Assessing Progress in Retinopathy Outcomes in Type 1 Diabetes

Comparing findings from the Wisconsin Diabetes Registry Study and the Wisconsin Epidemiologic Study of Diabetic Retinopathy

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OBJECTIVE—The Wisconsin Diabetes Registry Study (WDRS) cohort consisted of patients diagnosed with type 1 diabetes in the same geographic region as, but 8–34 years later than the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) cohort, providing a unique opportunity to assess changes in complications. We estimated the current prevalence and severity of diabetic retinopathy at 20 years of diabetes duration, compared these between eras, and evaluated the influence of diabetes management.

RESEARCH DESIGN AND METHODS—Twenty-year examinations, including fundus photographs, were completed on 305 WDRS subjects during 2007–2011. A subgroup of the WESDR cohort participated in one of four study visits during 1980–1996, at similar diabetes duration (n = 583). Adjusted ordinal logistic regression with three retinopathy severity categories was used to estimate odds ratios (ORs) of more severe retinopathy with diagnosis during an earlier era.

RESULTS—Mean hemoglobin A1c (HbA1c) was lower in WDRS than in WESDR (8.0% vs. 9.3% [P < 0.001], and 93% vs. 21% [P < 0.001]) used ≥3 daily insulin injections or an insulin pump. In WDRS, 18% had vision-threatening levels of retinopathy vs. 43% in WESDR. The adjusted OR of more severe retinopathy in the earlier era (OR 3.0, 95% CI 2.2–4.0) was reduced by including 20-year HbA1c in the model (OR 2.2 [1.6–3.0]).

CONCLUSIONS—Retinopathy severity at a diabetes duration of 20 years is lower in the more recent era of type 1 diabetes. Updated projections should be used when informing newly diagnosed individuals of prognosis and for health care cost assessments. Current glycemic control explained a limited amount of the difference.

The burden of type 1 diabetes mellitus is high. Because type 1 diabetes onset is typically in childhood and adolescence, the effort to manage the disease and its sequelae lasts a lifetime. The majority of the morbidity and mortality associated with type 1 diabetes comes from chronic microvascular and macrovascular complications (1,2), including diabetic retinopathy (DR), a leading cause of preventable blindness in adults (3). Previously, some evidence of DR was present in most individuals by 15–20 years of diabetes duration (4,5). Recent reports, however, suggest less or less severe DR in the current era of diabetes care, not only at early durations (6,7) but perhaps even in long-standing type 1 diabetes (8–11). Studies report a decline in the incidence of severe DR across those diagnosed during the 1960s, 1970s, and early 1980s (8–10), but they may still overestimate the current level of retinopathy at 20 years of the disease (12). “Glycemic memory” (13) implies that individuals practicing intensive diabetes management starting at early diabetes duration may have much lower rates or lesser severity of retinopathy today. Anti-hypertensive and lipid-lowering therapies now implemented earlier in the course of the disease could also impact the current level of retinopathy (8,14). The current course of retinopathy clearly has implications for individuals with type 1 diabetes as well as the health care system (15). Contemporary estimates on DR, DR severity, and diabetes self-management practices from population-based studies of individuals with type 1 diabetes in the U.S. are needed (12,15).

Differences in methods of identifying DR complicate the evaluation of time trends in retinopathy (16,17). In our two studies, protocols for data collection included the same gold standard methods for objectively measuring retinopathy. The Wisconsin Diabetes Registry Study (WDRS) has followed a population-based cohort of individuals comprehensively since diagnosis of type 1 diabetes (6,18). This cohort was enrolled from a geographically defined region overlapping the study area of the landmark and also population-based Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) (4). We sought to capitalize on the unique opportunity presented by these two cohorts to investigate change in the course of DR. Specifically, we aimed to do the following: 1) provide contemporary estimates of the prevalence and severity of DR and diabetes self-management in the population after type 1 diabetes duration of 20 years, 2) compare retinopathy severity between time periods, and 3) evaluate whether changes in glycemic control and related diabetes management factors explained the differences seen in retinopathy between these time periods.

