Incidence and progression of diabetic retinopathy in a multi-ethnic US cohort: the Multi-Ethnic Study of Atherosclerosis

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ABSTRACT

Aim To provide contemporary longitudinal data on the incidence and progression of diabetic retinopathy (DR) in a multi-ethnic population of whites, African Americans, Chinese and Hispanics in the United States.

Methods A prospective, multi-region, multi-ethnic population-based cohort study that included 498 participants with diabetes, aged 45–84 years at baseline, from the Multi-Ethnic Study of Atherosclerosis with retinal images obtained twice, on average 8 years apart. Presence and severity of DR were graded from these retinal images according to the modified Airlie House classification system. Main outcome measures were 8-year incidence, progression and improvement of DR, and their associated risk factors.

Results Over the 8 years, the cumulative rates were 19.2% for incident DR, 17.3% for DR progression, 23.3% for DR improvement, 2.7% for incident vision-threatening DR, 1.8% for incident proliferative DR and 2.2% for incident macular oedema. In multivariate analysis, significant risk factors associated with incident DR were higher glycosylated haemoglobin (relativerisk (RR) 1.28; 95% CI: 1.16 to 1.41) and higher systolic blood pressure (RR 1.14; 95% CI: 1.04 to 1.25). Significant factors associated with DR progression were higher glycosylated haemoglobin (RR 1.20; 95% CI: 1.00 to 1.43) and higher low-density lipoprotein cholesterol (RR 1.01; 95% CI: 1.00 to 1.03).

Conclusion Over an 8-year period, approximately one in five participants with diabetes developed DR, while almost a quarter of those with DR at baseline showed improvement, possibly reflecting the positive impact of clinical and public health efforts in improving diabetes care in the United States over the last two decades.

INTRODUCTION

Over 400 million people have diabetes worldwide, with numbers projected to increase to 650 million by 2040.[1] In the United States alone, about 30 million people have diabetes.[2] Diabetic retinopathy (DR) therefore remains a global threat to vision and the economy.[3 4] However, there are few sources of contemporary population-based longitudinal data on the incidence and progression of DR in the United States.[5]

A recent systematic review of all DR incidence studies reports that most of the contemporary studies (published after year 2000) were conducted in Asia.[5] All incidence studies from the United States were published before 2000, except for the Los Angeles Latino Eye Study (LALES).[6] Notably, the annual incidence of DR appears to be lower in studies published after 2000.[5] Long-term follow-up data from the Wisconsin Epidemiologic Study of Diabetic Retinopathy also corroborate this observation.[7 8] The trend of declining DR incidence may reflect earlier detection of diabetes, improved metabolic control and DR screening programmes.[9] Moreover, there is a lack of contemporary, longitudinal studies in the United States and other developed countries with accessible and high-quality healthcare systems, in which to assess possible race/ethnicity differences in DR incidence.

This study, conducted after 2000, estimates the incidence, progression and improvement of DR in a multi-ethnic population-based US sample.

METHODS

The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective cohort study of adults, aged 45–84 years at baseline (between 2000 and 2002), sampled from six communities in the United States, who were free of clinical cardiovascular disease at entry. Details of the MESA study design and methodology have been described previously.[10] We included 498 participants with diabetes at baseline for the current analyses (online supplemental figure). All participants underwent extensive assessment for atherosclerotic disease and its risk factors during the course of the study.[10–12] Diabetes was defined as fasting glucose ≥7.0 mmol/L (≥126 mg/dL) or use of insulin or oral hypoglycaemic medication. Written informed consent was obtained from all the participants.

Retinal photography and DR grading

A standardised study protocol was followed for fundus photography and retinopathy grading at the second and fifth MESA examinations.[12–14] Briefly, participants were seated in a darkened room where a 45-degree, 6.3-megapixel digital non-mydriatic camera (Canon, Lake Success, New York, USA) was used to capture two photographic fields of each eye, the first centred on the optic disc and the second centred on the fovea. Images were analysed at the University of Wisconsin-Madison Ocular Epidemiology Reading Center, where DR grading was performed according to standardised protocols and definitions.[12–14]

Retinopathy was considered to be present if any characteristic lesion as defined by the Early

