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The 3 Year Incidence and Cumulative Prevalence of Retinopathy:

The Atherosclerosis Risk In Communities Study

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Abstract

Purpose—To describe the 3 year incidence and cumulative prevalence of retinopathy and its risk factors.

Design—Population-based, prospective cohort study in four U.S. communities

Methods—In the Atherosclerosis Risk in Communities Study, 981 participants had retinal photography of one randomly selected eye at the 3rd examination (1993-95) and 3 years later at the 4th examination (1996). Photographs were graded on both occasions for retinopathy signs (e.g., microaneurysm, retinal hemorrhage, cotton wool spots). Incidence was defined as participants without retinopathy at the 3rd examination who developed retinopathy at the 4th examination, and cumulative prevalence was defined to include incident retinopathy as well as participants who had retinopathy at both the 3rd and 4th examinations.

Results—The 3-year incidence anad cumulative prevalence of any retinopathy in the whole cohort was 3.8% and 7.7%, respectively. In multivariable analysis, incident retinopathy was related to higher mean arterial blood pressure (OR 1.5, 95% CI 1.0, 2.3, per standard deviation increase in risk factor levels), fasting serum glucose (OR 1.6, 95% CI, 1.3, 2.1), serum total cholesterol (OR 1.4, 95% CI, 1.0, 2.0), and plasma fibrinogen (OR 1.4, 95% CI, 1.1, 1.9). Among persons without diabetes, the 3 year incidence and cumulative prevalence of non-diabetic retinopathy was 2.9% and 4.3%, respectively. Incident non-diabetic retinopathy was related to higher mean arterial blood pressure (OR 1.4, 95% CI, 0.9, 2.3) and fasting serum glucose (OR 1.5, 95% CI, 1.0, 2.3). Among persons with diabetes, the 3-year incidence and cumulative prevalence of diabetic retinopathy was 10.1% and 27.2%, respectively.

Conclusions—Retinopathy signs occur frequently in middle-aged people, even in those without diabetes. Hypertension and hyperglycemia are risk factors for incident retinopathy.

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Retinopathy signs (e.g., single microaneurysm, retinal hemorrhage, and/or cotton wool spots) are common fundus findings in older people, even in those without diabetes.[1, 2] Recent population-based studies show that among non-diabetic persons aged 40 years and older, up to 10% may have some retinopathy signs as detected from fundus photographs.[3-6] Although their underlying pathophysiology remains uncertain, these retinopathy signs have been shown to be a risk marker of subclinical cerebrovascular disease, and to predict incident hypertension,[7] clinical stroke,[8-11] congestive heart failure,[12] and cardiovascular mortality in people with and without diabetes.[13, 14]

There are few prospective data on the incidence of retinopathy signs in the general population.[15-17] The Beaver Dam Eye Study found that over a five year period, 6.0% of persons aged 43-86 years without diabetes developed retinopathy signs.[15] Hypertension, but not other cardiovascular risk factors (serum total and HDL cholesterol, glycosylated hemoglobin), was a significant predictor of incident retinopathy signs. The Hoorn Study in the Netherlands reported a 9-year retinopathy incidence of 11.6% in the general population, 7.3% among those with normal glucose tolerance.[16] Incident retinopathy signs were associated with hypertension and increased waist hip ratio, but not with serum lipids or cigarette smoking. In the Blue Mountains Eye Study in Australia, the 5-year incidence of retinopathy was 9.7% among persons without diabetes,[17] with age as the only significant risk factor.

In the current study, we describe the 3-year incidence and cumulative prevalence of retinopathy signs and associated risk factors in the Atherosclerosis Risk in Communities (ARIC) study, a prospective population-based study of cardiovascular disease in middle-aged people. Retinal photography was a component of the study during the third examination,[18-20] and was repeated on a sub-sample of the cohort at the fourth examination three years later.

