

Higher Prevalence of Retinopathy in Diabetic Patients of South Asian Ethnicity Compared With White Europeans in the Community

A cross-sectional study

NEIL T. RAYMOND, MSc¹
LAKSHMINARAYANAN VARADHAN, MRCP²
DILINI R. REYNOLD, MD³
KATE BUSH, BM⁴
SAILESH SANKARANARAYANAN, MRCP²
SRIKANTH BELLARY, MRCP⁵

ANTHONY H. BARNETT, FRCP⁵
SUDHESH KUMAR, FRCP⁶
J. PAUL O'HARE, FRCP⁶
ON BEHALF OF THE UK ASIAN DIABETES
STUDY RETINOPATHY STUDY GROUP

OBJECTIVE — The purpose of this study was to compare prevalence and risk factors for diabetic retinopathy among U.K. residents of South Asian or white European ethnicity.

RESEARCH DESIGN AND METHODS — This was a community-based cross-sectional study involving 10 general practices; 1,035 patients with type 2 diabetes were studied: 421 of South Asian and 614 of white European ethnicity. Diabetic retinopathy, sight-threatening retinopathy, maculopathy, and previous laser photocoagulation therapy were assessed after grading of retinal photographs. Data were collected on risk factors including age, duration, and treatment of diabetes, blood pressures, serum total cholesterol, and A1C.

RESULTS — Patients of South Asian ethnicity had significantly higher systolic (144 vs. 137 mmHg, $P < 0.0001$) and diastolic (84 vs. 74 mmHg, $P < 0.0001$) blood pressure, A1C (7.9 vs. 7.5%, $P < 0.0001$), and total cholesterol (4.5 vs. 4.2 mmol/l, $P < 0.0001$). Diabetic retinopathy was detected in 414 (40%) patients (189 South Asian [45%] versus 225 white European [37%]; $P = 0.0078$). Sight-threatening retinopathy was detected in 142 (14%) patients (68 South Asian [16%] versus 74 white European [12%]; $P = 0.0597$). After adjustment for confounders, there were significantly elevated risks of any retinopathy and maculopathy for South Asian versus white European patients.

CONCLUSIONS — Patients of South Asian ethnicity had a significantly higher prevalence of diabetic retinopathy and maculopathy, with significantly elevated systolic and diastolic blood pressure, A1C, and total cholesterol; lower attained age; and younger age at diagnosis. Earlier onset of disease and higher levels of modifiable risk factors make early detection of diabetes, annual referral for retinal screening, and intensive risk factor control key elements in addressing this health inequality.

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From the ¹Health Sciences Research Institute, Warwick Medical School, University of Warwick, Coventry, U.K.; ²SHO Diabetes, University Hospital Coventry and Warwickshire NHS Trust, Clifford Bridge Road, Coventry, U.K.; ³Warwick Medical School, University of Warwick, Coventry, U.K.; ⁴ST2 Ophthalmology, Southampton General Hospital, Southampton, U.K.; the ⁵Heart of England NHS Foundation Trust, Bordesley Green East, Birmingham, U.K.; and ⁶Clinical Sciences Research Institute, Warwick Medical School, University of Warwick, Coventry, U.K.

Corresponding author: J. Paul O'Hare, j.p.o-hare@warwick.ac.uk.

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N.T.R. and L.V. contributed equally to this study.

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Diabetes is one of the most common chronic conditions in the Western world, and its prevalence is increasing worldwide (1). Common risk factors for the development of its microvascular and macrovascular complications include duration of diabetes, poor glycemic control, elevated blood pressure, and dyslipidemia, the latter three of which are potentially amenable to therapeutic intervention (2,3). Diabetic retinopathy is the leading cause of blindness among the working age-group, the incidence of blindness is increasing rapidly, and the prevalence of visual impairment is higher in South Asians in the U.K. (4,5). There is conflicting evidence regarding the epidemiology of diabetic retinopathy in South Asians (6–9).

The U.K. Prospective Diabetes Study (UKPDS) showed similar prevalences of retinopathy at diagnosis and trial entry in its South Asian, Afro-Caribbean, and white European groups (10), whereas Mather et al. (6) showed that South Asians were 1.5 times more likely to have laser treatment for diabetic retinopathy. Recent studies in the U.K. reported higher prevalences of retinopathy in South Asians (7,8).

