Global Prevalence and Major Risk Factors of Diabetic Retinopathy

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OBJECTIVE—To examine the global prevalence and major risk factors for diabetic retinopathy (DR) and vision-threatening diabetic retinopathy (VTDR) among people with diabetes.

RESEARCH DESIGN AND METHODS—A pooled analysis using individual participant data from population-based studies around the world was performed. A systematic literature review was conducted to identify all population-based studies in general populations or individuals with diabetes who had ascertained DR from retinal photographs. Studies provided data for DR end points, including any DR, proliferative DR, diabetic macular edema, and VTDR, and also major systemic risk factors. Pooled prevalence estimates were directly age-standardized to the 2010 World Diabetes Population aged 20–79 years.

RESULTS—A total of 35 studies (1980–2008) provided data from 22,896 individuals with diabetes. The overall prevalence was 34.6% (95% CI 34.5–34.8) for any DR, 6.96% (6.87–7.04) for proliferative DR, 6.81% (6.74–6.89) for diabetic macular edema, and 10.2% (10.1–10.3) for VTDR. All DR prevalence end points increased with diabetes duration, hemoglobin A_{1c}, and blood pressure levels and were higher in people with type 1 compared with type 2 diabetes.

CONCLUSIONS—There are approximately 93 million people with DR, 17 million with proliferative DR, 21 million with diabetic macular edema, and 28 million with VTDR worldwide. Longer diabetes duration and poorer glycemic and blood pressure control are strongly associated with DR. These data highlight the substantial worldwide public health burden of DR and the importance of modifiable risk factors in its occurrence. This study is limited by data pooled from studies at different time points, with different methodologies and population characteristics.

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Diabetic retinopathy (DR) is the leading cause of blindness among working-aged adults around the world (1). Despite the significance of this problem, and the rising prevalence of diabetes notably in emerging Asian countries such as India and China (2,3), there are few precise contemporary estimates of the worldwide prevalence of DR, particularly severe vision-threatening stages of the disease, including proliferative DR (PDR) and diabetic macular edema (DME).

Previous individual studies have shown considerable variability in DR prevalence estimates among individuals with both diagnosed and undiagnosed diabetes, with rates ranging from 17.6% in a study in India (4) to 33.2% in a large U.S. study (5). Differences in study methodologies, population characteristics, and ascertainment and classification of DR have made direct comparisons between studies difficult. A meta-analysis summarized the U.S. prevalence of DR (6), but this study was limited to individuals with type 2 diabetes aged 40 years and older, and the data were largely derived from individuals of Caucasian background, with limited data on other racial groups. More important, this study did not include Asians, and an estimated 100 million people in China and 80 million in India have diabetes (2,3).

Although the major risk factors for DR (e.g., hyperglycemia, hypertension, dyslipidemia) have been examined in many epidemiologic studies and clinical trials (1), there is considerable variation in the consistency, pattern, and strength of these risk factors. This is particularly so with respect to severe stages of DR, because individual studies generally lack

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power to detect significant associations for PDR and DME. Thus, the importance of modifiable risk factors for these vision-threatening stages of DR remains unclear.

Generating a broader and more precise estimate of the prevalence of DR and its relationship with major modifiable risk factors, specifically for vision-threatening DR (VTDR), is crucial for guiding public health education and optimal clinical management of diabetes. We therefore conducted an individual participant analysis pooling population-based studies from the U.S., Australia, Europe, and Asia to determine the prevalence of DR and its sight-threatening end points (PDR and DME) as well as their relationship to key risk factors.

RESEARCH DESIGN AND METHODS

Study selection and inclusion criteria

We first performed a systematic literature review to identify all population-based studies that had ascertained DR from fundus (retinal) photographs. English-language articles were retrieved using Medline, EMBASE, Current Contents, EBSCO, JSTOR, and Science Direct using the following search terms: "diabetes" and "retinopathy" or "diabetic macular edema" and "population." We identified 3,539 citations identified to 10 February 2010. Irrelevant and duplicate citations were excluded after a review of the titles and abstracts. The full texts of the remaining articles were reviewed to ensure studies met inclusion and exclusion criteria. In addition, we manually reviewed bibliographies of included articles and consulted with colleagues to identify other potentially relevant population-based studies that had assessed DR from fundus photographs but which may not have published results or in which grading for DR was still ongoing.

Studies were excluded if they were not population-based and/or if fundus photographs were not undertaken to ascertain DR. Two investigators (J.Y., R.Kaw.) independently selected the studies for inclusion. Disagreements between the two were resolved by adjudication with two additional reviewers (S.R., T.Y.W.).

We identified 58 population-based studies in which fundus photographs were potentially assessed for DR. Principal investigators of these identified studies were then invited for collaboration in this individual participant meta-analysis. We requested individual participant data regarding presence and severity of DR, DME status, age, sex, ethnicity, diabetes type and duration, hemoglobin A_{1c} (HbA_{1c}), systolic and diastolic blood pressure, lipid profile, cigarette smoking status, BMI, and current use of diabetes, antihypertensive, and lipid-lowering medications.