METHODS

Study Population

The ARIC study included 15,792 participants aged 45 to 64 years selected by probability sampling from four U.S. communities: Forsyth County, NC; Jackson, MS; suburbs of Minneapolis, MN; and Washington County, MD.[21] The Jackson sample included African Americans only; in the other field centers, samples were representative of the populations in these communities (mostly white in Minneapolis and Washington County, and about 15% African American in Forsyth County). Of the participants at baseline, 14,346 (93% of survivors) returned for a 2nd examination in 1990-1992, and 12,887 (86% of the survivors) returned for a 3rd examination in 1993-95.

Retinal photographs were first taken on 12,536 persons at the 3rd examination. A sub-sample (n=1,084) of participants had a repeat retinal photograph of the same eye three years later at the beginning of the 4th examination over 5-month period (February to June 1996). This sub-sample was chosen as consecutive participants who consented to retinal photography; 99% of participants who were selected agreed to this component of the study. Of these, we excluded 2 participants whose race was neither African-American nor white, 4 African-American participants in Minneapolis and Maryland, 96 with ungradeable photographs at either the 3rd or 4th examination, and one with retinal vein occlusion, leaving 981 who had retinopathy data at both the 3rd and 4th examination for the current analysis.

Institutional review boards at each study site approved the study and written, informed consent was obtained at each examination.

Definition of Incidence and Cumulative Prevalence of Retinopathy

The retinal photography procedure followed a standardized protocol at both the 3rd and 4th examinations.[18] At both examinations, after five minutes of dark adaptation, a non-mydriatic 45-degree retinal photograph centred on the optic disc and macula were taken of one eye, which was randomly selected at the 3rd examination. The same eye was photographed at the 4th examination. The photographs were evaluated by trained graders masked to participant characteristics at the Fundus Photograph Reading Center, University of Wisconsin, Madison, WI.

Retinopathy was defined as present if any of the following lesions were graded definite or probable in any of the four fundus quadrants: microaneurysm, blot retinal hemorrhage, flame-shaped hemorrhage, cotton wool spot and hard exudate.[12] We defined "any retinopathy" as the presence of these signs in the study cohort and "non-diabetic retinopathy" as the presence of these signs in persons without diabetes.

For each of the two outcomes, we defined "incidence" as patients without retinopathy at the 3rd examination who had retinopathy at the 4th examination, and "cumulative prevalence" as patients who had retinopathy at both the 3rd and 4th examinations, and those who developed incident retinopathy at the 4th examination. In a sub-analysis, we also examined people who had retinopathy at the 3rd examination who did not have retinopathy signs in the same eye at the 4th examination, which we defined as "apparent regression" of retinopathy.

Quality control procedures for retinal grading have been previously reported.[18, 22] In general, weighted intra- and inter-grader kappa statistics were 0.91 and 0.81, respectively, for microaneurysms, 0.85 and 0.93 for retinal hemorrhage, and 1.00 and 0.95 for cotton wool spots.[22]

Definition of Cardiovascular Risk Factors

At each study visit, participants had an interview for demographic characteristics and medical history, a brief clinical examination and a set of core laboratory investigations.[23] Blood pressure was taken with a random-zero sphygmomanometer, and the mean of the last two measurements was used for analyses. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or use of anti-hypertensive medication during the previous 2 weeks. The mean arterial blood pressure was computed as 2/3 of the diastolic plus 1/3 of the systolic value.

