, risk of vision loss due to diabetic retinopathy can be reduced by effective control of serum glucose and blood pressure and by its early detection and timely treatment.[6-8] The efficacy and cost-effectiveness of early detection and treatment of diabetic retinopathy is well established.[9,10]

Investigating the prevalence of diabetic retinopathy is important because it is a key indicator of systemic diabetic microvascular complications, and as such, a sentinel indicator of the impact of diabetes. Despite the documented increase in the prevalence of diabetes in the US population,[11] national population-based data on the prevalence and severity of diabetic retinopathy remain scarce, with previous nationwide prevalence estimates dating back to 1988-1994 (National Health and Nutrition Examination Surveys III [NHANES III]).[12] In 2004, the Eye Diseases Prevalence Research Group estimated the prevalence of diabetic retinopathy from the compilation of 8 sepa-

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rate population-based studies from the United States and elsewhere conducted in the late 1980s or early 1990s.[13] Their report recommended that more recent estimates of diabetic retinopathy prevalence be obtained from the nationally representative sample of NHANES.

Moreover, several other population-based studies reported a decrease in the prevalence and incidence of severe diabetic retinopathy and related visual impairment.[14-16] However, these findings were limited to regional cohorts and the status of diabetic retinopathy at the national level remains unknown. Thus, the principal aim of this study is to describe the most recent prevalence and risk factors of diabetic retinopathy in the US population aged 40 years and older using NHANES 2005-2008.

METHODS

Study Population

NHANES are national representative surveys conducted by the National Center for Health Statistics, part of the Centers for Disease Control and Prevention. The data consist of samples of the US noninstitutionalized civilian population, which were obtained using a stratified multistage probability design with planned oversampling of certain age and racial/ethnic groups.[17] There were 6797 individuals aged 40 years and older interviewed for sociodemographic, medical, and family information and had a full medical examination at the medical examination center in NHANES 2005-2008. The NHANES 2005-2008 response rate for the interview sample aged 40 years and older was 71% and 69% for the examined sample.[18] The NHANES protocol was approved by a human subjects review board and written informed consent was obtained from all participants.

Fundus Photography

NHANES 2005-2008 used the Canon CR6-45NM ophthalmic digital imaging system and Canon EOS 10D digital camera (Canon, Tokyo, Japan) to take 2 digital images per eye (total 4 images per participant) through a nonpharmacologically dilated pupil. Participants were seated in a windowless room with the lights turned off to allow the pupils to dilate naturally in preparation for the retinal imaging examination. One image was centered on the macula and the second on the optic nerve. The digital images were graded by masked photo graders at the University of Wisconsin Ocular Epidemiologic Reading Center, Madison, using a modification of the Airlie House classification system.[19-21] Capture and grading of digital images and quality control by the Wisconsin group have been described in detail previously.[22]

Survey participants who had no light perception or severe visual impairment in both eyes or had a severe infection in one or both eyes were excluded (n=13). Complete data of fundus photographs of both eyes were obtained for 5371 (79%) participants aged 40 years and older who had full medical examinations.

Reasons for having incomplete data (n=1426, 21%) included insufficient time to finish the examination (ie, arrived late or left early; n=514; 42%), physical limitation (n=238; 19%), eye-specific limitation (n=193; 16%), participant's refusal (n=119; 10%), communication problems (n=40; 3%), and others. Those individuals with incomplete data were more likely to be older, non-Hispanic black, with less than a high school education, higher systolic blood pressure, higher glycated hemoglobin A_{1c} level, and a history of using insulin than participants with complete gradable photographs (all $P<.001$). We further examined the potential influence of nonresponse bias due to the exclusion of participants without complete gradable photographs by adjusting the original sampling weights using the standard weighting–class method.[23,24] Findings using these adjusted weights led to only minor differences in point and variance estimates (0%-0.5%), indicating minimal impact of nonresponse; therefore, we present all estimates using the original sampling weights.

Diabetic retinopathy was defined as the presence of 1 or more retinal microaneurysms or retinal blot hemorrhages with or without more severe lesions (hard exudates, soft exudates, intraretinal microvascular abnormalities, venous beading, retinal new vessels, preretinal and vitreous hemorrhage, and fibroproliferans) using the Early Treatment Diabetic Retinopathy Study (ETDRS) grading standards.[19]

Diabetic retinopathy was further categorized as nonproliferative and proliferative determined by assessment of the presence of retinal neovascularization or abnormal growth of new retinal blood vessels into the vitreous. Vision-threatening diabetic retinopathy, a level that may soon result in vision loss if left untreated, was defined as the presence of severe nonproliferative diabetic retinopathy, proliferative diabetic retinopathy, or clinically significant macular edema. Clinically significant macular edema was considered present when edema involved the fovea or was within 500 microns of the fovea, or when a 1+disc area of edema was present with at least a portion of it within the macula. Outcomes for this study were defined on the basis of the worse of the 2 eyes.