Table 1 Baseline characteristics of the MESA participants with diabetes

		Incident DR			DR progression		
	All	Yes	No		Yes	No	
	N=498*	N=70	N=295	P value	N=23	N=110	P value
Age, years	63.2 (8.9)	62.0 (9.4)	63.8 (8.8)	0.118	58.7 (7.5)	63.2 (8.8)	0.026
Gender, female	247 (49.6)	38 (54.3)	144 (48.8)	0.41	9 (39.1)	56 (50.9)	0.304
Ethnicity							
White	114 (22.9)	18 (25.7)	75 (25.4)	0.318	2 (8.7)	19 (17.3)	0.573
Chinese	57 (11.5)	11 (15.7)	35 (11.9)		2 (8.7)	9 (8.2)	
African American	169 (33.9)	16 (22.9)	99 (33.6)		12 (52.2)	42 (38.2)	
Hispanic	158 (31.7)	25 (35.7)	86 (29.2)		7 (30.4)	40 (36.4)	
Education							
High school or lower	214 (43.0)	35 (50.0)	122 (41.4)	0.189	10 (43.5)	47 (42.7)	0.947
College or higher	284 (57.0)	35 (50.0)	173 (58.6)		13 (56.5)	63 (57.3)	
Total household income							
<US$25 000	170 (34.1)	29 (41.4)	100 (33.9)	0.113	7 (30.4)	34 (30.9)	0.889
US$25 000 to US$50 000	165 (33.1)	25 (35.7)	89 (30.2)		8 (34.8)	43 (39.1)	
>US$50 000	163 (32.7)	16 (22.9)	106 (35.9)		8 (34.8)	33 (30.0)	
Diabetes duration, year	9.4 (7.9)	6.5 (3.8)	7.2 (6.3)	0.579	9.5 (6.0)	13.7 (9.6)	0.096
Cigarette smoker, current	54 (10.9)	10 (14.3)	27 (9.2)	0.208	5 (21.7)	12 (11.0)	0.163
Body mass index	31.2 (6.1)	32.1 (6.6)	31.0 (6.1)	0.219	31.1 (5.3)	31.3 (6.0)	0.887
Hip-to-waist ratio	1.04 (0.08)	1.05 (0.07)	1.05 (0.07)	0.975	1.05 (0.07)	1.04 (0.09)	0.697
Physical activity, hours/week	72.2 (73.4)	76.8 (77.4)	69.6 (75.4)	0.478	90.7 (65.7)	72.3 (67.1)	0.231
Hypertension	312 (63.8)	39 (55.7)	181 (63.3)	0.243	12 (52.2)	80 (72.7)	0.052
Anti-hypertensive medications							
Diuretics	107 (22.4)	20 (29.0)	57 (20.4)	0.125	8 (34.8)	22 (20.6)	0.142
Angiotensin 2 antagonist	46 (9.6)	5 (7.2)	18 (6.5)	0.812	4 (17.4)	19 (17.8)	0.967
ACE inhibitor	163 (34.1)	19 (27.5)	90 (32.3)	0.449	9 (39.1)	45 (42.1)	0.796
Systolic blood pressure, mm Hg	128.7 (21.4)	131.6 (19.7)	126.3 (19.1)	0.040	123.7 (19.2)	134.0 (26.9)	0.082
Diastolic blood pressure, mm Hg	70.9 (10.1)	71.9 (8.8)	70.8 (10.2)	0.403	71.6 (9.4)	70.6 (10.8)	0.669
Insulin use	42 (8.8)	5 (7.2)	11 (3.9)	0.241	4 (17.4)	22 (20.6)	0.73
HbA1c, %	7.3 (1.7)	7.9 (2.0)	6.9 (1.2)	<0.001	9.3 (2.7)	7.6 (1.7)	<0.001
Total cholesterol, mmol/L	181.0 (35.6)	183.6 (39.4)	180.4 (34.9)	0.493	193.5 (38.2)	178.6 (34.3)	0.071
HDL cholesterol, mmol/L	46.9 (12.5)	46.1 (13.8)	46.5 (11.5)	0.816	44.9 (10.4)	48.9 (14.5)	0.224
LDL cholesterol, mmol/L	103.5 (31.0)	101.7 (30.0)	103.3 (31.9)	0.709	122.9 (34.5)	101.7 (27.6)	0.002
Statin use	177 (37.0)	21 (30.4)	105 (37.6)	0.265	8 (34.8)	43 (40.2)	0.63
Homocysteine	9.2 (3.2)	8.4 (2.4)	9.5 (3.5)	0.021	9.3 (3.3)	8.8 (2.6)	0.393
C reactive protein	4.6 (5.8)	4.6 (4.6)	4.6 (6.1)	0.977	5.2 (8.8)	4.5 (4.7)	0.591
Proteinuria	116 (23.5)	17 (24.6)	57 (19.5)	0.344	6 (26.1)	36 (32.7)	0.533
Internal carotid IMT, mm	1.14 (0.63)	1.05 (0.51)	1.13 (0.64)	0.376	1.15 (0.56)	1.25 (0.66)	0.511
Z-score maximum IMT	0.18 (0.96)	0.08 (0.96)	0.15 (0.95)	0.591	0.15 (0.88)	0.32 (0.99)	0.452