Coronary heart disease was ascertained by standard procedure at baseline and follow-up examinations.[24] In the current study, the cumulative prevalence up to the 3rd examination was used to define absence versus presence of baseline coronary heart disease. Measurement of common carotid artery intima-media thickness (IMT) by ultrasound followed a detailed protocol.[25] Diabetes mellitus was defined as a fasting glucose ≥126 mg/dl (≥7.0 mmol/L), a non-fasting glucose ≥200mg/dl (≥11.1 mmol/L), or a self-reported history or treatment for diabetes.[26] Technicians measured height and weight of participants in scrub suits to compute the body mass index in units of weight/height^2 (kg/m2), as well as waist (umbilical level) and hips (maximum) to compute the waist-hip ratio. Blood collection and processing for total serum cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, serum glucose, white blood cell count, plasma fibrinogen and factor VIII are described elsewhere.[23] Physical activity, education, occupation, cigarette smoking and alcohol consumption were ascertained from interview. Physical activity was characterized by a sports index, with values ranging from 1 to 5.[27] All variables were based on data from the 3rd examination (considered baseline for this study), except for white blood cell count, plasma fibrinogen and factor VIII, which were measured at the 1st examination.

Statistical Methods

We calculated the incidence and cumulative prevalence of any retinopathy and non-diabetic retinopathy in the total cohort, and in sub-groups stratified by age, gender, race, diabetes and hypertension status and quartiles of fasting glucose and systolic blood pressure. We used binary logistic regression to calculate the odds ratio (OR) and its 95% confidence intervals (CI) for incidence and cumulative prevalence of retinopathy, comparing either presence or absence of a putative risk factor (e.g., hypertension) or per standard deviation increase in the level of the risk factor (e.g., systolic blood pressure), adjusting for age, gender, race and study center. Variables considered for multivariable models included those that were significant at $p<0.10$ in the age, gender, race and center adjusted models. The final multivariable model included adjustment for age, gender, race, study center, cigarette smoking, mean arterial blood pressure, total serum cholesterol, fasting serum glucose and plasma fibrinogen. All analyses were performed in SPSS version 12.1 (SPSS Inc, Chicago, Ill)

RESULTS

Comparisons of participants included (n=981) and excluded (n=11,555) from this study appear in Table 1. Persons included were more likely African-Americans and, after adjusting for age, gender, race and study center, were less likely to have completed high school education, and had lower serum HDL cholesterol and triglycerides, and decreased common carotid intima-media thickness as compared to those excluded. Persons included and excluded did not differ by age, gender and hypertension, diabetes and cigarette smoking status.

In the total cohort, the 3-year incidence of any retinopathy was 3.8% (36 cases / 941 persons at risk) and the cumulative prevalence 7.7% (76/981). There were 147 persons with diabetes, of which 143 were defined based on fasting glucose and 4 were based on self-reported history or treatment for diabetes; none were based on the non-fasting glucose cut-off. Among persons with diabetes, the corresponding 3-year incidence and cumulative prevalence of diabetic retinopathy was 10.1% (12/119) and 27.2% (40/147). Among persons without diabetes, the 3-year incidence and cumulative prevalence of non-diabetic retinopathy was 2.9% (24/822) and 4.3% (36/834).

Table 2 shows the incidence and cumulative prevalence of any retinopathy and non-diabetic retinopathy. The incidence and cumulative prevalence of retinopathy was not significantly associated with age or gender. The cumulative prevalence of any retinopathy was significantly greater in African-Americans (13.0%) than in whites (5.5%, $p<0.001$). The incidence and cumulative prevalence of any retinopathy was higher in people with diabetes and hypertension, and in those with higher quartiles of fasting glucose and systolic blood pressure. The cumulative prevalence of non-diabetic retinopathy was associated with higher quartiles of systolic blood pressure, but not hypertension status.

Table 3 shows logistic regression models of any retinopathy and non-diabetic retinopathy, adjusted for age, gender, race and center. The incidence of any retinopathy was related to baseline diabetes status and higher levels of systolic and mean arterial blood pressure, fasting serum glucose, total and LDL total cholesterol, triglycerides and plasma fibrinogen. The cumulative prevalence of any retinopathy was further associated with African-American race, hypertension status, and higher levels of diastolic blood pressure, waist hip ratio, common carotid IMT and factor VIII.

In persons without diabetes, the incidence and cumulative prevalence of non-diabetic retinopathy was related to higher levels of systolic, diastolic and mean arterial blood pressure, and total cholesterol levels.