Investigators from 35 of the 58 identified studies provided data for this analysis (Table 1). Investigators of the remaining 23 studies could not or did not want to participate, or did not respond to repeated invitations. All studies had institutional board review approval and provided appropriately deidentified data for analysis.

DR assessment and definition

Retinal photography was performed in all 35 studies according to standardized protocols. Most of the studies graded for DR using the Early Treatment Diabetic Retinopathy Scale (ETDRS) and its modification or the American Academy of Ophthalmology (AAO) International Clinical Diabetic Retinopathy Disease Severity Scale (Table 1).

DR severity was categorized as non-PDR (NPDR; level 20 through level 53) and PDR (level ≥60). DME was defined as absent or present. The four primary outcomes for this study were based on the severity in the worse eye or of the single eye that was photographed. Any DR was defined as the presence of NPDR, PDR, DME, or any combination thereof; and VTDR was defined as the presence of PDR and/or DME. These composite outcomes serve as the primary outcomes for this report, which respectively, indicate presence of any DR and severe DR likely to result in vision loss if left untreated.

Definition of diabetes and major risk factors

Not all studies reported information on diabetes type. If data on age at diagnosis of diabetes were available in these studies, participants were classified as type 1 if they were diagnosed before age 30 years and as type 2 if they were diagnosed with diabetes after age 30 years, as previously used in one study (7). Hypertension was defined in subjects with a blood pressure >140/90 or who reported being on treatment for hypertension. Serum cholesterol was categorized into levels <4.0 or ≥4.0 mmol/L.

Appraisal of study methodology and heterogeneity

Study methodology and heterogeneity were assessed independently by two investigators (J.Y., R.Kaw.). Any disagreement was settled by consensus or adjudication with a third reviewer (S.R.). Studies were assessed for a list of attributes as defined in Supplementary Table 1. Studies with similar methodologies and rigorous

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*A complete list of the study group can be found in the Supplementary Data online.

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Table 1—*Characteristics of diabetic participants in each study population* (N = 35)

							Fundus photography						Grading method	
Study	Country	Year of photo	T2DM (%)	Male (%)	Mean age (range)	Ethnicity (%)	Eyes/sub	Dilated	Mydriasis	Field	Deg	Stereo	DR	DME
T1DM only														
EDC	U.S.	1986–1988	0	50.6	27.6 (8–48)	98 EU, 2 AA	2	√	√	3	30	√	ETDRS	CSME
Fyn	Denmark	2007–2008	0	59.8	58.6 (37–88)	100 EU	2	√	√	9	45	X	ETDRS	CSME
New Jersey 725	U.S.	1993–1998	0	40.4	27.5 (3–60)	100 AA	2	√	√	7	30	√	EDTRS	Other[1]
Turin	Italy	2006–2008	0	53.0	29.5 (7–68)	100 EU	2	√	X	2	45	X	AAO	No data
T2DM only														
Aarhus	Denmark	2000	100	56.5	65.0 (32–90)	100 EU	2	√	√	2	60	X	EDTRS	CSME
ADDITION	Denmark	2003	100	56.5	63.8 (43–78)	100 EU	2	√	√	2	60	X	ETDRS†	CSME
CURES ES	India	2001–2002	100	44.8	50.8 (20–85)	100 AS	2	√	√	4	30	√	ETDRS	CSME
Funagata	Japan	2000–2002	100	57.3	67.1 (37–92)	100 AS	1	X	X	1	45	X	ETDRS	CSME
Hoorn	Netherlands	1989–1992	100	45.9	64.9 (50–76)	100 EU	2	√	√	2	45	X	Eurodiab	No data
Samutsakhon	Thailand	2007	100	28.3	59.2 (27–86)	100 AS	2	X	X	7	30	√	Other[2]	No data
San Luis Valley	U.S.	1984–1988	100	43.3	58.6 (22–75)	66 HI, 34 EU	2	√	√	3	30	√	ETDRS	CSME
UKADS	U.K.	2004–2007	100	53.1	64.3 (17–96)	59 EU, 41 AS	2	√	X	2	45	√	UK NSCG	UK NSCG
T1DM and T2DM														
AusDiab	Australia	1999–2000	96.5	51.4	63.0 (25–91)	92 EU, 5 AS	2	X	X	2.	45	X	ETDRS	Other[3]
BDES	U.S.	1988–1990	88.3	44.4	65.8 (44–86)	99 EU	2	√	√	7	30	√	ETDRS	CSME
Handan	China	2006–2007	99.7	35.9	57.6 (30–83)	100 AS	2	√	√	2	45	X	ETDRS	CSME
LALES	U.S.	2000–2003	97.6	43.8	58.5 (40–90)	100 HI	2	√	√	7	30	√	ETDRS	CSME
San Antonio	U.S.	1985–1986	97.8	40.6	54.4 (31–70)	82 HI, 18 EU	2	√	√	7	30	√	ETDRS	No data
WESDR	U.S.	1980–1982	58.5	48.5	50.9 (3–97)	99 EU, 1 AA	2	√	√	7	30	√	EDTRS	CSME
DM type not reported but deduced from age at diagnosis*														
Andhra Pradesh	India	1996–2000	97.9*	52.4	55.0 (25–86)	100 AS	1	√	√	2	30	√	Other[4]	Other[4]
Beijing	China	2006	100*	41.6	64.9 (45–87)	100 AS	2	√	X	2	45	X	ETDRS	CSME
BES	U.S.	1985–1988	95.6*	37.4	62.7 (40–91)	57 AA, 43 EU	2	√	√	2	45	√	Other[2]	No data
CHS	U.S.	1997–1998	99.1*	46.5	78.0 (69–95)	75 EU, 25 AA	1	X	X	1	45	X	ETDRS	CSME
EUREYE	7 European‡	2000–2003	99.2*	51.0	72.9 (64–93)	100 EU	2	√	√	1	35	√	Other[5]	No data
Hisayama	Japan	1998	98.5*	56.9	65.8 (43–96)	100 AS	2	√	X	1	45	X	ETDRS	No data
MVIP	Australia	1992–1994	96.7*	55.8	65.6 (42–97)	100 EU	2	√	X	2	30	√	AAO	CSME
NHANES	U.S.	2005–2008	95.4*	50.1	62.4 (40–85)	39 EU, 30 AA, 20 HI	2	X	X	2	45	√	ETDRS	CSME
Proyecto VER	U.S.	1997–1999	96.5*	37.3	60.5 (40–88)	100 HI	2	√	√	4	30	√	EDTRS	CSME
SINDI	Singapore	2007–2010	97.6*	52.3	61.0 (43–84)	89 AS	2	√	X	2	45	X	ETDRS	Other[6]
SNDREAMS	India	2004–2006	99.2*	53.0	56.3 (40–85)	100 AS	2	√	√	7	30	√	AAO	CSME