RESEARCH DESIGN AND METHODS

The WDRS population

The WDRS is an incident population-based cohort study of type 1 diabetes
Retinopathy progression in type 1 diabetes

complications and their risk factors, from diagnosis through a duration of 20 years (6,18–21). During May 1987 through April 1992, all residents ≤30 years of age in 28 counties of central and southern Wisconsin newly diagnosed with type 1 diabetes (by classic diabetes symptoms and requirement for exogenous insulin, according to World Health Organization criteria at the time [22]) were eligible. Patients were referred by physicians, nurses, diabetes educators, family members, or self-report. Hospitals and clinics were called every 3 months to ascertain missed cases. Case ascertainment was estimated to be 82%. Among 733 patients identified, 597 (81%) enrolled, and 589 remaining on insulin were eligible for long-term follow-up (20,21).

Follow-up during the 20 years after diabetes diagnosis included biannual or annual questionnaires for diabetes management and periodic clinical examinations, including blood samples and fundus photographs. Details on retinopathy during the first 14 years were published previously (6,21). Among 462 continuing subjects, 308 participated in a 20-year exam during November 2007 through July 2011, and 305 with fundus photographs were included in the current analysis.

**WDRS data collection**

Twenty-year examinations were completed at three clinic sites. Pupils were dilated, and color stereoscopic photographs were captured digitally of seven standard fields in both eyes (6,21,23). Images burned to compact disc were graded (levels 10–85) by the University of Wisconsin Ocular Epidemiology Reading Center in a masked fashion according to the modified Airle House Classification of Diabetic Retinopathy and the Early Treatment Diabetic Retinopathy Study severity of retinopathy system modified for WESDR (4). Retinopathy in the worse eye was classified as none (0–10), minimal (11–20), mild (21–30), moderate (31–40), or markedly severe to severe nonproliferative DR (47–53) or treated DR (panretinal photocoagulation) or proliferative DR (PDR) (60–85). These were further grouped into presence or absence of DR or PDR and into three categories of severity: none or minimal (levels 10–20), mild to moderate (21–43), and vision-threatening (moderately severe or worse, ≥47).

Weight was measured on a Health-o-meter (Health O Meter, Inc., Bridgeview, IL) physician beam scale, and height was measured with a standard stadiometer height rod fixed to the scale. Seated blood pressure, after measurement of arm circumference for cuff selection, was measured in the right arm with a random zero sphygmomanometer (Hawksley and Sons, Sussex, U.K.) according to the Hypertension Detection and Follow-up Program (24) protocol 5 minutes after cuff placement and repeated after a 5-minute rest. Questionnaires were completed on diabetes self-management, including continuous subcutaneous insulin infusion (CSII, insulin pump) use or number of insulin injections per day, blood glucose checks performed each day, average daily insulin dose, other medication use, and general health and socioeconomic factors, including total years of education.

Anticoagulated whole blood samples collected at the examination were analyzed for Diabetes Control and Complications Trial (DCCT)–equivalent hemoglobin A1c (HbA1c) within 7 days by automated high-performance liquid chromatography at the core DCCT laboratory at the University of Minnesota (Minneapolis, MN).

**Comparison with WESDR**
The WESDR identified 1210 persons with prevalent younger-onset (type 1) diabetes during 1979–1980 who were diagnosed before the age of 30 years, all of whom were using insulin and receiving their primary care within an 11-county area of southern and central Wisconsin; 996 participated in a baseline examination during 1980–1982 (4). The baseline (visit 1) and 4-, 10-, and 14-year follow-up examinations (visits 2–4) in 1984–1986, 1990–1992, and 1994–1996, respectively, included color stereoscopic photographs that were taken and graded as described above and previously (4,10). We included data from the first visit falling in a duration window (17–21 years) similar to that of the WDRS (n = 583).

As in the WDRS, WESDR study visits included measurement of height, weight, and seated blood pressure by random zero sphygmomanometer according to the Hypertension Detection and Follow-up Program (24), as well as questions on total years of education and on diabetes self-management, with the exception that blood glucose checks per day and insulin dose were not asked about at visit 1 and lipid medication use was not asked about at visits 1 and 2 (years in which these medications were not widely available). DCCT-equivalent HbA1c values were calculated for WESDR according to a regression equation determined after split sample testing with the core DCCT laboratory at the University of Minnesota (25).