Other Measurements

Diabetes was defined as self-report of a previous diagnosis of the disease by a clinician (excluding gestational diabetes mellitus) or hemoglobin A_{1c} of 6.5% or greater (American Diabetes Association's new diagnostic criterion for undiagnosed diabetes).[25] Although hemoglobin A_{1c} does not capture completely the increased risk of microvascular complications due to diabetes,[26] the diagnostic hemoglobin A_{1c} cut point of 6.5% was determined to be an inflection point for retinopathy prevalence, as is also true for the diagnostic thresholds of the glucose-based test.[25,27,28] The final analytic sample consisted of 1006 individuals with diabetes aged 40 years and older (n=795 for diagnosed diabetes; n=211 for undiagnosed diabetes).

All participants were asked about their age, sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, and others [including those who selected multiple races and non-Mexican American Hispanics]), educational attainment (less than high school, high school education, or higher), and health insurance status. Consistent with previous epidemiologic studies,[29-31] risk factors for diabetic retinopathy and vision-threatening diabetic retinopathy (hemoglobin A_{1c}, duration of diabetes, insulin use [yes/no], systolic and diastolic blood pressure, body mass index [BMI, calculated as weight in kilograms divided by height in meters squared], current smoking status [yes/no], and history of cardiovascular diseases [CVD; yes/no]) were examined. Hemoglobin A_{1c}, duration of diabetes, and systolic and diastolic blood pressure were used as continuous variables. Hemoglobin A_{1c} was used as the surrogate for blood glucose level and measured by a high-performance liquid chromatographic assay as used in the Diabetes Control and Complications Trial.[7] Insulin therapy indicated that the participant had type 1 diabetes or their diabetes could not otherwise be controlled without insulin. We used measured height and weight to calculate BMI and divided respondents into 3 groups: normal/underweight (BMI<25), overweight (BMI 25-<30), and obese (BMI ≥30). Prior history of CVD was ascertained by self-report of coronary heart disease, angina, myocardial infarction, stroke, or congestive heart failure.

Statistical Methods

Statistical analyses were conducted using SAS version 9.2 (SAS Institute, Cary, North Carolina) and SUDAAN version 10.1 software (Research Triangle Institute, Research Triangle Park, North Carolina) to calculate national estimates and their standard errors while accounting for the complex survey design of the survey. Taylor series linearization was used for variance estimation.[32] The NHANES 2005-2008 study has sufficient sample size to detect a relative difference of 6% (effective sample size = sample size/design effect = 1006/1.7 = 591) at 85% power and an α level of .05.

Characteristics of the study population are described using means for continuous variables and percentages for categorical variables. For continuous variables, *t* tests were used and for categorical variables the χ^2 test. We estimated the crude prevalence of diabetic retinopathy and vision-threatening diabetic retinopathy by age, sex, and race/ethnicity in the diabetic and overall US population. Multiple logistic regressions were used to assess the association between diabetic retinopathy and vision-threatening diabetic retinopathy, vs clinical potential risk factors for diabetic retinopathy and vision-threatening diabetic retinopathy after controlling for age, sex, race/ethnicity, and education attainment.

Predictive margins, odds ratios (OR), and 95% confidence intervals (CI) for each were calculated. Associations were considered to be significant if the *P* value was less than .05. Additionally, we compared the prevalence of diabetic retinopathy and vision-threatening diabetic retinopathy in NHANES 2005-2008 with NHANES III by using the right eye if the last digit of the participant identification number was even and the left eye if it was odd. The prevalence estimates were age standardized to the 2000 US census population.

RESULTS

In 2005-2008, the estimated (weighted) crude prevalence of diabetic retinopathy and vision-threatening diabetic retinopathy was 28.5% (95% CI, 24.9%-32.5%) and 4.4% (95% CI, 3.5%-5.7%), respectively, among persons with diabetes aged 40 years and older (**Table 1**). Extrapolating to the overall US population in the same period, the prevalence nation wide would be 3.8% (95% CI, 3.2%-4.5%) and 0.6% (95% CI, 0.5%-0.8%). Approximately 1.5% (95% CI, 1.1%-2.2%) of adults with diabetes had proliferative diabetic retinopathy and 2.7% (95% CI, 1.8%-4.0%) had clinically significant macular edema. In other words, approximately 0.2% (95% CI, 0.1%-0.3%) of adults aged 40 years or older had proliferative diabetic retinopathy and 0.4% (95% CI, 0.2%-0.5%) had clinically significant macular edema.

Among individuals with diabetes, no significant difference was found in the prevalence of diabetic retinopathy between those aged 40 to 64 years and those aged 65 years and older (28.0%; 95% CI, 23.0%-33.6%; vs 29.5%; 95% CI, 25.4%-33.9%; *P* = .64). Approximately 31.6% (95% CI, 26.8%-36.8%) of men with diabetes had diabetic retinopathy and approximately 25.7% (95% CI, 21.7%-30.1%) of women with diabetes had diabetic retinopathy (*P* = .04). Approximately 26.4% (95% CI, 21.4%-32.2%) of non-Hispanic white individuals, 38.8% (95% CI, 31.9%-46.1%) of non-Hispanic black individuals, and 34.0% (95% CI, 26.7%-42.1%) of Mexican American individuals with diabetes had diabetic retinopathy (*P* = .008). Prevalence of vision-threatening diabetic retinopathy was not statistically different between individuals aged 40 to 64 years and those aged 65 years and older (4.1%; 95% CI, 2.8%-5.8%; vs 5.1%; 95% CI, 3.5%-7.3%; *P* = .41). There was no significant difference in the prevalence of vision-threatening diabetic retinopathy between men and women (4.2%; 95% CI, 2.8%-6.1%; vs 4.7%, 95% CI, 3.2%-6.9%; *P* = .67). Approximately 3.2% (95% CI, 2.0%-5.1%) of non-Hispanic white individuals, 9.3% (95% CI, 5.9%-14.4%) of non-Hispanic black individuals, and 7.3% (95% CI, 3.9%-13.3%) of Mexican American individuals with diabetes had vision-threatening diabetic retinopathy (*P* = .006).