Data for a given column are expressed as numbers (percentages) for categorical variables or means (SDs) for continuous variables; p values calculated based on simple χ^2 or Wilcox test (categorical), or independent sample t tests, comparing characteristics between participants with and without incident DR or DR progression.
*Of these, 133 participants had DR at baseline eye examination (ie, were not at risk of incident DR at follow-up eye examination).
ACE, angiotensin converting enzyme; DR, diabetic retinopathy; HbA1c, glycosylated hemoglobin; HDL, high-density lipid; IMT, intima-media thickness; LDL, low-density lipoprotein ; MESA, Multi-Ethnic Study of Atherosclerosis.

Treatment Diabetic Retinopathy Study severity scale was present: microaneurysms, haemorrhages, cotton wool spots, intraretinal microvascular abnormalities, hard exudates, venous beading and new vessels. For each eye, retinopathy severity was assigned according to the modified Airlie House Classification system (online supplemental table).[12–14] The DR level for a participant at a given examination was derived by concatenating the collapsed retinopathy levels for the two eyes, giving the eye with the higher-level greater weight. This scheme provided a 15-step scale (10/10, 20<20, 20/20, 31<31, 31/31, 41<41, 41/41, 51<51, 51/51, 60<60, 60/60, 65<65, 65/65, 70<70, 70/70). For purposes of classification, if the DR severity could not be graded in an eye, it was considered to have a score equivalent to that in the other eye. The cumulative incidence of any DR was estimated from all persons who had no DR at examination 2 (severity level step 1, that is, 10/10) and who participated in the follow-up examination and had a severity level at step 2 are higher (eg, 20<20). For analysis of PDR, steps 12 and above (60+) were grouped as one level. Incidence of PDR was estimated from all persons who were free of this complication at examination 2 but had this level of severity at examination 5. For persons with no or only non-proliferative DR at examination 2 (step 9 or less), progression was defined as an increase in the severity of DR by two steps or more at examination 5. Similarly, improvement in DR was defined for persons with levels 20/20 to 51/51 (severity levels at nine or under) at examination

Table 2 Eight-year incidence and progression of DR in the MESA

	Incident DR		DR progression		DR improvement		Incident VTDR		Incident PDR		Incident CSME	
	No at risk	Incidence (%)	No at risk	Incidence (%)	No at risk	Incidence (%)	No at risk	Incidence (%)	No at risk (%)	Incidence (%)	No at risk	Incidence (%)
Total	365	70 (19.2)	133	23 (17.3)	133	31 (23.3)	482	13 (2.7)	491	9 (1.8)	465	10 (2.2)
White	93	18 (19.4)	21	2 (9.5)	21	3 (14.3)	112	1 (0.9)	113	1 (0.9)	106	1 (0.9)
African American	115	16 (13.9)	54	12 (22.2)	54	15 (27.8)	164	3 (1.8)	167	3 (1.8)	154	2 (1.3)
Hispanic	111	25 (22.5)	47	7 (14.9)	47	10 (21.3)	151	8 (5.3)	156	4 (2.6)	149	6 (4.0)
Chinese	46	11 (23.9)	11	2 (18.2)	11	3 (27.3)	55	1 (1.8)	55	1 (1.8)	56	1 (1.8)
P value		0.318		0.573		0.623		0.116		0.794		0.285

DR progression/improvement was defined as a two-step or more change (+/–) in the DR severity scale as described in online supplemental table 1.
CSME, clinically significant macular oedema; DR, diabetic retinopathy; MESA, Multi-Ethnic Study of Atherosclerosis; PDR, proliferative diabetic retinopathy; VTDR, vision-threatening diabetic retinopathy.