This study was performed in accordance with the Declaration of Helsinki. WDRS and WESDR study participants provided informed consent for follow-up, and the institutional review board of the University of Wisconsin approved the related protocols.

**Statistical methods**

Analyses were performed with the statistical software package SAS v9.2 (26). The cohorts were described by means, SDs, and percentages. The prevalences of DR and PDR at 20 years were estimated for each cohort. Diabetic retinopathy severity categories were also described. Tests for significant trends across severity category were completed by univariate linear and logistic regression models within each study cohort for glycemic control and related care variables as well as for potentially confounding factors. Data from the two cohorts were then pooled for fitting ordinal (proportional odds) logistic regression models of retinopathy severity category, where the estimated odds ratios (ORs) for higher vs. lower retinopathy are considered the same regardless of where the cutoff points are placed across the 3 categories. The model first included an indicator variable for study cohort, age at exam, and sex. Diabetes duration at exam and years of education were added to the model as significant (P ≤ 0.05) and having attenuated the OR for retinopathy severity in the WESDR vs. WDRS by 7 and 13%, respectively. The steps of Baron and Kenny (27) were followed to assess mediation by glycemic control (HbA1c) or diabetes care or blood pressure. Interaction terms were tested in a stepwise manner. Model fit was confirmed by the Hosmer-Lemeshow goodness of fit test and χ² tests for the proportional odds assumption.

Sensitivity analyses were completed to assess potential participation bias at a diabetes duration of 20 years on prevalence and regression models. Analyses were repeated with weighting by the inverse of the probability of participation in the examination, thereby giving more weight to participants who resemble nonparticipants (28). Probability was estimated by logistic regression of participation status on sociodemographic
factors, diabetes care, and glycemic control at earlier durations (6,28). By similar methods, a sensitivity analysis was also completed for the WESDR cohort among those subjects examined in the diabetes duration window of 17–21 years.

**RESULTS**—WDRS participants in the 20 year exam were representative of the entire enrolled cohort with respect to age, sex, year and study area at diagnosis, and mean glycemic control in the first year and first 3 years after onset (data not shown), although fewer nonwhite individuals participated. Individuals were on average 11.2 years of age at diagnosis and 30.9 years of age, with a mean diabetes duration of 19.7 years, at the examination (Table 1). Participants were 49% male and 97% white. Characteristics of the WESDR group and significant differences between cohorts are also presented in Table 1. The cohorts were similar with respect to sex, race, and diabetes duration, although WESDR participants were slightly older (14.1 years at diagnosis and 33.4 years at the exam, each \(P < 0.001\)). Persons in the WESDR had less education than those in WDRS (13.8 vs. 15.2 years, \(P < 0.001\)). WESDR participants were diagnosed on average nearly two decades earlier than those in WDRS.

**Diabetes management at 20 years**

There were more intensive insulin management practices in WDRS than in WESDR (93.4% vs. 21.3%) with CSII or \(\geq 3\) insulin injections per day (multiple daily injection [MDI]) and lower HbA1c (8.0% vs. 9.3%) (Table 1). More individuals in WDRS were taking antihypertensive medications (28.5% vs. 18.5%), and blood pressures were higher in WESDR, especially among those taking these medications (data not shown). WDRS subjects checked blood glucose more often (mean 4.8 vs. 1.9 checks per day) and were more likely to use lipid-lowering medications (22.6% vs. 2.2%) than the WESDR subjects with blood glucose check and lipid medication data. Body weight, BMI, and insulin dose were greater in WDRS than in WESDR (Table 1).

**Diabetic retinopathy**

At a diabetes duration of 20 years, most individuals had evidence of some DR; however, retinopathy was less frequent and less severe in the WDRS cohort than in the WESDR cohort (Table 2). In WDRS, 92% (95% CI 89–95%) showed any DR, compared with 97% (95% CI 96–99%) in WESDR. Only 10% (95% CI 7–14%) showed evidence of PDR or treated DR in WDRS, vs. 36% (95% CI 32–40%) in WESDR. Weighting by inverse participation probability affected the prevalence estimates of DR and PDR in WDRS (<0.4 and 1.4%) and WESDR (<0.2 and 0.7%) little. The majority of WDRS participants displayed no DR or minimal DR (34%) or mild to moderate (48%) nonproliferative DR; 18% in WDRS had vision-threatening preproliferative or proliferative levels vs. 43% in WESDR.