Extrapolating survey findings to the entire US adult population in the same period (without regard for diabetes status), the prevalence of diabetic retinopathy was significantly higher among individuals who were aged 65 years or older than those younger than 65 years of age (6.1%; 95% CI, 5.1%-7.3%; vs 3.1%; 95% CI, 2.4%-3.9% *P* < .001). Approximately 4.3% (95% CI, 3.5%-

5.3%) of adult men in the United States had diabetic retinopathy compared with 3.3% (95% CI, 2.7%-4.1%) of adult women ($P=.046$). Non-Hispanic black individuals and Mexican American individuals had a higher prevalence of diabetic retinopathy than non-Hispanic white individuals (9.6%; 95% CI, 7.7%-11.9%; 6.7%; 95% CI, 5.4%-8.4%; vs 2.9%; 95% CI, 2.2%-3.9%; both $P<.001$).

Prevalence of vision-threatening diabetic retinopathy was higher among people aged 65 years or older than those aged 40 to 64 years (1.0%; 95% CI, 0.7%-1.5%; vs 0.4%; 95% CI, 0.3%-0.7%; $P=.009$). There was no significant difference in the prevalence of vision-threatening diabetic retinopathy between men and women observed (0.6%; 95% CI, 0.4%-0.9%; vs 0.6%; 95% CI, 0.4%-0.9%; $P=.81$). Approximately 0.4% (95% CI, 0.2%-0.6%) of non-Hispanic white individuals, 2.3% (95% CI, 1.5%-3.6%) of non-Hispanic black individuals, and 1.4% (95% CI, 0.8%-2.7%) of Mexican American individuals had vision-threatening diabetic retinopathy ($P<.001$).

Among individuals with diabetes, those with diabetic retinopathy were more likely to be men (53.7%; 95% CI, 47.4%-59.9%; vs 46.5%; 95% CI, 41.5%-51.6%; $P=.04$) than those without diabetic retinopathy (TABLE 2). Diabetic individuals with diabetic retinopathy had a longer duration of diabetes (15.0 years; 95% CI, 13.4-16.5; vs 7.3 years; 95% CI, 6.5-8.1; $P<.001$), higher systolic blood pressure (134.2 mm Hg; 95% CI, 131.6-136.9; vs 130.1 mm Hg; 95% CI, 127.9-132.4; $P=.04$), and higher hemoglobin A_{1c} level (7.9%; 95% CI, 7.6%-8.1%; vs 7.0%; 95% CI, 6.8%-7.1%; $P<.001$) than those without diabetic retinopathy. Diabetic individuals with diabetic retinopathy were more likely to use insulin than those with diabetes but no diabetic retinopathy (44.6%; 95% CI, 38.5%-50.9%; vs 10.2%; 95% CI, 8.1%-12.7%; $P<.001$).

TABLE 3 shows the associations of various risk factors with diabetic retinopathy and vision-threatening diabetic retinopathy among individuals with diabetes. In multivariate analysis, independent risk factors for diabetic retinopathy include male sex (38.1%; 95% CI, 32.6%-43.6%; vs 27.1%; 95% CI, 22.4%-31.8%; OR, 2.07; 95% CI, 1.39-3.10), higher hemoglobin A_{1c} level (OR, 1.45; 95% CI, 1.20-1.75), longer diabetes duration (OR, 1.06

Table 1. Estimated Prevalence of Diabetic Retinopathy and Vision-Threatening Diabetic Retinopathy in Individuals With Diabetes Aged 40 Years and Older and in the Adult US Population, by Age, Sex, and Race/Ethnicity: NHANES 2005-2008