2 who had a two-step or more decrease in the severity of DR at examination 5.

Macular oedema was defined as hard exudate in the presence of microaneurysm and blot haemorrhage within one-disc diameter from the foveal centre or presence of focal photocoagulation scars in the macular area. Clinically significant macular oedema (CSME) was considered present when the macular oedema was within 500 µm of the foveal centre or if focal photocoagulation scars were present in the macular area. Vision-threating diabetic retinopathy (VTDR) was defined as the presence of severe NPDR-proliferative retinopathy or CSME. If an eye was ungradable, the scores for the other eye were used to define these outcomes.

Risk factor assessment

All participants underwent an extensive assessment for atherosclerotic disease and its risk factors during the course of the study.[10] Data for this analysis were based on those collected at the baseline examination. Standardised questionnaires were used to obtain information about medical history, education level, annual household income, cigarette smoking, alcohol consumption, use of hormone replacement therapy and antihypertensive and antidiabetic medications taken. Smoking was defined as current, former or never. Duration of diabetes was estimated from the age of first use of diabetic medication. Diabetic medication use was defined to include oral hypoglycaemic medications and/or insulin. Diabetes was defined as fasting glucose ≥7.0 mmol/L (≥126 mg/dL) or use of insulin or oral hypoglycaemic medication. Resting blood pressure was measured three times with participants in the seated position. The average of the last two measurements was used in analysis. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg or current use of antihypertensive medications. Height and weight were measured with participants wearing light clothing and no shoes. Body mass index was calculated as weight in kilograms divided by height in square metres. The waist-hip ratio was defined as the ratio of the waist circumference and the hip circumference, measured in centimetres.

Blood samples were assayed for putative biochemical risk factors, including levels of cholesterols, glycosylated haemoglobin, homocysteine and C reactive protein. Analyses were performed at a central site at the Collaborative Studies Clinical Laboratory at Fairview–University Medical Center (Minneapolis, Minnesota, USA). Low-density lipoprotein (LDL) cholesterol was calculated with the Friedewald equation. Carotid artery intima-media thickness was measured using B-mode ultrasound according to a standardised protocol as detailed elsewhere.[15]

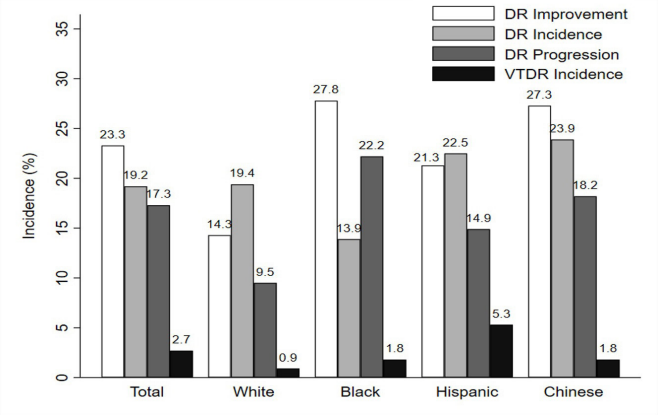

Figure 1 Incidence and progression of DR by ethnic groups in the Multi-Ethnic Study of Atherosclerosis. DR, diabetic retinopathy; VTDR, vision-threatening diabetic retinopathy; DR progression/improvement was defined as a two-step or more change (+/–) in the DR severity scale as described in online supplemental table.

Statistical analysis

Incidence and progression estimates were calculated, with participants having DR at examination 2 excluded from the estimate of incidence, but only these individuals contributed to analyses of progression and improvement. Comparisons of traditionally associated risk factors, as listed in table 1, with incident DR outcomes were interrogated by race/ethnic group using χ^2 (for categorical variables) and independent sample t tests (for continuous variables). Univariate Poisson regression models were performed to examine associations, with significant factors associated with DR incidence or progression ($p<0.05$), along with age, gender and race/ethnicity, being included in a multivariable model. All statistical analyses were performed using STATA statistical software: release 15.0 (StataCorp LP).