In multivariable analysis (Table 3), any retinopathy was associated with higher levels of mean arterial blood pressure (OR 1.5, 95% CI 1.0, 2.3, per standard deviation increase in risk factor levels), fasting serum glucose (OR 1.6, 95% CI, 1.3, 2.1), serum total cholesterol (OR 1.4, 95% CI, 1.0, 2.0), and plasma fibrinogen (OR 1.4, 95% CI, 1.1, 1.9). Non-diabetic retinopathy was associated with higher levels of mean arterial blood pressure (OR 1.4, 95% CI, 0.9, 2.3) and fasting serum glucose (OR 1.5, 95% CI, 1.0, 2.3).

Of the 70 people with any retinopathy signs at the 3rd examination, 40 (57.1%) had persistent retinopathy signs at the 4th examination, but 30 (42.9%) did not have retinopathy signs in the same eye at the 4th examination. After controlling for age, gender, race and center, these 30 persons with "apparent regression" of retinopathy were less likely to have diabetes, were never/past cigarette smokers, and had smaller waist hip ratios, higher levels of physical activity, and lower levels of fasting glucose and factor VIII (data not shown). Of the 33 non-diabetic persons with retinopathy signs at the 3rd examination, 21 (63.6%) did not have these signs at the 4th examination. These 21 persons were more likely to be never/past cigarette smokers, and had lower levels of factor VIII (data not shown).

DISCUSSSION

We found in this population-based cohort a 3-year incidence of any retinopathy of 3.8% and a cumulative prevalence of 7.7%. Among participants without diabetes, the 3-year incidence was 2.9% and the cumulative prevalence 4.3%. We showed that risk factors for incidence and cumulative prevalence of any retinopathy in middle aged people were higher levels of blood pressure, fasting glucose, total cholesterol and plasma fibrinogen. Among middle-aged persons without diabetes, risk factors for non-diabetic retinopathy were higher blood pressure and fasting serum glucose.

Our study findings should be compared to three other prospective studies that have examined the incidence of retinopathy signs in the general population.[15-17] In the Beaver Dam Eye Study, the 5-year incidence of non-diabetic retinopathy was 6% among participants of similar age (55-74 years).[15] In the Hoorn Study, the 9 year incidence of retinopathy was 7% among non-diabetic participants aged 50-74 years.[16] The Blue Mountains Eye Study reported a 5-year retinopathy incidence of 8% among non-diabetic participants aged 49-59 years and 9% among those aged 60-69 years.[17] If we assume linear yearly incidence, then the annual incidence of non-diabetic retinopathy is 1.0% in the current ARIC study, which is comparable to the annual incidence of 1.2% in the Beaver Dam Eye Study and 0.8% in the Hoorn Study. These rates are lower than the 1.7% annual incidence reported in the Blue Mountains Eye Study. Direct comparison of rates of retinopathy between studies is limited by differences in the method of ascertaining retinopathy; we used a 45° non-mydriatic retinal photograph of only one eye to define presence or absence of retinopathy signs, while the Beaver Dam Eye Study used 30° stereoscopic mydriatic photographs of two eyes,[15] the Hoorn study used 45° mydriatic retinal photographs of two eyes,[16] and the Blue Mountains Eye Study defined retinopathy from six-field 30° stereoscopic retinal photographs of two eyes. Additionally, both the Blue Mountains and Beaver Dam Eye studies validated incident cases by a side-by-side assessment of the retinal photographs performed at baseline and follow up of patients who developed incident retinopathy. Differences in study participant characteristics (e.g., age and prevalence of hypertension between studies) may also contribute to the variation in incidence rates of retinopathy.