				Crude Prevalence of Diabetic Retinopathy			
			Weighted Size, in Thousands[c]	Diabetes Population		US Population	
Characteristics	No.[a]	No.[b]		% (95%CI)	*P* Value	% (95%CI)	*P* Value
Total	1006	324	4202	28.5 (24.9-32.5)		3.8 (3.2-4.5)	
Age, y							
40-64	575	189	2588	28.0 (23.0-33.6)	.64	3.1 (2.4-3.9)	<.001
≥65	431	135	1613	29.5 (25.4-33.9)		6.1 (5.1-7.3)	
Sex							
Male	504	173	2257	31.6 (26.8-36.8)	.04	4.3 (3.5-5.3)	.046
Female	502	151	1944	25.7 (21.7-30.1)		3.3 (2.7-4.1)	
Race/ethnicity							
Non-Hispanic white	396	107	2507	26.4 (21.4-32.2)	.008	2.9 (2.2-3.9)	<.001
Non-Hispanic black	306	119	1006	38.8 (31.9-46.1)		9.6 (7.7-11.9)	
Mexican American	197	70	401	34.0 (26.7-42.1)		6.7 (5.4-8.4)	
Other	107	28	286	19.7 (12.5-29.7)		3.3 (2.3-4.7)	
				Crude Prevalence of Vision-Threatening Diabetic Retinopathy			
Total	1006	62	655	4.4 (3.5-5.7)		0.6 (0.5-0.8)	
Age, y							
40-64	575	36	376	4.1 (2.8-5.8)	.41	0.4 (0.3-0.7)	.009
≥65	431	26	278	5.1 (3.5-7.3)		1.0 (0.7-1.5)	
Sex							
Male	504	24	298	4.2 (2.8-6.1)	.67	0.6 (0.4-0.9)	.81
Female	502	38	356	4.7 (3.2-6.9)		0.6 (0.4-0.9)	
Race/ethnicity							
Non-Hispanic white	396	13	304	3.2 (2.0-5.1)	.006	0.4 (0.2-0.6)	<.001
Non-Hispanic black	306	28	241	9.3 (5.9-14.4)		2.3 (1.5-3.6)	
Mexican American	197	16	85	7.3 (3.9-13.3)		1.4 (0.8-2.7)	
Other	107	5	22	1.6 (0.6-3.8)[d]		0.3 (0.1-0.6)	

Abbreviations: CI, confidence interval; NHANES, National Health and Nutrition Examination Surveys.
[a] Number of participants with diabetes in NHANES 2005-2008.
[b] Number of participants with diabetes who had diabetic retinopathy or vision-threatening diabetic retinopathy in NHANES 2005-2008.
[c] Weighted total number of US adult population who had diabetic retinopathy or vision-threatening diabetic retinopathy.
[d] Estimate is considered unreliable because relative standard error is greater than 30%.

per year duration; 95% CI, 1.03-1.10), use of insulin (47.4%; 95% CI, 39.1%-55.8%; vs 26.7%; 95% CI, 21.9%-31.5%; OR, 3.23; 95% CI, 1.99-5.26), and higher systolic blood pressure (OR, 1.03 per mm Hg; 95% CI, 1.02-1.03). Moreover, longer diabetes duration (OR=1.03 per year duration; 95% CI, 1.01-1.05), use of insulin (7.5%; 95% CI, 4.8%-10.1%; vs 3.3%; 95% CI, 1.9%-4.7%; OR=2.63; 95% CI, 1.34-5.15), and higher systolic blood pressure (OR, 1.03 per mm Hg; 95%CI, 1.01-1.06) were also associated with increased odds of vision-threatening diabetic retinopathy. The odds of vision-threatening diabetic retinopathy were significantly higher among non-Hispanic black individuals than in non-Hispanic white individuals, even after controlling for all other factors considered (9.8%; 95% CI, 5.7%-13.8%; vs 3.3%; 95% CI, 1.6%-5.0%; OR, 3.77; 95% CI, 1.47-9.69).

Additionally, we found that the age-standardized prevalence of diabetic retinopathy was statistically significantly different between 2 periods (15.8%; 95% CI, 12.7%-19.6% in NHANES III vs 22.1%; 95% CI, 18.4%-26.3% in NHANES 2005-2008; $P=.01$). A statistically significant difference of vision-threatening diabetic retinopathy was also observed; 1.3% (95% CI, 0.7%-2.3%) had vision-threatening diabetic retinopathy from the NHANES III data and 3.3% (95% CI, 2.4%-4.4%) from NHANES 2005-2008 ($P=.002$).

Table 2. Comparison of Characteristics of Individuals With Diabetes Aged 40 Years and Older, by Diabetic Retinopathy Status: NHANES 2005-2008

Characteristics	Weighted Mean (95% CI)		*P* Value
	With Diabetic Retinopathy	Without Diabetic Retinopathy	
Age at examination, y	61.6 (60.2-62.9)	60.0 (58.9-61.0)	.04
Duration of diabetes, y	15.0 (13.4-16.5)	7.3 (6.5-8.1)	<.001
Systolic blood pressure, mm Hg	134.2 (131.6-136.9)	130.1 (127.9-132.4)	.04
Diastolic blood pressure, mm Hg	67.5 (66.0-69.0)	71.6 (70.2-73.0)	<.001
Hemoglobin A_{1c}, %	7.9 (7.6-8.1)	7.0 (6.8-7.1)	<.001
	Weighted % (95% CI)		
Male sex	53.7 (47.4-59.9)	46.5 (41.5-51.6)	.04
Race/ethnicity			
Non-Hispanic white	59.7 (49.5-69.1)	66.4 (56.7-74.9)	.008
Non-Hispanic black	24.0 (18.2-30.8)	15.1 (10.6-21.1)	
Mexican American	9.6 (6.2-14.4)	7.4 (4.9-11.2)	
Other	6.8 (4.5-10.3)	11.1 (7.0-17.2)	
Less than high school education	31.8 (25.1-39.3)	25.4 (21.2-30.1)	.08
With health insurance	85.9 (80.3-90.1)	89.5 (85.5-92.5)	.26
Insulin use	44.6 (38.5-50.9)	10.2 (8.1-12.7)	<.001
BMI[a]			
Normal <25	11.3 (8.1-15.5)	11.1 (8.5-14.4)	.21
Overweight 25-<30	31.6 (23.0-41.7)	23.8 (20.2-27.9)	
Obese ≥30	57.1 (48.5-65.2)	65.0 (60.4-69.4)	
Smoker	17.2 (12.3-23.5)	18.0 (14.2-22.6)	.78
History of CVD (yes)	27.8 (22.6-33.8)	20.6 (16.8-25.1)	.06

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular diseases; NHANES, National Health and Nutrition Examination Surveys.
[a]BMI was calculated as weight in kilograms divided by height in meters squared.