Retinopathy severity is further described in Table 3. Significant trends were noted for correlation of less education and greater diabetes duration with increasing retinopathy severity in each cohort. Trends for lower HbA1c and related factors, including more intensive insulin care and more blood glucose checking, were observed with decreasing retinopathy severity in both WDRS and WESDR cohorts. Blood pressures and use of antihypertensive medications increased with increasing severity category in both cohorts. A greater proportion of males was noted with increasing retinopathy severity in both cohorts, but the trend was only significant in the WESDR group. There was no effect of race on retinopathy outcome in either of the primarily non-Hispanic white cohorts.

### Table 1—Characteristics of the WDRS and WESDR study groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>WDRS</th>
<th>WESDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>305</td>
<td>583</td>
</tr>
<tr>
<td>Male</td>
<td>150 (49.2)</td>
<td>292 (50.1)</td>
</tr>
<tr>
<td>White</td>
<td>297 (97.4)</td>
<td>574 (98.6)</td>
</tr>
<tr>
<td>Age at diagnosis (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>11.2 ± 7.0</td>
<td>14.1 ± 7.3</td>
</tr>
<tr>
<td>0–4</td>
<td>54 (17.7)</td>
<td>51 (8.8)</td>
</tr>
<tr>
<td>5–9</td>
<td>98 (32.1)</td>
<td>135 (23.2)</td>
</tr>
<tr>
<td>10–14</td>
<td>76 (24.9)</td>
<td>176 (30.2)</td>
</tr>
<tr>
<td>15–19</td>
<td>38 (12.5)</td>
<td>87 (14.9)</td>
</tr>
<tr>
<td>≥20</td>
<td>39 (12.8)</td>
<td>134 (23.0)</td>
</tr>
<tr>
<td>Age at exam (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>30.9 ± 7.0</td>
<td>33.4 ± 7.4</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>19.7 ± 1.2</td>
<td>19.2 ± 1.4</td>
</tr>
<tr>
<td>Education (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>15.2 ± 2.6</td>
<td>13.9 ± 2.5</td>
</tr>
<tr>
<td>&lt;7%</td>
<td>72 (23.7)</td>
<td>40 (7.4)</td>
</tr>
<tr>
<td>Insulin pump (CSII)</td>
<td>146 (47.9)</td>
<td>10 (1.7)</td>
</tr>
<tr>
<td>Daily insulin injections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>157 (51.0)</td>
<td>573 (98.3)</td>
</tr>
<tr>
<td>1–2</td>
<td>18 (5.9)</td>
<td>459 (78.7)</td>
</tr>
<tr>
<td>3</td>
<td>19 (6.2)</td>
<td>66 (11.3)</td>
</tr>
<tr>
<td>≥4</td>
<td>120 (39.3)</td>
<td>48 (8.2)</td>
</tr>
<tr>
<td>Intensive care (MDI or CSII, %)</td>
<td>285 (93.4)</td>
<td>124 (21.3)</td>
</tr>
<tr>
<td>Insulin dose, units/kg/day (n = 417)</td>
<td>0.75 ± 0.30</td>
<td>0.70 ± 0.24</td>
</tr>
<tr>
<td>BMI, kg/m² (n = 529)</td>
<td>28.3 ± 5.9</td>
<td>26.1 ± 4.6</td>
</tr>
<tr>
<td>Weight, kg (n = 537)</td>
<td>83.8 ± 19.8</td>
<td>73.1 ± 14.9</td>
</tr>
<tr>
<td>Blood glucose checks/day (n = 378)</td>
<td>4.8 ± 4.5</td>
<td>1.9 ± 1.7</td>
</tr>
<tr>
<td>&lt;1</td>
<td>30 (9.8)</td>
<td>145 (38.4)</td>
</tr>
<tr>
<td>≥1</td>
<td>51 (16.7)</td>
<td>119 (31.5)</td>
</tr>
<tr>
<td>Systolic BP (mmHg, n = 531)</td>
<td>122 ± 13</td>
<td>125 ± 19</td>
</tr>
<tr>
<td>Diastolic BP (mmHg, n = 530)</td>
<td>77 ± 9</td>
<td>79 ± 11</td>
</tr>
<tr>
<td>Antihypertensive medication</td>
<td>87 (28.5)</td>
<td>108 (18.5)</td>
</tr>
<tr>
<td>Lipid-lowering medication (n = 358)</td>
<td>69 (22.6)</td>
<td>8 (2.2)</td>
</tr>
</tbody>
</table>