In the current study, hypertension and hyperglycemia were the only consistent risk factors for the incidence and cumulative prevalence of any retinopathy and non-diabetic retinopathy. The presence of clinical coronary heart disease or subclinical carotid atherosclerosis, as defined from carotid artery IMT, was not related to development of any retinopathy or non-diabetic

retinopathy after controlling for blood pressure and glucose in multivariable analyses. Findings from other prospective studies have been largely inconsistent. In the Beaver Dam Eye Study, hypertension, but not glycosylated hemoglobin, was associated with 5-year incident non-diabetic retinopathy.[15] Incident retinopathy signs in the Hoorn Study was associated with hypertension but inconsistently associated with obesity (associated with a higher waist hip ratio but not BMI), and not associated with serum lipids and cigarette smoking.[16] The Blue Mountains Eye Study examined a range of cardiovascular risk factors, but showed that older age was the only significant risk factor for incident retinopathy in non-diabetic persons.[17]

In the general cohort, any retinopathy was associated with higher total cholesterol and plasma fibrinogen that was independent of blood pressure and glycemia, although these associations were not significant once participants with diabetes were excluded. The association of total cholesterol with retinopathy has been reported previously in a previous cross-sectional analysis,[28] but has not been found in most other studies [2, 15-17, 29] Plasma fibrinogen is a hemostatic factor and a non-specific marker of systemic inflammation. Higher plasma fibrinogen levels has been previously associated with incident cardiovascular disease,[30] and retinal vascular diseases, such as retinal vein occlusion and arteriolar emboli.[31] In the Hoorn study, retinopathy was associated with elevated levels of C-reactive protein, another more specific biomarker of systemic inflammation, among people with and without diabetes.[32] However, neither C-reactive protein or plasma fibrinogen were associated with retinopathy in the Cardiovascular Health Study.[5]

In the current study, we found that 43% of any retinopathy signs and 64% of retinopathy signs among persons without diabetes seen at the 3rd examination were not present at the 4th examination three years later. A possible explanation of the "apparent regression" of retinopathy signs is misclassification of retinopathy status at either the 3rd or 4th examination. However, the reliability of retinopathy assessment was high in the ARIC study, with repeated grading of photographs during the study showing intra-grader and inter-grader weight kappas ranging from 0.81 to 1.00 for microaneurysm, retinal hemorrhage and cotton wool spots.[22] Furthermore, in the Blue Mountains Eye Study, a similar pattern and magnitude of "apparent regression" of retinopathy signs was observed. Of the 195 participants with non-diabetic retinopathy at baseline, 72% did not have these retinopathy signs after 5 years.[17] As discussed above, the Blue Mountains Study validated this observation by a side-by-side assessment of the retinal photographs performed at baseline and follow up among participants that had this "apparent regression" of retinopathy; this was not performed in the ARIC study. Despite the possibility of misclassification, there is strong biological rationale for regression of mild retinopathy signs. Microaneurysms become non-perfused and retinal hemorrhages can be resorbed. We further note that regression of any retinopathy in our study was related to lower levels of cardiovascular risk factors (absence of diabetes, never/past cigarette smoking status, lower waist hip ratio, and higher levels of physical activity). Thus, the data in this paper support the concept that the appearance of retinopathy is a response to one or more stimuli, and that retinopathy signs are more likely to subside in people with lower levels of these risk factors.

Strengths of our study include a prospective design, a community-based study population, standardized retinopathy evaluation from photographs, and measurement of a number of risk factors. Our study is limited by the following. First, retinal photography data were available from only one eye for each patient, and a proportion of photographs was ungradeable, largely because of poor pupil dilation. Additionally, as mentioned, there was no side-by-side comparison of retinal data. Thus, a person's retinopathy status may be misclassified, possibly resulting in either an over- or under-estimation of incidence (and apparent regression) rates. Whether there was differential misclassification with respect to the risk factors examined here is less clear. It is possible, for example, that the apparent regression of retinopathy was related to differential misclassification, and participants with lower levels of cardiovascular risk

factors classified as having retinopathy at the 3rd examination only are more likely to have been misclassified. Second, selection biases may have accentuated or obscured associations, as retinal photography was performed only on a small subset of the total cohort at the 4th examination. We noted differences in participants' characteristics between those who were included and excluded from the study. Finally, retinopathy signs can be caused by factors other than those measured here (e.g., anemia, retinal inflammatory disease). However, these conditions would be relatively infrequent in the general population and not significantly affect the incidence rates reported.