COMMENT

This study provides the latest nationally representative estimates on the prevalence and risk factors for diabetic retinopathy in the United States. Earlier population-based studies showed that almost all individuals with type 1 diabetes and more than 60% of those with type 2 diabetes develop diabetic retinopathy during the first 2 decades of the disease.[2] With the expected increased prevalence of type 2 diabetes in the population, due in part to increasing rates of obesity and decreasing physical activity, the burden of diabetic retinopathy might be expected to increase as well.[33] However, improved access to screening for and treatment of diabetic retinopathy may reduce the burden of diabetes-related vision loss.

Our prevalence estimates are somewhat lower than those from a previous meta-analysis that compiled data from 8 population-based studies of non-Hispanic white, non-Hispanic black, and Hispanic people with diabetes from the United States and elsewhere that reported an overall estimate of prevalence of diabetic retinopathy of 40% and a prevalence of vision-threatening diabetic retinopathy of 8%.[13] However, the studies that were included in the meta-analysis were from regional cohorts, many were from prior decades, and most did not include individuals with undiagnosed diabetes. If undiagnosed diabetes were excluded from our sample, our estimates for diabetic retinopathy and vision-threatening diabetic retinopathy among self-reported diagnosed diabetes would be 32.8% (95% CI, 28.6-37.2) and 5.2% (95% CI, 4.0-6.7), respectively.

It is also possible that the lower prevalence reported in this study reflects a true reduction in the prevalence of diabetic retinopathy. Rates of other diabetic complications have declined during recent decades. For example, Geiss et al[34] found that hospitalization rate for lower extremity amputations among individuals with diabetes began decreasing in 1997. Another recent study found that age-adjusted diabetes-related end-stage renal disease decreased between 1996 and 2006.[35] Improved diabetes care, such as effective management of blood glucose levels, blood pressure, and serum lipid levels, is likely to reduce the incidence of diabetic retinopathy. Conversely, it might also lead to increased

survival resulting in higher prevalence of diabetic retinopathy. Moreover, a recent longitudinal cohort study suggested that low vision and blindness could be substantially reduced among individuals with diagnosed diabetes who received guideline-recommended levels of care.[36]

We found that the age-standardized prevalences of diabetic retinopathy and vision-threatening diabetic retinopathy were statistically significantly different between NHANES III and NHANES 2005-2008. These differences between surveys may be real or may be attributed to improved methods used to photograph the fundus in the more recent NHANES 2005-2008 compared with NHANES III. Two digital 45° color images of both eyes were taken in the NHANES 2005-2008 while in NHANES III only one 45° color film image from 1 eye was taken. Although some studies have shown grading of digital images to have similar sensitivity for detecting diabetic retinopathy as grading of film images, it is possible that the current method led to increased detection of both diabetic retinopathy and vision-threatening diabetic retinopathy because of more retina being assessed in 2 images compared with 1 and higher-quality digital images compared with earlier film images used in NHANES III, thus limiting our ability to directly compare results from NHANES III and current NHANES 2005-2008 study (R.K., unpublished data, 2009).

A previous analysis of NHANES III data by Harris et al[12] suggests that the prevalence of diabetic retinopathy was 46% higher in non-Hispanic black individuals and 84% higher in Mexican American individuals than in non-Hispanic white individuals. Although not statistically significant at a .05 level, we also found that among individuals with diabetes, non-Hispanic black individuals (47% higher) and Mexican American individuals (29% higher) had a higher crude prevalence of diabetic retinopathy than their non-Hispanic white counterparts. Moreover, the prevalence of vision-threatening diabetic retinopathy in individuals with diabetes was 190% higher in non-Hispanic black individuals and 130% higher in Mexican American individuals than in non-Hispanic white individuals. This may be due to individuals of non-Hispanic black and Mexican American heritage being more likely to have poorer glycemic control and being less likely to be screened and treated for diabetic retinopathy.[37] Data from National Health Interview Survey also suggest that non-Hispanic black individuals and Hispanics are less likely to use eye care services.[38] These findings lend further insight to inform national efforts to reduce disparities in care among racial/ethnic and socioeconomic groups and preserve sight for all adults in the United States.