Data are mean ± SD or n (%) unless otherwise specified. Boldface type indicates significant (\(P < 0.01\)) differences between study groups. Variables with missing data in WESDR group are noted with available \(n\) in parentheses. BP, blood pressure.
Retinopathy progression in type 1 diabetes

Table 2—DR in the WDRS and WESDR studies at diabetes duration of 20 years

<table>
<thead>
<tr>
<th>Retinopathy</th>
<th>WDRS</th>
<th>WESDR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Any retinopathy (DR)</td>
<td>281</td>
<td>92.1</td>
</tr>
<tr>
<td>None (10–13)</td>
<td>24</td>
<td>7.9</td>
</tr>
<tr>
<td>Nonproliferative DR</td>
<td>249</td>
<td>81.6</td>
</tr>
<tr>
<td>Minimal (14, 15, 20)</td>
<td>80</td>
<td>26.2</td>
</tr>
<tr>
<td>Mild (31)</td>
<td>59</td>
<td>19.3</td>
</tr>
<tr>
<td>Mild to moderate (37)</td>
<td>52</td>
<td>17.0</td>
</tr>
<tr>
<td>Moderate (43)</td>
<td>35</td>
<td>11.5</td>
</tr>
<tr>
<td>Moderately severe to severe (47, 53)</td>
<td>23</td>
<td>7.5</td>
</tr>
<tr>
<td>PDR or treated DR (≥60)</td>
<td>32</td>
<td>10.5</td>
</tr>
</tbody>
</table>

DR grade levels are noted in parentheses.

Ordinal logistic regression models for the three retinopathy severity categories confirmed higher, unadjusted average odds of more severe retinopathy in the WESDR era than in the WDRS era (OR 3.3 [95% CI 2.5–4.3]). With adjustment for age, sex, diabetes duration, and education, the OR was reduced to 3.0 (95% CI 2.2–4.0) (Table 4). The inclusion of 20-year HbA1c in the model further reduced the OR for WESDR vs. WDRS (from 3.0 to 2.9). No interaction terms were significant, and weighting for participation did not affect the final results.

CONCLUSIONS—The frequency and severity of diabetic retinopathy after a diabetes duration of 20 years was lower for individuals with type 1 diabetes diagnosed in a more recent era. This result extends our previous findings of a lower than expected prevalence of retinopathy at a diabetes duration of 4–14 years (6) and is consistent with findings of several other studies (8–10). A similar decline in diabetes-related macular edema has also been suggested (29). In WDRS, only 12% of individuals had evidence of macular edema (4% with clinically significant edema) at 20 years (T.J.L., unpublished observations). This provides support that diabetes care is having a “positive and sustained influence on diabetes complications” (13).

Many of the recent reports on individuals followed up for longer durations of type 1 diabetes come from clinic-based studies in Europe (8,9), and only few are truly population based (11,30,31). Further, very little data exist on retinopathy prevalence among those with a diabetes duration of ≥20 years and a diagnosis after 1980, especially for type 1 diabetes alone (32).