Table 1—*Continued*

Study	Country	Year of photo	T2DM (%)	Male (%)	Mean age (range)	Ethnicity (%)	Fundus photography						Grading method	
							Eyes/sub	Dilated	Mydriasis	Field	Deg	Stereo	DR	DME
DM type not reported and could not be deduced														
ARIC	U.S.	1993–1995	NR	47.5	60.8 (50–71)	64 EU, 36 AA	1	X	X	1	45	X	ETDRS	CSME
BMES	Australia	1992–1994	NR	53.0	67.9 (51–96)	97 EU, 2 AS	2	√	√	6	30	√	ETDRS	CSME
MESA	U.S.	2002–2004	NR	52.0	65.5 (46–86)	36 AA, 30 HI, 22 EU, 12AS	2	X	X	2	45	X	EDTRS	Other[7]
Rotterdam	Netherlands	1990–1993	NR	39.4	72.9 (55–96)	96 EU, 4 O	2	√	√	1	35	√	Other[5]	No data
Shihpai	Taiwan	1999–2000	NR	61.1	71.7 (65–90)	100 AS	2	√	√	2	35	X	AAO	CSME
SiMES	Singapore	2004–2006	NR	43.3	62.6 (40–80)	100 AS	2	√	X	2	45	X	ETDRS	Other[6]