Consistent with previous research, we found that higher levels of hemoglobin A_{1c}, longer duration of diabetes, insulin use, and higher systolic blood pressure were independently associated with diabetic retinopathy in the NHANES data.[29,39-41] This is

Table 3. Multiple Logistic Regressions for Risk Factors of Diabetic Retinopathy and Vision-Threatening Diabetic Retinopathy in Individuals With Diabetes Aged 40 Years and Older: NHANES 2005-2008

	Diabetic Retinopathy		Vision-Threatening Diabetic Retinopathy	
Characteristics	PM (95%CI)	OR (95%CI)	PM (95%CI)	OR (95%CI)
Age per y	NA	0.99 (0.95-1.02)	NA	1.00 (0.95-1.05)
Sex				
Male	38.1 (32.6-43.6)	2.07 (1.39-3.10)	6.1 (3.4-8.8)	1.79 (0.67-4.80)
Female	27.1 (22.4-31.8)	1 [Reference]	3.8 (1.9-5.7)	1 [Reference]
Race/ethnicity				
Non-Hispanic white	31.2 (25.4-37.0)	1 [Reference]	3.3 (1.6-5.0)	1 [Reference]
Non-Hispanic black	38.9 (30.4-47.4)	1.62 (0.81-3.26)	9.8 (5.7-13.8)	3.77 (1.47-9.69)
Mexican American	31.7 (19.5-43.9)	1.03 (0.39-2.76)	9.5 (2.0-17.0)	3.63 (1.05-12.56)
Other	29.3 (19.9-38.6)	0.88 (0.42-1.82)	2.9 (0-6.5)	0.86 (0.19-3.82)
Education				
<High school	33.8 (26.9-40.7)	1 [Reference]	6.3 (3.2-9.3)	1 [Reference]
≥High school	31.8 (26.8-36.7)	0.87 (0.51-1.50)	4.0 (2.1-5.9)	0.59 (0.22-1.54)
Health insurance				
Yes	31.8 (27.2-36.4)	0.74 (0.34-1.59)	5.1 (3.6-6.6)	2.27 (0.54-9.52)
No	36.5 (25.4-47.6)	1 [Reference]	2.5 (0-5.5)	1 [Reference]
Hemoglobin A_{1c} per percentage point	NA	1.45 (1.20-1.75)	NA	1.21 (0.97-1.50)
Duration of diabetes per y	NA	1.06 (1.03-1.10)	NA	1.03 (1.01-1.05)
Insulin use				
Yes	47.4 (39.1-55.8)	3.23 (1.99-5.26)	7.5 (4.8-10.1)	2.63 (1.34-5.15)
No	26.7 (21.9-31.5)	1 [Reference]	3.3 (1.9-4.7)	1 [Reference]
Systolic blood pressure per mm Hg	NA	1.03 (1.02-1.03)	NA	1.03 (1.01-1.06)
Diastolic blood pressure per mm Hg	NA	0.96 (0.93-0.98)	NA	0.96 (0.94-0.98)
BMI[a]				
Normal <25	30.9 (21.2-40.6)	1 [Reference]	4.0 (0-8.0)	1 [Reference]
Overweight 25-<30	37.0 (29.4-44.6)	1.49 (0.71-3.13)	4.8 (2.2-7.4)	1.25 (0.29-5.41)
Obese ≥30	30.3 (25.4-35.3)	0.96 (0.47-1.96)	5.0 (2.7-7.2)	1.31 (0.34-5.05)
Smoking status				
Yes	36.8 (25.4-48.3)	1.40 (0.67-2.92)	3.3 (1.1-5.5)	0.61 (0.25-1.47)
No	31.6 (27.3-35.9)	1 [Reference]	5.0 (3.5-6.5)	1 [Reference]
History of CVD				
Yes	33.5 (27.0-40.0)	1.10 (0.72-1.71)	6.4 (2.7-10.1)	1.69 (0.58-4.92)
No	32.0 (27.4-36.5)	1 [Reference]	4.2 (2.3-6.0)	1 [Reference]

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; NA, not applicable; NHANES, National Health and Nutrition Examination Surveys; OR, odds ratio; PM, predictive margin.
[a]BMI was calculated as weight in kilograms divided by height in meters squared.

consistent with findings from randomized controlled clinical trials that showed that modifying identified risk factors such as glycemic control and blood pressure control could reduce the burden of diabetic retinopathy and also prevent vision loss caused by it.[7,8] Prevention efforts may also need to target individuals with longer duration of diabetes and those using insulin. The new availability of care for vulnerable sections of the population should have demonstrable effect on risk of blindness in diabetes. Furthermore, primary prevention of diabetes, including identifying and protecting individuals at risk (ie, by reduced body weight and increased physical activity), may also help delay the onset of type 2 diabetes and reduce complications of diabetic retinopathy. We also found an inverse relationship between diastolic blood pressure and the presence of diabetic retinopathy. The underlying reason remains unexplained and requires further exploration. It could be due to selective participation bias. However, previous studies from Singapore[42] and Africa[43] also suggested a possible association between pulse pressure (difference between systolic and diastolic blood pressure) and diabetic retinopathy.

The strengths of this study include its population-based national sample, its inclusion of individuals with undiagnosed diabetes, and improved detection of retinopathy due to use of digital fundus images of both eyes. This improved methodology results in estimates that are less biased than those obtained from NHANES III. However, individuals without diabetes may have retinopathy because of higher glucose level or hypertension, which is not assessed in the current study. Also, due to the infrequency of proliferative diabetic retinopathy (n=23) and clinically significant macular edema (n=37), we were unable to provide meaningful estimates by age, sex, and race/ethnicity.