RESULTS

Table 1 summarises baseline characteristics for the 498 participants with diabetes. Compared with participants without incident DR, those with incident DR had higher levels of systolic blood pressure and glycosylated haemoglobin and lower levels of homocysteine. Compared with those without DR progression, participants whose DR progressed were younger and had higher levels of glycosylated haemoglobin and LDL cholesterol.

Incidence rates were 19.2% for DR, 17.3% for DR progression, 23.3% for DR improvement, 2.7% for VTDR, 1.8% for

Table 3 Risk factors for DR incidence and progression in the MESA

	DR incidence		DR progression	
Risk factors	**RR (95% CI)***	**RR (95% CI)†**	**RR (95% CI)***	**RR (95% CI)†**
Age, per year	0.98 (0.96 to 1.01)	0.99 (0.97 to 1.02)	**0.95 (0.91 to 0.99)**	0.99 (0.94 to 1.04)
Gender, female	1.19 (0.78 to 1.82)	1.05 (0.67 to 1.63)	0.67 (0.31 to 1.45)	0.44 (0.17 to 1.09)
Ethnicity				
White	Reference	Reference	Reference	Reference
Chinese	1.24 (0.64 to 2.40)	1.21 (0.63 to 2.34)	1.91 (0.31 to 11.85)	1.13 (0.23 to 5.51)
African American	0.72 (0.39 to 1.33)	0.56 (0.30 to 1.07)	2.33 (0.57 to 9.60)	1.86 (0.49 to 7.11)
Hispanic	1.16 (0.68 to 2.00)	0.91 (0.52 to 1.57)	1.56 (0.35 to 6.94)	1.11 (0.25 to 5.03)
Diabetes duration, per year	0.98 (0.94 to 1.03)		0.94 (0.88 to 1.00)	
Education				
College or higher	Reference		Reference	
High school or lower	1.32 (0.87 to 2.02)		1.03 (0.48 to 2.18)	
Total household income				
>US$50 000	Reference		Reference	
US$25 000 to US$50 000	1.67 (0.94 to 2.97)		0.80 (0.33 to 1.96)	
<US$25 000	1.71 (0.98 to 3.00)		0.88 (0.35 to 2.20)	
Cigarette smoker, current	1.47 (0.82 to 2.62)		1.88 (0.80 to 4.41)	
Body mass index, per unit	1.02 (0.99 to 1.05)		1.00 (0.94 to 1.06)	
Hip-to-waist ratio, per 0.1 unit	1.00 (0.74 to 1.33)		1.09 (0.75 to 1.58)	
Physical activity, per hour/week	1.00 (1.00 to 1.00)		1.00 (1.00 to 1.01)	
Hypertension	0.78 (0.51 to 1.18)		0.49 (0.23 to 1.01)	
Hypertension medications				
Diuretics	1.44 (0.91 to 2.26)		1.78 (0.83 to 3.79)	
Angiotensin 2 antagonists	1.10 (0.49 to 2.47)		0.98 (0.37 to 2.62)	
ACE inhibitor	0.83 (0.52 to 1.34)		0.90 (0.42 to 1.94)	
Systolic blood pressure, per 10 mm Hg	**1.11 (1.01 to 1.22)**	**1.14 (1.04 to 1.25)**	0.85 (0.72 to 1.01)	
Diastolic blood pressure, per 10 mm Hg	1.09 (0.90 to 1.32)		1.08 (0.79 to 1.46)	
Insulin use	1.62 (0.76 to 3.47)		0.84 (0.31 to 2.27)	
HbA1c, per %	**1.32 (1.19 to 1.45)**	**1.28 (1.16 to 1.41)**	**1.29 (1.13 to 1.47)**	**1.20 (1.00 to 1.43)**
Total cholesterol, per mmol/L	1.00 (1.00 to 1.01)		1.01 (1.00 to 1.02)	
HDL cholesterol, per mmol/L	1.00 (0.98 to 1.02)		0.98 (0.95 to 1.01)	
LDL cholesterol, per mmol/L	1.00 (0.99 to 1.01)		**1.02 (1.01 to 1.03)**	**1.01 (1.00 to 1.03)**
Statin use	0.77 (0.48 to 1.23)		0.83 (0.38 to 1.81)	
Homocysteine	**0.91 (0.84 to 0.98)**	0.93 (0.85 to 1.00)	1.05 (0.94 to 1.18)	
C reactive protein	1.00 (0.97 to 1.03)		1.02 (0.95 to 1.09)	
Proteinuria	1.27 (0.78 to 2.06)		0.76 (0.32 to 1.81)	
Internal carotid IMT, mm	0.85 (0.60 to 1.19)		0.79 (0.41 to 1.52)	
Z-score maximum IMT	0.94 (0.74 to 1.19)		0.85 (0.57 to 1.26)	