AA, African American; AAO, American Academy of Ophthalmology; AS, Asian; CSME, clinically significant macular edema; DM, diabetes mellitus; ETDRS, Early Treatment Diabetic Retinopathy Study; EU, Caucasian, European ancestry; Eyes/sub, eyes per subject; HI, Hispanic; NR, not reported and could not be deduced; O, others; UK NSCG, United Kingdom National Screening Committee guidelines. ADDITION, Anglo-Danish-Dutch study of Intensive Treatment in People with Screen-detected Diabetes in Primary Care; ARIC, Atherosclerosis Risk in Communities Study; Andhra Pradesh, Andhra Pradesh Eye Disease Study; AusDiab, Australian Diabetes, Obesity and Lifestyle Study; BDES, Beaver Dam Eye Study; BES, Baltimore Eye Survey; BMES, Blue Mountains Eye Study; Beijing, Beijing Eye Study; CHS, Cardiovascular Health Study; CURES ES, Chennai Urban Rural Epidemiology Study (Eye Study); EDC, Pittsburgh Epidemiology of Diabetes Complications Study; EUREYE; European Eye Study; Funagata, Funagata Study; Handan, Handan Eye Study; Hisayama, Hisayama Study; Hoorn, Hoorn Study; LALES, Los Angeles Latino Eye Study; MESA, Multiethnic Study of Atherosclerosis; MVIP, Melbourne Vision Impairment Project; NHANES, National Health and Nutrition Examination Survey; Proyecto VER, Proyecto Vision and Eye Research; Rotterdam, Rotterdam Study; SiMES, Singapore Malay Eye Study; SINDI, Singapore Indian Eye Study; SNDREAMS, Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study; T1DM, type 1 diabetes; T2DM, type 2 diabetes; UKADS, UK Asian Diabetes Study; WESDR, Wisconsin Epidemiologic Study of Diabetic Retinopathy. * DM type not reported by study but could be deduced from provided information regarding subject's age and duration of diabetes: Type 1 diabetes was assumed if subject was aged less than 30 years at diagnosis; type 2 diabetes was assumed if subject was aged 30 years or older at diagnosis. †ETDRS includes modified WESDR, modified Airlie House, modified ETDRS. ‡7 European countries: Norway, Estonia, UK, France, Italy, Greece, Spain. [1]Other: Macular edema (ME) = retinal thickening within 1 disc diameter of center of macula or history of ME with history of photocoagulation confirmed by treating physician. [2]Other: Not reported. [3]Other: Hard exudates (HE) within 1 disc diameter of macula. [4]Other: Adapted from Olk RJ, Lee CM. *Diabetic Retinopathy: Practical Management*. Philadelphia: JB Lippincott, 1993:3–20. [5]Other: Graded for presence of microaneurysms (MA) and/or dot hemorrhages with ICD codes. [6]Other: ME = HE in the presence of MA and blot hemorrhage within 1 disc diameter from foveal center or presence of focal photocoagulation scars in the macular area. [7]Other: Clinically significant macular edema (CSME) = macular edema within 500 μm of foveal center, or if photocoagulation scars were present in the macular area.

ophthalmologic definitions were defined as those with a score of ≥9 (maximum, 11).

Statistical analysis

Data from each study were checked for consistency in variable definition before pooling, and where appropriate, data were recategorized according to a common definition. Race/ethnicity was categorized as Caucasian (Europeans and those of European origin), Asian (Chinese, Chinese American, Japanese, Malay, Indian, or people of Asian origin), African American, and Hispanic (Mexican Americans). Asians were further subdivided into Chinese or Japanese origin, and South Asian (Indian, Malay, South Indian, Thai, etc). Study-specific and pooled-data estimates of the prevalence of any DR, PDR, DME, and VTDR were directly age-standardized to the 2010 world diabetes population aged 20–79 years (8) using age strata 20–39, 40–59, and 60–79 years. We calculated 95% CIs for standardized prevalence rates using a normal approximation and Breslow-Day standard errors, after being modified to use a binomial assumption for the variance of the crude stratum-specific rates (9).

Initial analyses included data from all 35 studies, and subsequent analyses were performed using only data from studies with similar methodologies and outcome definitions (i.e., studies with a score of ≥9). Results from the latter analyses are presented throughout this report because of their similar methodologies.

Poisson regression models with robust error variance were used to estimate relative risks for DR, PDR, DME, and VTDR by categories of risk factors (e.g., hypertension, duration), adjusting for age (continuous, from 20–79 years), race (five categories), hypertension (yes/no), HbA_{1c} (four categories) and study, as appropriate. We also performed supplementary analyses on the interaction between diabetes type and duration, using people with type 2 diabetes for <10 years as the reference group. Including sex in regression models generally did not improve the model fit and did not appreciably alter the results.

Global estimates

The total number of patients with diabetes with DR aged between 20 and 79 years was estimated by multiplying the 2010 country-specific totals of people with diabetes (sourced from Diabetes Atlas) by our pooled racial group–specific rates of DR using the most predominant racial

group per country; for example, in Brazil, where 53.7% of country is "white" (according to 2000 census results listed in Central Intelligence Agency, *The World Factbook*) (10), our pooled Caucasian rate was applied, and in countries where the predominant racial group did not easily align with our limited pooled racial groups (e.g., Melanesians in Papua New Guinea), the overall pooled world rate was applied.

All analyses were undertaken using Stata Intercooled 11.1 software (StataCorp LP, College Station, TX).

RESULTS—Data were collated from 22,896 individuals from 35 studies in the U.S., Australia, Europe, and Asia. Of these, 52% were female, 44.4% were Caucasian, 30.9% were Asian, 13.9% were Hispanic, and 8.9% were African American. The mean age was 58.1 years (range 3–97), median diabetes duration was 7.9 years (interquartile range [IQR] 3–16), and median HbA_{1c} was 8.0% (6.7–9.9%). Summary characteristics of the diabetic participants from each of the included studies are presented in Table 1 and Supplementary Table 2.