Our study is subject to several limitations. First, individuals who were institutionalized (eg, nursing home residents) were not included in the NHANES, which may have led to an underestimate of diabetic retinopathy prevalence. Second, we could not distinguish between type 1 and type 2 diabetes and the specific risk of diabetic retinopathy complications. Third, there were substantial numbers of eligible individuals with diabetes who did not have photographs that could be graded, which may negatively bias estimates of diabetic retinopathy prevalence. Survey participants who had no light perception or severe visual impairment in both eyes, or a severe infection in 1 or both eyes were excluded—this might negatively bias the prevalence estimates. Small sample sizes might have prevented us from detecting differences, if they existed, between and among subgroups. Due to limitations inherent with the NHANES sampling frame, we were unable to estimate the prevalence of diabetic retinopathy and vision-threatening diabetic retinopathy among racial/ethnic groups other than non-Hispanic white individuals, non-Hispanic black individuals, and Mexican American individuals.

CONCLUSIONS

Our data demonstrate that a high prevalence of diabetic retinopathy and vision-threatening diabetic retinopathy in the United States exists, especially among racial/ethnic minorities. Male sex, higher hemoglobin A_{1c} level, longer duration of diabetes, insulin use, and higher systolic blood pressure were independently associated with the presence of diabetic retinopathy. These estimates provide policy makers updated information for use in planning eye care services and rehabilitation. With the aging of the population and the increasing proportion of the population with diverse racial/ethnic heritage, the number of cases of diabetic retinopathy and vision-threatening diabetic retinopathy will likely increase. Furthermore, the need for eye care and for culturally appropriate interventions that can reduce disparity and improve access to eye care among diverse populations is also likely to increase.

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Study concept and design: Zhang, Saaddine, Cotch, Cheng, Albright.
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Analysis and interpretation of data: Zhang, Saaddine, Chou, Cotch, Cheng, Geiss, Gregg, Albright.
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REFERENCE

1. Klein R, Klein B. Vision disorders in diabetes. In: National Diabetes Data Group, ed. *Diabetes in America*. 2nd ed. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 1995:293–337.
2. Fong DS, Aiello L, Gardner TW, et al; American Diabetes Association. Retinopathy in diabetes. *Diabetes Care*. 2004;27(suppl 1):S84-S87.
3. Cheung N, Wong TY. Diabetic retinopathy and systemic vascular complications. *Prog Retin Eye Res*. 2008; 27(2):161-176.
4. Liew G, Wong TY, Mitchell P, Cheung N, Wang JJ. Retinopathy predicts coronary heart disease mortality. *Heart*. 2009;95(5):391-394.
5. Javitt JC, Aiello LP, Chiang Y, Ferris FL III, Canner JK, Greenfield S. Preventive eye care in people with diabetes is cost-saving to the federal government: implications for health-care reform. *Diabetes Care*. 1994; 17(8):909-917.
6. National Diabetes Data Group. *Diabetes in America*. 2nd ed. Bethesda, MD: National Institutes of Health,