The aim of this study was to evaluate the prevalence of diabetic retinopathy and its risk factors among South Asians compared with white Europeans in a community setting in the U.K., using data from the Coventry Diabetes Retinopathy Screening service and general practitioner records.

RESEARCH DESIGN AND METHODS

In brief, the U.K. Asian Diabetes Study (UKADS) was a cluster randomized controlled trial designed to evaluate the benefits of an enhanced diabetes care package for people of South Asian ethnicity with type 2 diabetes in Coventry and Birmingham, U.K. (11,12). The current study was a substudy of UKADS, comprising a cross-sectional

prevalence survey using data from 10 general practices in the Foleshill area of Coventry in central England. Retinal photographs and demographic data were collected from the Coventry and Warwickshire Diabetes Retinal Screening Centre (CWDRSC) for UKADS patients, all of South Asian ethnicity, plus a comparison group of white European patients from the same geographical area of Coventry. Digital retinal photographs (2 eyes \times 2 fields), taken using a 3072 \times 2906 Canon D20 back on a Canon DGI nonmydriatic camera at 45°, were examined independently by two qualified retinal photography graders following quality assurance protocols. A confirmatory grading by ophthalmologists for all films with changes greater than R1 (background retinopathy) was undertaken, and a research ophthalmologist (K.B.) undertook a quality assurance check of 10% of photographs, following audit specifications of the national screening guidelines. As a result of this process, no instances of discordance in grade were identified.

The grading of diabetic retinopathy was based on the U.K.'s National Screening Committee guidelines, and retinopathy was classified as none (R0), background (R1), preproliferative (R2), and proliferative (R3), with or without maculopathy (M) or previous photocoagulation (P) (13). Final grading was based on the worst eye, with any grade of diabetic retinopathy more severe than R1 (i.e., R2, R3, M, or P) classified as sight-threatening retinopathy (STR). CWDRSC has an overall ungradable rate of 2.4% of photographs; patients with ungradable photographs were excluded.

Clinical data were collected for all patients from their general practice records; for UKADS patients, annual review data collected at research clinics were used. Details on risk factors including blood pressure, duration of diabetes, age of onset of diabetes, A1C, serum creatinine, and cholesterol were recorded. For Foleshill general practitioners, biochemical measurement processing is all undertaken by a central laboratory service based in University Hospital Coventry and Warwickshire.

Prevalence of any retinopathy, STR, maculopathy, and previous photocoagulation was estimated overall and for South Asian versus white European patients. Age- and sex-standardized prevalence and 95% CIs were estimated for any retinopathy and STR plus maculopathy. Demographic and risk factors distributions were compared between the groups, us-

Table 1—Characteristics of patients with type 2 diabetes by ethnicity group

	South Asian	White European	Total	P
<i>n</i>	421	614	1,035	
Sex				
Female	190 (45)	289 (48)	479 (47)	0.3386
Male	231 (55)	311 (52)	542 (53)	
Treatment:				
Insulin	71 (17)	127 (21)	198 (20)	0.1249
Tablets/diet	350 (83)	487 (79)	817 (80)	
Any retinopathy (yes)	189 (45)	225 (37)	414 (40)	0.0078
STR (yes)	68 (16)	74 (12)	142 (14)	0.0597
Maculopathy (yes)	53 (13)	52 (8)	105 (10)	0.0310
Previous photocoagulation (yes)	15 (4)	28 (5)	43 (4)	0.4296

Data are *n* (%). *n* = 1,035. Data are missing regarding the sex of 14 individuals.

ing the χ^2 test, *t* test, and Mann-Whitney *U* test as appropriate.

Multiple logistic regression was used to estimate crude and adjusted odds ratios (ORs) (95% CIs) to allow for differences between groups with respect to demographic and risk factors and control for potentially confounding variables. *P* < 0.05 was considered to be statistically significant. In developing logistic models, the strategy was to fit the simplest models that adequately fit the data to adjust for potential confounding. Interaction effects were investigated and excluded where not statistically significant. Terms for sex, age at diagnosis, and duration of diabetes were included in all models, irrespective of statistical significance. For an expected difference of 8–10% in retinopathy prevalence, with 80% power and *P* = 0.05, it was estimated that 900–1,000 patients were needed.