Analyses of these 35 studies showed that the overall age-standardized prevalence of any DR was 34.6% (95% CI 34.5–34.8), PDR was 6.96% (6.87–7.04), DME was 6.81% (6.74–6.89), and VTDR was 10.2% (10.1–10.3; data not shown). Analyses confined to studies with similar methodologies and rigorous outcome definitions showed that the age-standardized prevalence was 35.4% (35.2–35.6) for any DR, 7.24% (7.15–7.33) for PDR, 7.48% (7.39–7.57) for DME, and 11.7% (11.6–11.8) for VTDR (Table 2). There was no discernible sex difference in the prevalence of any DR or for PDR, DME, or VTDR. Extrapolating these prevalence rates to the 2010 world diabetes population, we estimate that 92.6 million (91.2–94.0) adults had any DR, 17.2 million (16.6–17.7) had PDR, 20.6 million (19.6–21.6) had DME, and 28.4 million (27.6–29.2) had VTDR.

Table 3 reports the age-standardized prevalence of any DR by retinopathy risk factors and other subgroups of interest. The prevalence of any DR varied across ethnic groups and was highest among African Americans and lowest among Asians. The prevalence of any DR increased with diabetes duration (21.1 vs. 76.3%, comparing <10 with ≥20 years), HbA_{1c} (18.0 vs. 51.2%, comparing levels ≤7.0 with >9.0%), and blood pressure (30.8 vs. 39.6%, comparing blood pressure ≤140/90 or >140/90), and was higher in people with type 1 than type 2 diabetes (77.3 vs. 25.2%). Similar relationships were also evident in the prevalence patterns of PDR, DME, and VTDR. There was a trend toward a higher prevalence of VTDR stages, but not any DR, in people with cholesterol levels ≥4.0 mmol/L. Analysis by year/period of fundus photography suggests a decline in the prevalence of any DR in the post-2000 era (Table 3).

Table 2—*Age-standardized prevalence of DR in diabetic subjects aged 20–79 years, using studies with similar methodologies and ophthalmologic definitions*

Overall	Studies included (*n*)	Total (*N*)	Cases (*n*)	Age-standardized prevalence per 100 (95% CI)
Any DR	18	12,620	4,487	35.36 (35.17–35.56)
PDR	21	13,436	957	7.24 (7.15–7.33)
DME	20	14,554	1,039	7.48 (7.39–7.57)
VTDR	18	12,710	1,481	11.72 (11.61–11.83)
Men				
Any DR	18	6,252	2,263	36.27 (35.99–36.55)
PDR	21	6,376	469	7.53 (7.39–7.66)
DME	20	7,010	486	7.44 (7.30–7.57)
VTDR	18	6,051	704	11.74 (11.57–11.90)
Women				
Any DR	18	6,368	2,224	34.46 (34.19–34.73)
PDR	21	7,060	488	6.98 (6.86–7.10)
DME	20	7,544	553	7.54 (7.42–7.66)
VTDR	18	6,659	777	11.70 (11.55–11.86)

After adjusting for known risk factors, individuals with type 1 diabetes for ≥20 years were 2.7 times more likely to have any DR (relative risk 2.69 [96% CI 2.47–2.93]), 15 times more likely to have PDR (15.3 [11.3–20.8]), 5 times more likely to have DME (4.83 [3.71–6.30]), and 8.7 times more likely to have VTDR (8.69 [7.10–10.63]) compared with those with type 2 diabetes for <10 years (Table 4).

CONCLUSIONS—This study provides a global estimate of the prevalence of DR and the severe stages of DR (PDR, DME) using individual-level data from population-based studies worldwide. On the basis of the data from all 35 studies on more than 20,000 participants with diabetes, we estimated that among individuals with diabetes, the overall prevalence of any DR was 34.6%, PDR was 7.0%, DME was 6.8%, and VTDR was 10.2%. Analyses confined only to studies with similar methodologies and ophthalmologic definitions showed that the age-standardized prevalence of any DR was 35.4%, PDR was 7.2%, DME was 7.4%, and VTDR was 11.7%, among individuals with diabetes. The prevalence estimates of any DR and VTDR were similar in men and women and were highest in African Americans and lowest in Asians. Prevalence rates were substantially higher in those with type 1 diabetes and increased with duration of diabetes, and values for HbA_{1c}, blood pressure, and cholesterol. Extrapolated to the world diabetes population in 2010, we estimate that approximately 93 million may have some DR, and 28 million may have sight-threatening stages of DR.

The prevalence of DR has been previously reported in a number of population-based samples (11–16). However, prevalence estimates varied considerably across some studies, depending on the population and study methodology. For example, variable prevalence rates were reported between populations of different ethnicities (e.g., 32.4% in an Australian Caucasian cohort (14) vs. 48.0% in a Mexican American cohort (15)) as well as between different populations of the same ethnicity (e.g., 35% in a U.S. Caucasian cohort (13) and 15.3% in a more recent Australian Caucasian cohort). More important, prevalence estimates for the more severe and vision-threatening end points, such as PDR and DME, are scarce, due to the small numbers of these cases from individual population-based studies. Published estimates for VTDR prevalence (17–20), for example, ranges widely, from 1.2 (17) to 32.2% (18). Our study provides the first precise estimates for these important clinical subgroups of DR.