Systolic blood pressure and hypertension were evaluated in separate multivariable models due to high collinearity.
Bold values represent statistically significant associations (p<0.05)
Multivariate adjusted RR (95% CI).
*Univariate unadjusted relative risk (RR) and 95% CI.
†Multivariate adjusted RR (95% CI).
ACE, angiotensin converting enzyme; DR, diabetic retinopathy; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; IMT, intima-media thickness; LDL, low-density lipoprotein; MESA, Multi-Ethnic Study of Atherosclerosis.

proliferative DR and 2.2% for CSME (table 2). Although Hispanics were most likely to develop VTDR (5.3%), followed by African Americans (1.8%), Chinese (1.8%) and whites (0.9%) (figure 1), these differences were not statistically significant (p=0.116). Risk factors significantly associated with incident DR were higher glycosylated haemoglobin and higher systolic blood pressure (table 3). Risk factors significantly associated with DR progression were higher glycosylated haemoglobin and LDL cholesterol.

In supplementary analyses (data not shown), we observed no significant difference between age or gender groups for the incidence of DR outcomes. None of the factors examined in table 3 was significantly associated with DR improvement.

DISCUSSION

In this multi-ethnic population-based cohort study, we provide contemporary US estimates on the incidence and progression of DR. We found that over an 8-year period, approximately one in every five participants with diabetes developed incident DR, whereas 23% of participants with DR showed improvement in disease severity. The incidence for VTDR was 2.7%, despite the potential for prompt treatment to prevent this complication. Higher blood pressure and poorer glycaemic control, both treatable, were associated with increased risk of incident DR. Respectively, each per cent higher glycosylated haemoglobin and each

10 mm Hg higher systolic blood pressure were associated with 28% and 14% increased risk of developing DR over 8 years.

Directly comparable studies with contemporary data on the incidence and progression of DR in countries with high income economies are lacking. Of the 14 population-based studies with incidence data on DR, only 8 were conducted after year 2000.[5] Sample sizes of these studies ranged from 117 to 775 participants. None of these studies was conducted in the United States, except for the LALES that focused on Hispanics (Mexican Americans) only. In the LALES, the 4-year incidence of DR was 34% and progression of DR was 39%.[6] These are much higher estimates than observed in MESA. Although our data showed that Hispanics were most likely to develop VTDR, their 8-year DR incidence was 22.5% and DR progression was 14.9%. These differences may reflect differences in study populations and/or methodologies. The MESA population was free of clinically overt cardiovascular disease at baseline and may therefore be healthier than that of the LALES, as reflected by younger age (mean age of 55 years vs 63 years in the LALES), fewer participants with long duration of diabetes (21% vs 47% >10 years) and better glycaemic control (mean HbA1c of 6.4% vs 8.5%). Moreover, MESA used two-field non-stereoscopic retinal imaging to assess DR, whereas the LALES used seven-field stereoscopic retinal imaging. This could also partly explain the differences in the results. Nevertheless, it has been shown that two-field retinal imaging performs generally well against seven-field imaging in the assessment of DR.[16]

Strengths of our study include its multi-ethnic, population-based sample, prospective design, standardised photographic assessment of DR by trained graders in a central grading centre with a low number of ungradable photographs and standardised assessment of risk factors. However, our sample size was relatively small, and the low incidence rates limited the precision of the risk estimates and power to assess some of the less common risk factors. It also limited our ability to perform more in-depth analyses for the less common but more severe forms of DR.