RESULTS— A total of 1,079 patients with gradable photographs were identified, including 430 (40%) of South Asian and 649 (60%) white European ethnicity. Of these, 44 patients were excluded as having probable type 1 diabetes on the basis of age of onset <30 years and the need for insulin treatment at or near diagnosis. Of 1,035 patients remaining, there were 421 (41%) of South Asian and 614 (59%) of white European ethnicity, including 53% male and 47% female patients, with no difference in proportions comparing ethnicity-defined subgroups (Table 1). More white European than South Asian patients received insulin treatment, but the difference was not statistically significant (Table 1).

A total of 414 (40%) patients had diabetic retinopathy, with significantly

more South Asian than white European patients (Table 1). STR was detected in 142 (14%) patients, with more STR in the South Asian group and a difference of borderline statistical significance (Table 1). Maculopathy was detected in 105 (10%) patients, with a significant difference between groups: 55 South Asian (13%) versus 60 white European (9%) patients (Table 1). Age- and sex-standardized prevalences showed a significant difference for any retinopathy (South Asian 48.3% [95% CI 43.5–53.1] versus white European 37.2% [33.3–41.0]) but not STR (South Asian 17.3% [13.7–20.9] versus white European 12.4% [9.7–15.0]) and were of borderline significance for maculopathy (South Asian 14.4% [11.1–17.8] versus white European 8.8% [6.5–11.1]). A total of 43 patients, 15 (4%) South Asian and 28 (5%) white European, had previously had laser photocoagulation therapy, with no significant difference between the groups (Table 1).

Clinical data were collected and analyzed for 421 South Asian and 465 white European patients. Patients of South Asian ethnicity were significantly younger, were younger at diagnosis of diabetes, and had shorter duration of diabetes (Table 2). There were significant differences with respect to cardiovascular risk profiles: the South Asian group had higher systolic and diastolic blood pressures, A1C, and total cholesterol, indicating considerably higher overall cardiovascular risk (Table 2).

Levels of mean systolic blood pressure and A1C were elevated in patients with any retinopathy and further raised in those with STR, whereas similar increasing patterns were apparent for both ethnicity-defined groups. The South Asians had significantly raised systolic BP

Table 2—Clinical data: potentially confounding risk factors by ethnicity

Risk factors comparison	South Asian	White European	P (t test)
n	421	492	
Attained age	60.6 ± 11.2	67.5 ± 11.6	<0.0001
Duration of diabetes (years)	7.6 ± 7.3	8.8 ± 5.7	<0.0001
Age at diagnosis (years)	53.0 ± 12.0	58.6 ± 12.3	<0.0001
Systolic blood pressure (mmHg)	144.1 ± 20.8	137.0 ± 18.7	<0.0001
Diastolic blood pressure (mmHg)	84.2 ± 11.5	74.3 ± 10.3	<0.0001
Total cholesterol (mmol/l)	4.5 ± 1.2	4.2 ± 1.1	<0.0001
A1C (%)	7.9 ± 1.6	7.5 ± 1.6	<0.0001
Plasma creatinine (μmol/l)	101.5 ± 26.8	114.5 ± 38.9	<0.0001

Data are means ± SD. No. of individuals with missing data: 1, attained age; 19, duration of diabetes; 13, systolic blood pressure; 22, diastolic blood pressure; 13, total cholesterol; 11, A1C; and 13, plasma creatinine.

at all stages and higher A1C when no retinopathy or background retinopathy only was present (Fig. 1A and B).

Treatment with insulin was significantly associated with higher prevalences of any retinopathy, STR, maculopathy, and previous photocoagulation (all with $P < 0.0001$). In unadjusted logistic regression models, the South Asians had a nonsignificantly elevated OR (95% CI) for any retinopathy of 1.30 (0.99–1.71) and STR of 1.38 (0.95–2.02) with maculopathy of borderline significance of 1.54 (1.00–2.38) (Table 3). In models for both any retinopathy and maculopathy, a statistically significant interaction effect for ethnicity × duration was identified, implying that the ethnicity effect varied depending on diabetes duration. ORs (95% CIs) for South Asian versus white European, adjusted for potential confounders, for increasing duration of diabetes were estimated: any retinopathy 2.40 (1.37–4.22), 2.06 (1.22–2.56), and 1.77 (0.93–1.83), and maculopathy 3.44 (1.50–7.89), 2.86 (1.28–4.40), and 2.38 (1.00–2.71) for durations of 0, 5, and 10 years, respectively. In STR models, the effect of ethnicity was not statistically significant.