More intensive diabetes care from early diabetes on appears to have changed the prognosis for individuals whose diagnoses were made in the current era of diabetes care (7,9,33). CSII or multiple daily insulin injections, more frequent blood glucose checking, and rapid- or prolonged-acting insulin analogs are improvements not available to the WESDR cohort during earlier diabetes durations, and for some even by a duration of 20

Table 3—Characteristics by DR category in the WDRS and WESDR study groups at diabetes duration of 20 years

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>WDRS</th>
<th>WESDR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None or minimal</td>
<td>Mild to moderate</td>
</tr>
<tr>
<td></td>
<td>n (% )</td>
<td>n (% )</td>
</tr>
<tr>
<td>C</td>
<td>N (%)</td>
<td>Male (%)</td>
</tr>
<tr>
<td>N (%)</td>
<td>104 (34.1)</td>
<td>45.2</td>
</tr>
<tr>
<td>Male (%)</td>
<td>146 (47.9)</td>
<td>48.0</td>
</tr>
<tr>
<td>White (%)</td>
<td>55 (18.0)</td>
<td>60.0</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>100.0</td>
<td>98.3</td>
</tr>
<tr>
<td>Male (%)</td>
<td>239 (40.5)</td>
<td>47.5</td>
</tr>
<tr>
<td>White (%)</td>
<td>253 (43.4)</td>
<td>56.1</td>
</tr>
</tbody>
</table>

Data are mean ± SD except as indicated. Boldface type indicates significant test for trend P values (P < 0.05), determined within study by linear regression for continuous and logistic regression for dichotomous variables modeled on DR category (1–3). Variables with missing data in WESDR group are noted with available n in parentheses. BP, blood pressure.
years (34). Shortly after the WDRS sub-
jects were diagnosed, the benefits of in-
tensive therapy, especially when started
earlier in the course of type 1 diabetes,
were proved to reduce the risk of diabetes
complications (35). WESDR participants
included in this investigation were at 14–
35 years after diabetes onset at the time of
the first DCCT report.

Contemporary data on diabetes man-
gement practices of individuals with
longer type 1 diabetes duration in the
U.S. are scarce. Diabetes management in
the WDRS cohort at 20 years was similar
to that recently reported among both the
conventional and intensively treated arms
of the primary prevention group of the
DCCT at a mean diabetes duration of 24
years, where approximately 50% were
using insulin pumps, 50% were using
MDI, and 60% were checking blood
glucose 4 or more times daily (34). HbA1c
levels were also similar in the con-
ventional, intensive, and WDRS groups,
at 7.7%, 7.8%, and 8.0%, respectively.
Consistent with our finding of less severe
retinopathy among those showing better
diabetes management, the prevalence of
PDR was 4.4% in the intensively treated
group and 12.7% in the group originally
randomized to conventional therapy (34).

Cross-sectional data from WESDR suggest
that PDR was more common in those
with lower HbA1c levels, even after
adjustment for glycemic control, when
comparing the DCCT and WESDR groups.

Although BMI differed between the
cohorts, it had little effect on retinopathy
outcome, remaining nonsignificant in re-
gression analysis. Inclusion of HbA1c in
the model and greater BMI in WDRS
was no longer associated with achieving
better glycemic control. This may repre-
sent the additional impact of better self-
care practices, better access to care, ability
to afford testing supplies, or health liter-
acy, all of which may result from better
socioeconomic status (36) and are other-
wise unmeasured in the current analysis.

It may be noted that the DCCT was a trial
of management and not of the impact
of lower HbA1c in isolation. Despite this,
the aspects of diabetes management consist-
tently measured in both studies did not
further explain the difference in retinopathy
outcome. A meta-analysis of PDR pre-
vention has not been conducted in either
cohort.

Better glycemic control was the stron-
gest predictor for decreasing severe reti-

nopathy with time in some previous
reports (7,9); however, current HbA1c
levels only partially explained the difference
in retinopathy between the cohorts. The sta-

bility or level of glycemic control during
diabetes duration may be an im-
portant variable in setting the course
of retinopathy even through 20 years
(13). Although data on early glycemic
control are available for WDRS, the

variable (1) Univariate (2) Adjusted (3) Adjusted with HbA1c (4) Adjusted with BP (5) Adjusted with HbA1c and BP