In summary, our study provides contemporary population-based data on the incidence and progression of DR in the United States. Our data suggest that compared with estimates reported in older studies, the incidence and progression of DR have decreased substantially, consistent with earlier detection of diabetes and improved clinical management, which has occurred over the last two decades. The suggestion of disparities in outcomes and the association of DR progression with treatable risk factors indicate further opportunity for improvement.

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Contributors NC contributed to data analysis and interpretation, initial drafting, critical review and final revision of the manuscript; MLC contributed to data analysis, critical review and final revision of the manuscript; RK, BEKK, SS, MFC and TYW contributed to securing funding and conducting the study, critical review and final revision of the manuscript; C-YC contributed to critical review and final revision of the manuscript.

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Competing interests None declared.

Patient consent for publication Obtained.

Ethics approval The MESA cohort is being drawn from six regions in the United States: Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; New York, New York; and St Paul, Minnesota. The institutional review boards of the six field centers have approved the study protocol. References: Bild DE, *et al*. *Am J Epidemiol*. 2002;156:871–81. No approval number or ID, but you can refer to references above or link below for detailed study protocol, which is public information (https://www.mesa-nhlbi.org).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data are de-identified participant data from the Multi-Ethnic Study of Atherosclerosis. Approval was given to use these data from the study committee.

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REFERENCES

1 Ogurtsova K, da Rocha Fernandes JD, Huang Y, *et al*. IDF diabetes atlas: global estimates for the prevalence of diabetes for 2015 and 2040. *Diabetes Res Clin Pract* 2017;128:40–50.
2 Prevention CfDCa. *National diabetes statistics report 2017*. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services, 2017. https://www.cdc.gov/diabetes/data/statistics/statistics-report.html
3 Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. *Lancet* 2010;376:124–36.
4 Tan GS, Cheung N, Simó R, *et al*. Diabetic macular oedema. *Lancet Diabetes Endocrinol* 2017;5:143–55.
5 Sabanayagam C, Banu R, Chee ML, *et al*. Incidence and progression of diabetic retinopathy: a systematic review. *Lancet Diabetes Endocrinol* 2019;7:140–9.
6 Varma R, Choudhury F, Klein R, *et al*. Four-year incidence and progression of diabetic retinopathy and macular edema: the Los Angeles Latino eye study. *Am J Ophthalmol* 2010;149:752–61.
7 Klein R, Knudtson MD, Lee KE, *et al*. The Wisconsin epidemiologic study of diabetic retinopathy XXIII: the twenty-five-year incidence of macular edema in persons with type 1 diabetes. *Ophthalmology* 2009;116:497–503.
8 Klein R, Knudtson MD, Lee KE, *et al*. The Wisconsin epidemiologic study of diabetic retinopathy: XXII the twenty-five-year progression of retinopathy in persons with type 1 diabetes. *Ophthalmology* 2008;115:1859–68.
9 Cheung N, Wong TY. Changing trends of blindness: the initial harvest from translational public health and clinical research in ophthalmology. *Am J Ophthalmol* 2012;153:193–5.
10 Bild DE, Bluemke DA, Burke GL, *et al*. Multi-Ethnic study of atherosclerosis: objectives and design. *Am J Epidemiol* 2002;156:871–81.
11 Bertoni AG, Whitt-Glover MC, Chung H, *et al*. The association between physical activity and subclinical atherosclerosis: the multi-ethnic study of atherosclerosis. *Am J Epidemiol* 2009;169:444–54.
12 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;31:544–9.
13 Wong TY, Liew G, Tapp RJ, *et al*. Relation between fasting glucose and retinopathy for diagnosis of diabetes: three population-based cross-sectional studies. *Lancet* 2008;371:736–43.
14 Wong TY, Klein R, Islam FMA, *et al*. Diabetic retinopathy in a multi-ethnic cohort in the United States. *Am J Ophthalmol* 2006;141:446–55.
15 Folsom AR, Kronmal RA, Detrano RC, *et al*. Coronary artery calcification compared with carotid intima-media thickness in the prediction of cardiovascular disease incidence: the multi-ethnic study of atherosclerosis (MESA). *Arch Intern Med* 2008;168:1333–9.
16 Scanlon PH, Malhotra R, Greenwood RH, *et al*. Comparison of two reference standards in validating two field mydriatic digital photography as a method of screening for diabetic retinopathy. *Br J Ophthalmol* 2003;87:1258–63.