The most comparable study to ours is the pooled analysis for prevalence of DR

Table 3—*Age-standardized prevalence of DR by subgroups of interest, in diabetic subjects aged 20–79 years, using studies with similar methodologies and ophthalmologic definitions*

	Any DR (cases/total)	PDR (cases/total)	DME (cases/total)	VTDR (cases/total)	Age-standardized prevalence per 100 (95% CI)			
					Any DR	PDR	DME	VTDR
Sex								
Male	2,263/6,252	469/6,376	486/7,010	704/6,051	36.27 (35.99–36.55)	7.53 (7.39–7.66)	7.44 (7.30–7.57)	11.74 (11.57–11.90)
Female	2,224/6,368	488/7,060	553/7,544	777/6,659	34.46 (34.19–34.73)	6.98 (6.86–7.1)	7.54 (7.42–7.66)	11.7 (11.55–11.86)
Race								
Caucasian	2,814/6,021	666/5,573	453/5,345	856/5,516	45.76 (45.44–46.07)	12.04 (11.87–12.21)	8.42 (8.28–8.57)	15.45 (15.25–15.64)
Chinese	202/751	26/1,025	31/568	42/751	25.08 (24.25–25.91)	2.67 (2.26–3.07)	8.12 (6.88–9.36)	6.14 (5.55–6.73)
South Asian	886/4,463	40/3,196	270/5,220	165/3,100	19.12 (18.88–19.35)	1.29 (1.22–1.36)	4.93 (4.82–5.04)	5.2 (5.05–5.34)
African Americans	378/678	61/670	70/673	111/678	49.56 (48.59–50.52)	8.99 (8.58–9.40)	10.35 (9.90–10.79)	16.89 (16.32–17.46)
Hispanic	151/448	159/2,830	209/2,490	301/2,523	34.56 (33.24–35.87)	5.10 (4.91–5.29)	7.15 (7.0–7.3)	10.85 (10.44–11.25)
Asian (combined)	1,088/5,214	66/4,221	301/5,788	207/3,851	19.92 (19.7–20.14)	1.54 (1.48–1.61)	5.0 (4.89–5.12)	5.25 (5.12–5.39)
Diabetes type*								
Type 1	1,740/2,277	594/2,314	305/1,864	716/2,315	77.31 (76.34–78.28)	32.39 (31.76–33.01)	14.25 (13.86–14.64)	38.48 (37.80–39.16)
Type 2	2,633/9,666	356/1,0464	671/1,1244	742/9,814	25.16 (24.96–25.36)	2.97 (2.91–3.02)	5.57 (5.48–5.66)	6.92 (6.83–7.02)
Diabetes duration								
<10 years	1,394/6,747	88/7,207	243/7,685	238/6,771	21.09 (20.87–21.30)	1.23 (1.18–1.28)	3.15 (3.08–3.23)	3.53 (3.45–3.62)
10 to <20 years	1,544/2,702	278/2,852	368/2,842	479/2,698	54.22 (53.73–54.71)	9.06 (8.86–9.25)	13.43 (13.19–13.66)	17.78 (17.5–18.05)
≥20 years	1,338/1,752	582/1,840	344/1,734	727/1,789	76.32 (75.61–77.04)	31.66 (31.21–32.11)	19.96 (19.58–20.34)	40.87 (40.35–41.38)
HbA_{1c}								
≤7.0%	562/3,290	85/3,285	125/3,975	147/3,038	17.99 (17.64–18.33)	3.1 (2.93–3.26)	3.59 (3.42–3.76)	5.40 (5.19–5.60)
7.1–8.0%	624/1,856	129/1,896	133/2,344	202/1,860	33.13 (32.64–33.62)	6.87 (6.63–7.10)	6.30 (6.06–6.54)	10.82 (10.53–11.10)
8.1–9.0%	701/1,546	168/1,652	141/1,843	230/1,626	43.1 (42.53–43.66)	9.64 (9.37–9.90)	7.69 (7.46–7.93)	13.64 (13.33–13.95)
>9.0%	1,995/3,700	485/4,098	546/4,346	773/4,076	51.2 (50.8–51.6)	10.93 (10.76–11.11)	12.49 (12.31–12.67)	18.35 (18.13–18.58)
Blood pressure								
Normal	2,037/5,900	307/6,243	369/6,516	521/6,122	30.84 (30.59–31.09)	4.16 (4.07–4.25)	5.45 (5.35–5.55)	7.60 (7.48–7.72)
Hypertensive†	2,407/6,583	632/6,791	661/7,900	958/6,568	39.55 (39.19–39.91)	12.32 (12.08–12.57)	10.59 (10.37–10.81)	17.63 (17.36–17.9)
Total cholesterol								
<4 mmol/L	503/1,619	56/1,064	69/1,624	89/1,056	31.64 (31.11–32.17)	5.12 (4.87–5.36)	4.60 (4.37–4.83)	8.09 (7.78–8.40)
≥4.0 mmol/L	2,491/8,074	409/7,072	534/8,289	664/6,798	31.06 (30.82–31.29)	5.67 (5.56–5.78)	6.78 (6.67–6.9)	9.55 (9.42–9.69)
Era of study‡								
Pre-2000	2,502/4,645	692/6,162	505/5,139	907/5,530	49.57 (49.21–49.93)	10.58 (10.43–10.73)	9.28 (9.14–9.43)	15.62 (15.43–15.81)
Post-2000	1,985/7,975	265/7,274	534/9,415	574/7,180	24.79 (24.57–25.00)	3.47 (3.40–3.55)	5.46 (5.35–5.56)	7.86 (7.74–7.98)