In conclusion, our study provides data on the incidence and cumulative prevalence of retinopathy signs in middle-aged people over a three year period. The 3-year incidence and cumulative prevalence of any retinopathy in the whole cohort was 3.8% and 7.7%, respectively. Among persons without diabetes, the 3 year incidence and cumulative prevalence of non-diabetic retinopathy was 2.9% and 4.3%, respectively. Among persons with diabetes, the corresponding figures were 10.3% and 27.8%, respectively. We showed that risk factors for incidence and cumulative prevalence of any retinopathy were higher levels of blood pressure, fasting glucose, total cholesterol and plasma fibrinogen. Among participants without diabetes, risk factors for non-diabetic retinopathy were higher blood pressure and fasting serum glucose. These data provide further understanding of the evolution of retinopathy signs as risk markers of systemic cardiovascular disease.

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Table 1

Participant Characteristics, the Atherosclerosis Risk In Communities Study

	Included (n=981)	Excluded (n=11,555)	P value*
Age, yrs, mean (SE)	60.3 (0.18)	59.9 (0.50)	0.18
Men, number (%)	548 (55.9)	6411 (55.5)	0.79
African-Americans, number (%)	292 (29.8)	2519 (21.8)	<0.001
High school education, number (%)	752 (77.0)	9271 (80.3)	0.01
Professional occupation, number (%)	216 (22)	2773 (24)	0.69
Prevalent coronary heart disease, number (%)	35 (3.7)	466 (4.1)	0.52
Hypertension, number (%)	426 (43.6)	4654 (40.5)	0.07
Diabetes, number (%)	147 (15.0)	1750 (15.2)	0.60
Current cigarette smoker, number (%)	155 (15.8)	2057 (17.8)	0.20
Current alcohol consumption, number (%)	497 (50.7)	6072 (52.7)	0.05
Body mass index, kg/m^2, mean (SE)	28.7 (0.15)	28.5 (0.05)	0.11
Physical activity index, mean (SE)	2.6 (0.80)	2.8 (0.76)	0.24
Common carotid IMT, mm, mean (SE)	0.74 (0.17)	0.77 (0.22)	0.001
Fasting glucose, mg/dL, mean (SE)	111.5 (0.29)	111.0 (0.39)	0.62
Total cholesterol, mg/dL, mean (SE)	209.1 (1.22)	207.4 (0.35)	0.19
HDL cholesterol, mg/dL, mean (SE)	49.2 (0.53)	52.4 (0.17)	<0.001
Triglycerides, mg/dL, mean (SE)	136.4 (2.41)	143.2 (0.86)	0.03

*Adjusted for age and sex (except for age and men, unadjusted for age and sex, respectively).

Table 2

Three-Year Incidence and Cumulative Prevalence of Any Retinopathy and Retinopathy in Persons without Diabetes (Non-Diabetic Retinopathy)