CONCLUSIONS— This primary care-based study shows that U.K. resident South Asians with diabetes have a significantly higher prevalence of any retinopathy and maculopathy than indigenous white Europeans. As reported previously, the South Asian group in this study was younger at diagnosis and had a shorter duration of diabetes (14). Significantly higher

systolic and diastolic blood pressures, A1C, and cholesterol levels—all risk factors potentially amenable to treatment—were observed compared with those for the white European group. After adjustment for these differences, the excess risk of both any retinopathy and maculopathy for the South Asian group remained significantly elevated, suggesting further risk attributable to ethnicity. The risk of STR was raised for South Asians but not statistically significantly so, perhaps reflecting the extra white European patients already treated with laser photocoagulation. Excluding patients who had previously undergone photocoagulation from the STR category would result in a significant excess risk of STR for the South Asian patients.

Duration of diabetes and glycemic control are well-established risk factors for retinopathy, confirmed in the current study findings (2). The significant interaction of ethnicity and duration of diabetes observed complicates interpretation of the ethnicity effect in this study. Differential risk of retinopathy between South Asian and white European patients is largely observed in those with diabetes duration of <10 years. This finding has not been reported previously and emphasizes the need for effective screening and earlier diagnosis of diabetes among the South Asian population and suggests that the pathogenesis of diabetic retinopathy in this group may be more aggressive than that in white Europeans. Hypertension has been shown to be strongly associated with diabetic retinopathy in previous trials and was an important modifiable factor in the current study (2,15). As in

previous trials, no significant association of diabetic retinopathy and total cholesterol was observed (15,16). There was a strong association between retinopathy and treatment with insulin. Tightening glycemic control rapidly may precipitate progression of diabetic retinopathy, and it is possible that insulin therapy has contributed to the progression of retinopathy in these patients (17). It seems more likely that insulin treatment is only initiated in response to the identification of complications; recent evidence confirms resistance to early conversion to insulin therapy in this population (12).

The current study found a higher prevalence of retinopathy than was observed in the UKPDS, reflecting the longer duration of diabetes and risk factors profile (2,10). A large screening-based study in Liverpool during the 1990s reported 27% retinopathy including 6% STR (18). This result is significantly lower than the Coventry prevalence, possibly reflecting a secular trend over time plus differences in the ethnicity composition of the samples; the Liverpool study had no comparison of ethnicity-defined groups. In Bradford patients aged 40+ years attending a diabetic outpatient's clinic, a 60% prevalence of retinopathy was detected, including 38% STR, with statistically significantly excess STR in the South Asian group (8). The prevalence is significantly higher than that in Coventry and includes ethnicity comparisons, but these were hospital clinic patients, who are unlikely to be representative of the community at large. Studies from the U.S. have reported retinopathy prevalences of up to 40%, with significant variation between ethnicity-defined groups (19,20). Taken together, these studies illustrate the potential effects of sample selection, lending weight to the importance of using population-based screening data in retinopathy studies—with ethnicity recorded, as in the current study.

In the U.K., ethnic minority populations including South Asians are concentrated mainly in identifiable urban areas, reflecting historical migration patterns. Areas such as Coventry and Birmingham are appropriate for comparative studies, and high recruitment (61%) and retention (90% after 1 year) rates were achieved for the UKADS trial (12). The current study included South Asian and white European patients from the same inner city practices, sharing the same high deprivation scores. Previous hospital-based studies were smaller, and samples