National Institute of Diabetes and Digestive and Kidney Diseases; 1995.
7. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329(14):977-986.
8. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ*. 1998;317(7160):703-713.
9. Vijan S, Hofer TP, Hayward RA. Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus. *JAMA*. 2000; 283(7):889-896.
10. Javitt JC, Aiello LP. Cost-effectiveness of detecting and treating diabetic retinopathy. *Ann Intern Med*. 1996;124(1 pt 2):164-169.
11. Centers for Disease Control and Prevention. National diabetes fact sheet: general information and national estimates on diabetes in the United States, 2007. http://www.cdc.gov/diabetes/pubs/factsheet07.htm. Accessed February 2, 2010.
12. Harris MI, Klein R, Cowie CC, Rowland M, Byrd-Holt DD. Is the risk of diabetic retinopathy greater in non-Hispanic blacks and Mexican Americans than in non-Hispanic whites with type 2 diabetes? a US population study. *Diabetes Care*. 1998;21(8):1230-1235.
13. Kempen JH, O'Colmain BJ, Leske MC, et al; Eye Diseases Prevalence Research Group. The prevalence of diabetic retinopathy among adults in the United States. *Arch Ophthalmol*. 2004;122(4): 552-563.
14. Hovind P, Tarnow L, Rossing K, et al. Decreasing incidence of severe diabetic microangiopathy in type 1 diabetes. *Diabetes Care*. 2003;26(4):1258-1264.
15. Nordwall M, Bojestig M, Arnqvist HJ, Ludvigsson J; Linköping Diabetes Complications Study. Declining incidence of severe retinopathy and persisting decrease of nephropathy in an unselected population of type 1 diabetes-the Linköping Diabetes Complications Study. *Diabetologia*. 2004;47(7):1266-1272.
16. Klein R, Lee KE, Knudtson MD, Gangnon RE, Klein BE. Changes in visual impairment prevalence by period of diagnosis of diabetes: the Wisconsin Epidemiologic Study of Diabetic Retinopathy. *Ophthalmology*. 2009;116(10):1937-1942.
17. Centers for Disease Control and Prevention; National Center for Health Statistics. National Health and Nutrition Examination Survey questionnaire (or examination protocol, or laboratory protocol). http://www.cdc.gov/nchs/nhanes/nhanes2003-2004/analytical_guidelines.htm. Accessed February 2, 2010.
18. Centers for Disease Control and Prevention; National Center for Health Statistics. National Health and Nutrition Examination Surveys: response rates & CPS population totals. http://www.cdc.gov/nchs/nhanes/response_rates_CPS.htm. Accessed February 22, 2010.
19. Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs—an extension of the modified Airlie House classification: ETDRS report number 10: Early Treatment Diabetic Retinopathy Study Research Group. *Ophthalmology*. 1991; 98(5)(suppl):786-806.
20. Klein R, Klein BE, Magli YL, et al. An alternative method of grading diabetic retinopathy. *Ophthalmology*. 1986;93(9):1183-1187.
21. The Diabetic Retinopathy Study Research Group. Diabetic retinopathy study report number 6: design, methods, and baseline results; report number 7: a modification of the Airlie House classification of diabetic retinopathy. *Invest Ophthalmol Vis Sci*. 1981; 21(1 pt 2):1-226.
22. Klein R, Meuer SM, Moss SE, Klein BE, Neider MW, Reinke J. Detection of age-related macular degeneration using a nonmydriatic digital camera and a standard film fundus camera. *Arch Ophthalmol*. 2004; 122(11):1642-1646.
23. Wang C-Y, Haskell WL, Farrell SW, et al. Cardiorespiratory fitness levels among US adults 20-49 years of age: findings from the 1999-2004 National Health and Nutrition Examination Survey. *Am J Epidemiol*. 2010;171(4):426-435.
24. Holt D, Elliot D. Methods of weighting for unit non-response. *Statistician*. 1991;40(3):333-342 doi: 10.2307/2348286.
25. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010; 33(suppl 1):S62-S69.
26. Hirsch IB, Brownlee M. Beyond hemoglobin A_{1c}—need for additional markers of risk for diabetic microvascular complications. *JAMA*. 2010;303 (22):2291-2292.
27. Cheng YJ, Gregg EW, Geiss LS, et al. Association of A_{1c} and fasting plasma glucose levels with diabetic retinopathy prevalence in the US population: implications for diabetes diagnostic thresholds. *Diabetes Care*. 2009;32(11):2027-2032.
28. International Expert Committee. International Expert Committee report on the role of the A_{1c} assay in the diagnosis of diabetes. *Diabetes Care*. 2009; 32(7):1327-1334.
29. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy III: prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. *Arch Ophthalmol*. 1984;102(4):527-532.
30. Mitchell P, Smith W, Wang JJ, Attebo K. Prevalence of diabetic retinopathy in an older community: the Blue Mountains Eye Study. *Ophthalmology*. 1998; 105(3):406-411.
31. Klein R, Klein BE, Moss SE, Linton KL. The Beaver Dam Eye Study: retinopathy in adults with newly discovered and previously diagnosed diabetes mellitus. *Ophthalmology*. 1992;99(1):58-62.
32. Korn EL, Graubard BI. *Analysis of Health Surveys*. New York, NY: Wiley; 1999.
33. Saaddine JB, Honeycutt AA, Narayan KM, Zhang X, Klein R, Boyle JP. Projection of diabetic retinopathy and other major eye diseases among people with diabetes mellitus: United States, 2005-2050. *Arch Ophthalmol*. 2008;126(12):1740-1747.
34. Geiss L, Engelgau M, Pogach L, et al. A national progress report on diabetes: successes and challenges. *Diabetes Technol Ther*. 2005;7(1): 198-203.
35. Burrows NR, Li Y, Geiss LS. Incidence of treatment for end-stage renal disease among individuals with diabetes in the US continues to decline. *Diabetes Care*. 2010;33(1):73-77.
36. Sloan FA, Grossman DS, Lee PP. Effects of receipt of guideline-recommended care on onset of diabetic retinopathy and its progression. *Ophthalmology*. 2009;116(8):1515-1521.
37. Nsiah-Kumi P, Ortmeier SR, Brown AE. Disparities in diabetic retinopathy screening and disease for racial and ethnic minority populations—a literature review. *J Natl Med Assoc*. 2009;101(5):430-437.
38. Zhang X, Saaddine JB, Lee PP, et al. Eye care in the United States: do we deliver to high-risk people who can benefit most from it? *Arch Ophthalmol*. 2007; 125(3):411-418.
39. Wong TY, Klein R, Islam FM, et al. Diabetic retinopathy in a multi-ethnic cohort in the United States. *Am J Ophthalmol*. 2006;141(3):446-455.
40. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy II: prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol*. 1984;102(4):520-526.
41. Stratton IM, Kohner EM, Aldington SJ, et al. UKPDS 50: risk factors for incidence and progression of retinopathy in type II diabetes over 6 years from diagnosis. *Diabetologia*. 2001;44(2):156-163.
42. Wong TY, Cheung N, Tay WT, et al. Prevalence and risk factors for diabetic retinopathy: the Singapore Malay Eye Study. *Ophthalmology*. 2008; 115(11):1869-1875.
43. Nkondi Mbadi ANL-MB, Longo-Mbenza B, Mvitu Muaka M, Mbungu FS, Lemogoum D. Relationship between pulse pressure, visual impairement and severity of diabetic retinopathy in sub-Saharan Africa. *Mali Med*. 2009;24(3):17-21.