Data are *n*/*n* unless otherwise indicated. Note: Data in this table come from high-quality studies only. High-quality studies were those that scored ≥9/11 on our score, and, for "Any DR" outcome, the DR grading could distinguish ≥level 20 and the study provided DME data; for "PDR outcome," the DR grading could distinguish ≥level 60; for DME outcome the study provided DME data; for "VTDR outcome," the DR grading could distinguish ≥level 60 and the study provided DME data. *Diabetes type includes the diabetes type information provided by each study plus the calculated diabetes type based on the age at diagnosis assumption. Type is missing if this information was not provided, and/or age at diagnosis could not be determined. †Hypertension was defined in subjects with a blood pressure >140/90 mmHg or who reported being on treatment for hypertension. ‡Era of study was the period during which the fundus photography was undertaken.

Table 4—*Age-standardized prevalence of DR by diabetes type and duration, in diabetic subjects aged 20–79 years, using studies with similar methodologies and ophthalmologic definitions*

DM type	DM duration (years)	Total (*N*)	Cases (*n*)	Age-standardized prevalence per 100 (95% CI)	Adjusted relative risk* (95% CI)
Any DR					
Type 1	<10	456	202	20.53 (18.73–22.34)	1.38 (1.19–1.59)
Type 1	10 to <20	794	624	55.55 (51.34–59.76)	2.43 (2.19–2.69)
Type 1	20+	1,026	914	86.22 (85.07–87.37)	2.69 (2.47–2.93)
Type 2	<10	6,291	1,192	18.11 (17.91–18.31)	1.0
Type 2	10 to <20	1,908	920	51.10 (49.53–52.66)	2.06 (1.91–2.23)
Type 2	20+	726	424	52.15 (51.12–53.19)	2.45 (2.24–2.68)
PDR					
Type 1	<10	458	10	0.37 (0.31–0.43)	0.90 (0.44–1.86)
Type 1	10 to <20	803	141	19.46 (16.38–22.53)	6.72 (4.70–9.61)
Type 1	20+	1,052	443	40.36 (39.60–41.12)	15.33 (11.29–20.80)
Type 2	<10	6,749	78	1.06 (1.02–1.10)	1.0
Type 2	10 to <20	2,049	137	6.92 (6.41–7.42)	4.32 (3.16–5.91)
Type 2	20+	788	139	15.13 (14.64–15.63)	9.79 (7.14–13.43)
DME					
Type 1	<10	399	13	0.55 (0.48–0.63)	0.59 (0.32–1.07)
Type 1	10 to <20	587	91	12.27 (11.43–13.1)	2.50 (1.77–3.52)
Type 1	20+	877	201	17.31 (16.83–17.8)	4.83 (3.71–6.30)
Type 2	<10	7,286	230	3.07 (2.99–3.16)	1.0
Type 2	10 to <20	2,255	277	11.94 (11.42–12.47)	3.22 (2.68–3.87)
Type 2	20+	857	143	16.47 (15.93–17.01)	4.56 (3.67–5.67)
VTDR					
Type 1	<10	456	20	0.74 (0.65–0.82)	0.85 (0.52–1.38)
Type 1	10 to <20	804	178	14.29 (13.61–14.97)	3.97 (3.08–5.12)
Type 1	20+	1,054	518	47.2 (46.38–48.03)	8.69 (7.10–10.63)
Type 2	<10	6,315	218	3.37 (3.28–3.47)	1.0
Type 2	10 to <20	1,894	301	16.14 (15.41–16.87)	3.73 (3.10–4.49)
Type 2	20+	735	209	25.95 (25.26–26.65)	6.27 (5.14–7.65)

DM, diabetes. *Adjusted for age (continuous, from 20–79 years), race (5 categories), hypertension (yes/no), HbA_{1c} (4 categories) and study.

in the U.S. (6). On the basis of eight population studies derived from the U.S. and Australia, an overall prevalence of 40% for any DR and 8% for VTDR was reported (6). These estimates, however, represented findings limited to individuals aged older than 40 years and only with type 2 diabetes, were largely derived from individuals of Caucasian background, did not evaluate PDR and DME separately, and did not include studies from Asia. Ours is the first synthesis of individual-level data from all eligible population-based studies worldwide with a sufficiently large sample to allow a more precise estimation of the prevalence of PDR and DME.