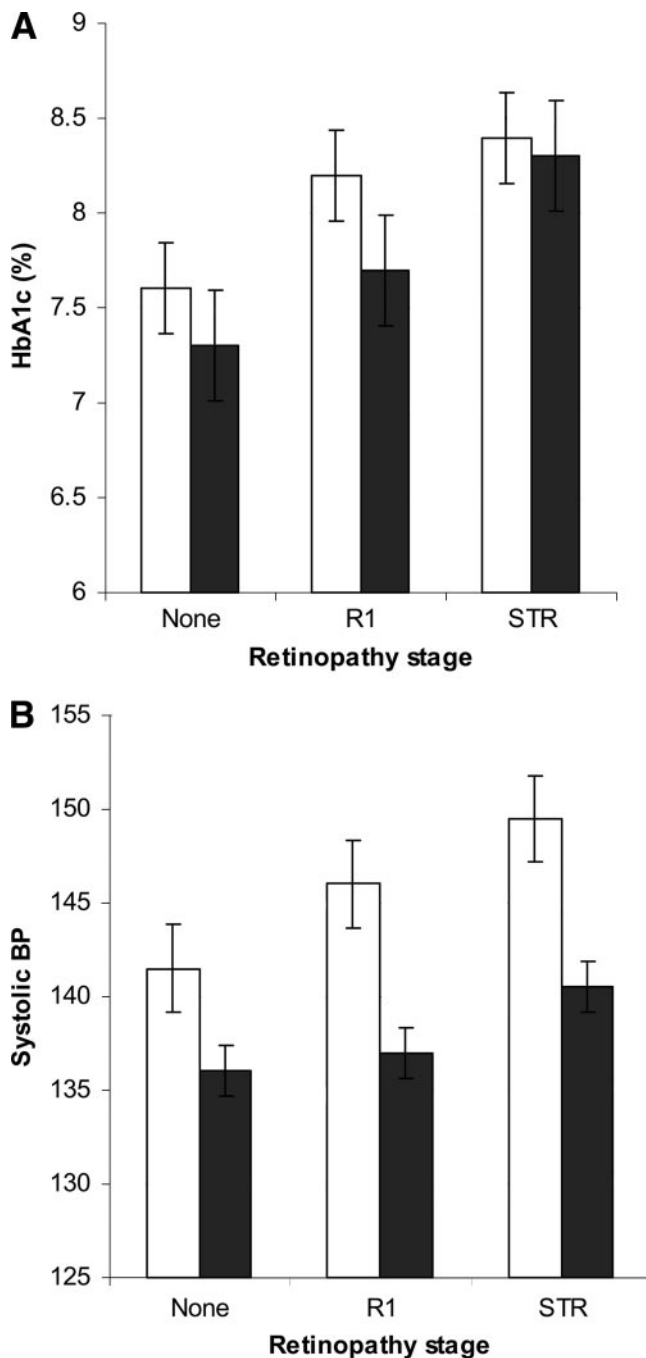


Figure 1—Retinopathy stage, mean A1C (± 1 SEM), and mean systolic blood pressure (± 1 SEM) by ethnicity. A: South Asian, $n = 413$; white European, $n = 475$. B: South Asian, $n = 414$; white European, $n = 478$. □, South Asian; ■, white European.

selected may not have excluded a socioeconomic status bias or other biases related to secondary care referral or access. As with any study involving informed consent, we cannot entirely exclude the possibility of selection bias, but by using a community-based screening program with a high proportion of patients recruited and retained, this was minimized. One limitation may be generalization of findings to nonurban populations be-

cause cultural factors may have an impact on diabetes, its management, patient concordance, and development of diabetic retinopathy. One strength of this study was the use of high-resolution digital photographs graded according to standard national quality-assurance protocols, although this grading is not as detailed as and uses less grades than the grading systems used in previous research (15).

Large-scale studies of South Asians in India have reported prevalences of diabetic retinopathy lower than those observed in white European populations; one study reported a prevalence of 17.6%, with increasing risk for men, elevated A1C levels, older age, treatment with insulin, and longer duration of diabetes (9). The prevalence reported was much lower compared with the current and previous estimates for U.K.-resident South Asian patients (8). Although most risk factors appear similar, it is of interest that systolic blood pressure in the younger South Asians in India was not a significant predictor of retinopathy and that mean blood pressures were much lower than those in the current study (9). Studies in India have shown differential rural and urban population lifestyle profiles associated with differential risk factor profiles, particularly increasing insulin resistance and hyperglycemia; these observations may help explain higher rates of diabetes and diabetes complications, including retinopathy, reported in South Asians in the U.K. (21).

Across the world, wide variations in retinopathy prevalences have been reported, identifying ethnic groups such as Maoris and Pacific Islanders and African, Mexican, and Hispanic Americans as having a particularly high risk (22,23). Differential risk may be explained by different levels of the potentially modifiable risk factors hyperglycemia and hypertension, with varying diabetes duration possibly reflecting earlier disease onset in these population groups. Whereas genetic differences between racial groups might contribute, such a contribution is relatively small compared with that of the modifiable risk factors (8,9,24). Systematic screening for retinopathy combined with intensive management of diabetes, including reduction of blood glucose and blood pressure to international targets, could help to reduce the incidence of visual impairment and blindness in ethnic minority groups across the world, addressing an important health inequality.