	Any Retinopathy								Non-Diabetic Retinopathy							
	3-yr Incidence				3-yr Cumulative Prevalence				3-yr Incidence				3-yr Cumulative Prevalence			
	N	n	%	p	N	n	%	p	N	n	%	p	N	n	%	p
Age group, years																
50-54	191	4	2.1	0.38	197	10	5.1	0.81	175	4	2.3	0.49	176	5	2.8	0.10
55-59	261	12	4.6		274	25	9.1		228	7	3.1		230	9	3.9	
60-64	239	7	2.9		246	14	5.7		207	5	2.4		210	8	3.8	
65-73	250	13	5.2		264	27	10.2		214	8	3.7		220	14	6.4	
Gender																
Women	522	16	3.1	0.24	549	43	7.8	0.71	464	12	2.6	0.53	473	21	4.4	0.83
Men	419	20	4.8		432	33	7.6		360	12	3.3		363	15	4.1	
Race																
Whites	675	24	3.6	0.49	689	38	5.5	<0.001	605	18	3.0	0.86	610	23	3.8	0.21
African-Americans	266	12	4.5		292	38	13.0		219	6	2.7		226	13	5.8	
Diabetes status																
Absent	822	24	2.9	<0.001	834	36	4.3	<0.001	--	--	--	--	--	--	--	--
Present	119	12	10.1		147	40	27.2		--	--	--		--	--	--	
Fasting serum glucose, mg/dL																
1st quartile, <95	275	6	2.2	0.006	278	9	3.2	<0.001	272	6	2.2	0.48	273	7	2.6	0.18
2nd quartile, 95-102	221	7	3.2		227	13	5.7		217	7	3.2		222	12	5.4	
3rd quartile, 102-113	248	8	3.2		252	12	4.8		243	8	3.3		247	12	4.9	
4th quartile, >113	196	15	7.7		223	42	18.8		92	3	3.3		94	5	5.3	
Hypertension status																
Absent	545	15	2.8	0.06	553	23	4.2	<0.001	497	14	2.8	0.84	500	17	3.4	0.11
Present	394	21	5.1		426	53	12.2		327	10	3.1		336	19	5.7	
Systolic blood pressure, mmHg																
1st quartile, <112	250	7	2.8	0.01	253	10	4.0	<0.001	235	6	2.6	0.07	237	8	3.4	0.01
2nd quartile, 112-122	225	3	1.3		232	10	4.3		192	1	0.5		195	4	2.1	
3rd quartile, 122-136	246	12	4.9		253	19	7.5		215	8	3.7		215	8	3.7	
4th quartile, >136	220	14	6.4		243	37	15.2		182	9	4.9		189	16	8.5	

N: Number at risk and n: number at retinal endpoint.

Table 3

Independent Predictors of Three-Year Incidence and Cumulative Prevalence of Any Retinopathy and Retinopathy in Persons without Diabetes (Non-Diabetic Retinopathy)

		Any Retinopathy		Non-Diabetic Retinopathy	
		3-yr Incidence	3-yr Cumulative Prevalence	3-yr Incidence	3-yr Cumulative Prevalence
Age	10 year increase†	1.5 (0.8, 2.8)	1.6 (1.0, 2.6)	1.1 (0.5, 2.4)	1.6 (0.9, 3.0)
Race	African-Africans vs Whites	1.1 (0.5, 2.4)	1.7 (0.9, 3.1)	0.7 (0.2, 1.9)	1.2 (0.6, 2.7)
Cigarette smoking	Current vs Past/Never	1.3 (0.6, 2.7)	1.3 (0.5, 2.1)	1.2 (0.4, 3.8)	2.0 (0.8 4.7)
Fasting serum glucose	Per SD (42 mg/dL) h	1.6 (1.3, 2.1)	1.3 (1.0, 1.7)	1.5 (1.0, 2.3)	1.5 (1.1, 2.1)
Mean arterial blood pressure	Per SD (13 mmHg) increase	1.5 (1.0, 2.3)	1.7 (1.2, 2.2)	1.4 (0.9, 2.3)	1.6 (1.1, 2.4)
Total cholesterol	Per SD (38 mg/dL) increase	1.4 (1.0, 2.0)	2.1 (1.8, 2.6)	1.2 (0.2, 7.1)	2.0 (0.5, 8.4)
Plasma fibrinogen	Per SD (66mg/dL) increase	1.4 (1.1, 1.9)	1.3 (1.0, 1.6)	1.2 (0.8, 1.8)	1.2 (0.8, 1.6)

Data show odds ratio (95% confidence interval) from logistic regression models, adjusted for all variables shown plus gender and center