Some of the differences in DR prevalence between individual studies may be partly attributed to the differing periods of the studies (Table 1 and Supplementary Table 3). Improvements in the management of DR and diabetes, and increased screening for diabetes, may have led to lower DR incidence and prevalence over time (21). Furthermore, DR susceptibility may also vary among ethnic groups. In support of the latter hypothesis, a number of multiethnic cohort studies have reported a higher DR prevalence among Mexican Americans than in non-Hispanic whites (5,22,23). Others, however, showed a similar or lower prevalence of DR in African Americans (18) and Mexican Americans (24) than in non-Hispanic whites. In some studies (5), after adjusting for putative DR risk factors, racial differences in the prevalence of DR was attributed to differing levels of risk factors for DR, but in others, the excess risk was unexplained (22,23,25). Differences in socioeconomic factors, including access to and the level of diabetes care, and possibly genetic susceptibility (26), may also possibly explain some of the disparities in rates and severity of DR in the different ethnic groups. In addition, racial differences in the effect of DR risk factors could also have accounted for some of these variations (23,27). Population-based studies incorporating host and environmental data are needed to further clarify the effect of race and ethnicity on DR prevalence.

We highlight several key points regarding the major risk factors for DR: First, we confirm the importance of the three major risk factors for DR—diabetes duration (17,19,28), HbA_{1c} (17,28–32), and blood pressure (17,28,33)—and suggest that they apply broadly across the mild to vision-threatening stages of DR.

Second, we establish that higher total serum cholesterol was associated with a higher prevalence of DME, bringing clarity to previously conflicting reports about this risk factor (19). This is particularly relevant to recent reports from trials suggesting that fenofibrate, a lipid-altering agent, may slow the development and progression of DR (34). Fenofibrate, however, acts mostly on triglycerides, and its effects on retinopathy in those trials were independent of lipid levels achieved. Statins, however, did not affect DR severity in the few studies in which this was evaluated, although not as a primary outcome (35,36).

Third, we provide estimates of risk of DR by diabetes type, in which studies in individuals with type 1 diabetes are currently scarce. We showed that the prevalence of DR is substantially higher in type 1 than in type 2 diabetes (11,37), an outcome independent of diabetes duration. However, because we classified type of diabetes by age of onset (younger or older than age 30 years), in some studies there may be potential misclassification (e.g., some people with type 2 diabetes will be younger than 30 years).

The strengths of our study include a large sample size to determine prevalence and risk factor associations for sight-threatening end points (PDR, DME), the inclusion of diverse ethnic population samples from around the world, and studies that had used photographic documentation of DR.

Our study has limitations. Pooling of data from various sources introduces many potential sources of heterogeneity that could influence accuracy; thus, although our estimates are highly precise, their accuracy is unknown. Samples of different study designs could have considerably

different inclusion criteria, sample selection, and study protocols. For example, population samples could have varied considerably between a cardiovascular disease study and an eye survey, or a study on diabetes complications.

There was also a range of methods used in ascertaining diabetes status. Studies in which diagnosis of diabetes was based on self-report, without confirmation from blood tests, could have resulted in an overestimate of DR prevalence rates because those with undiagnosed diabetes might have been erroneously excluded from the sample denominator.

Furthermore, there were differences in the methodologies used to detect and diagnose DR, such as the number of eyes photographed per subject, number of retinal fields examined per eye, and the grading protocols and definitions used. In studies that did not collect data on diabetes type, this information was defined on the basis of age of diagnosis, with a cutoff at age 30 years to use as many studies with detailed information other than types of diabetes. Misclassification could have occurred as a result of this assumption. This, however, would not have affected the overall prevalence estimates but could have had a small effect of attenuating the comparative estimates between the type 1 and type 2 diabetes groups. A few studies with large numbers of participants could have influenced our results. Finally, the absence of studies from the Middle East, Africa, or South America could also affect the accuracy of our findings.

In conclusion, our current study provides the first global estimate of DR and, more important, the two sight-threatening end points (PDR and DME), based on a pooled individual participant analysis of more than 20,000 participants from 35 studies around the world. Our study shows that 35% of people with diabetes had some form of DR, and that 7% had PDR, 7% had DME, and 10% were affected by these vision-threatening stages. We estimate that in 2010, approximately 93 million were affected by DR, and 28 million by VTDR. This suggests that DR has the potential to be the leading cause of visual impairment and blindness worldwide. We confirmed the importance and impact of three major modifiable risk factors—hyperglycemia, hypertension, and dyslipidemia—on the risk of all DR end points, including for the first time, PDR and DME. These results highlight the substantial public health effect of diabetes, and thus, the need for effective screening and management of DR risk factors.

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