Health care professionals in developed and developing countries need to be aware of the potential contribution of diabetic retinopathy to visual loss in South Asian communities. High-quality data are needed to monitor retinopathy incidence as well as prevalence and to investigate the effectiveness of interventions to modify known risk factors through aggressive treatment of blood pressure and glycemia. Screening for diabetic retinopathy is

Table 3—Multiple logistic regression results for 396 South Asian versus 459 white European patients

	Model 1: unadjusted	Model 2: adjusted for confounders	Model 3: adjusted for confounders and interactions
Any retinopathy			
Ethnicity (SA vs. WH)	1.30 (0.99–1.71), 0.0601	1.46 (1.06–2.02), 0.0225	$P = 0.0023$
Duration of diabetes		1.11 (1.08–1.14), <0.0001	$P < 0.0001$
Age at diagnosis		1.00 (0.98–1.02), 0.5629	1.00 (0.98–1.01), 0.6176
Sex (male vs. female)		1.39 (1.02–1.87), 0.0343	1.35 (1.00–1.83), 0.0499
Systolic blood pressure		1.01 (1.00–1.02), 0.0085	1.01 (1.00–1.02), 0.0095
A1C		1.11 (1.01–1.23), 0.0354	1.12 (1.01–1.24), 0.0260
Insulin treated (yes vs. no)		2.23 (1.52–3.28), <0.0001	2.18 (1.48–3.21), <0.0001
Duration × ethnicity		—	$P = 0.0324$
STR			
Ethnicity (SA vs. WH)	1.38 (0.95–2.02), 0.0954	1.44 (0.94–2.23), 0.0968	
Duration of diabetes		1.09 (1.06–1.12), <0.0001	
Age at diagnosis		1.00 (0.98–1.02), 0.7675	
Sex (male vs. female)		1.29 (0.86–1.94), 0.2262	
Systolic blood pressure		1.01 (1.00–1.02), 0.0445	
A1C		1.14 (1.01–1.29), 0.0322	
Insulin treated (yes vs. no)		1.89 (1.18–3.00), 0.0072	
Maculopathy			
Ethnicity (SA vs. WH)	1.54 (1.00–2.38), 0.0505	1.53 (0.94–2.49), 0.0842	$P = 0.0035$
Duration of diabetes		1.06 (1.02–1.09), 0.0009	$P = 0.0002$
Age at diagnosis		1.00 (0.98–1.03), 0.8052	1.00 (0.98–1.03), 0.7993
Sex (male vs. female)		1.09 (0.69–1.72), 0.7030	1.08 (0.68–1.70), 0.7531
Systolic blood pressure		1.01 (1.00–1.02), 0.0243	1.01 (1.00–1.02), 0.0365
A1C		1.18 (1.03–1.34), 0.0168	1.19 (1.04–1.36), 0.0124
Insulin treated (yes vs. no)		1.96 (1.17–3.26), 0.0102	1.83 (1.09–3.08), 0.0225
Duration × ethnicity		—	$P = 0.0157$

Data are odds ratio (95% CI), P value. SA, South Asian; WH, white European.

becoming more systematic in the U.K. and across the developed world, but coverage rates and uptake among ethnic minority groups in inner city areas may be much lower than those for white Europeans (4). An awareness that these patients have the highest risk of visual impairment or blindness through a combination of inadequate screening, early onset of disease, and poorly controlled risk factors, particularly glycemia and blood pressure, is the first step toward development of programs to rectify these important health inequalities (7,12).

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APPENDIX

Members of the UKADS Retinopathy Study Group are as follows: Warwick Medical School, Warwick University, and University Hospital Coventry and Warwickshire, Coventry, U.K.: J.P. O'Hare, N.T. Raymond, S. Kumar, K. Johal, L. Varadhan, D.R. Reynold, K. Bush, S. Sankaranarayanan, A. Szczepura, A. Gumber, I.C. Agarwal, D.K. Mistry, F.F. Lyall, M.R. Dhadhanian, K.L. Kakad, U. Jetty, J.F. Sihota, S. Mall, K. Webb, S. Khatoon, R. Parker, P. Claire, G. Turner, S. Alijah, R.K. Dutta, and K. Mishra; and University of Birmingham and Heart of England NHS Trust, Birmingham, U.K.: S. Bellary, A.H. Barnett, and S. Mughal.

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