<table>
<thead>
<tr>
<th>Variable</th>
<th>(1) Univariate</th>
<th>(2) Adjusted</th>
<th>(3) Adjusted with HbA1c</th>
<th>(4) Adjusted with BP</th>
<th>(5) Adjusted with HbA1c and BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>WESDR study cohort</td>
<td>3.33 (2.52–4.39)</td>
<td>3.01 (2.24–4.04)</td>
<td>2.23 (1.63–3.03)</td>
<td>2.88 (2.13–3.88)</td>
<td>2.21 (1.62–3.02)</td>
</tr>
<tr>
<td>Age (per 1 year)</td>
<td>1.00 (0.98–1.02)</td>
<td>1.00 (0.98–1.02)</td>
<td>0.99 (0.97–1.01)</td>
<td>0.99 (0.97–1.01)</td>
<td>0.99 (0.97–1.01)</td>
</tr>
<tr>
<td>Male</td>
<td>1.42 (1.10–1.85)</td>
<td>1.40 (1.08–1.83)</td>
<td>1.10 (0.84–1.45)</td>
<td>1.09 (0.83–1.44)</td>
<td>1.09 (0.83–1.44)</td>
</tr>
<tr>
<td>Duration (per 1 year)</td>
<td>1.17 (1.06–1.30)</td>
<td>1.21 (1.09–1.34)</td>
<td>1.18 (1.06–1.31)</td>
<td>1.21 (1.08–1.34)</td>
<td>1.21 (1.08–1.34)</td>
</tr>
<tr>
<td>Education (per 1 year)</td>
<td>0.88 (0.83–0.93)</td>
<td>0.90 (0.85–0.95)</td>
<td>0.80 (0.84–0.94)</td>
<td>0.90 (0.86–0.96)</td>
<td>0.90 (0.86–0.96)</td>
</tr>
<tr>
<td>HbA1c (per 1%)</td>
<td>1.34 (1.23–1.47)</td>
<td>1.34 (1.23–1.47)</td>
<td>1.34 (1.23–1.47)</td>
<td>1.34 (1.23–1.47)</td>
<td>1.34 (1.23–1.47)</td>
</tr>
<tr>
<td>Systolic BP (per 3 mmHg)</td>
<td>1.04 (1.00–1.07)</td>
<td>1.04 (1.00–1.08)</td>
<td>1.04 (1.00–1.08)</td>
<td>1.04 (1.00–1.08)</td>
<td>1.04 (1.00–1.08)</td>
</tr>
<tr>
<td>Diastolic BP (per 3 mmHg)</td>
<td>1.12 (1.07–1.18)</td>
<td>1.11 (1.05–1.17)</td>
<td>1.11 (1.05–1.17)</td>
<td>1.11 (1.05–1.17)</td>
<td>1.11 (1.05–1.17)</td>
</tr>
</tbody>
</table>

Data are ORs (95% CIs). Models are represented in columns as follows: (1) model with study cohort only; (2) model 1 with adjustment for age, sex, diabetes duration, and subject’s total years of education; (3) model 2 with adjustment for HbA1c; (4) model 2 with adjustment for systolic and diastolic blood pressures; (5) model 2 with adjustment for HbA1c and blood pressures (final model).

In conclusion, WESDR participants
tended to have lower blood pressures and
in adjusted analysis, lower HbA1c levels
were associated with a lower risk of
retinopathy development. Although BMI
and other factors may have contributed
to the lower prevalence of retinopathy,
these results suggest that glycemic con-

control was the primary factor.

References (37–39)

1. Diabetes Care (37–39)

2. Diabetes Care (37–39)

3. Diabetes Care (37–39)

4. Diabetes Care (37–39)

5. Diabetes Care (37–39)
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not shown). This variation, however, had little impact on the reported difference in outcome between the study periods.

The WDRS and the WESDR provided a unique opportunity to compare outcomes of individuals with type 1 diabetes across time. Few population-based studies exist that followed individuals from diagnosis for such a long period. The overlapping study area and the same approach to definition of retinopathy also reduced bias from differing methodologies and demographics. Still, limitations do exist. The current analysis was cross-sectional and captured the point prevalence at 20 years, previously determined as the time by which nearly all individuals would have some level of DR. Those who chose not to participate in the examination or were no longer continuing WDRS subjects could have displayed more severe retinopathy. This was not seen, however, in questionnaire responses regarding whether participants had ever been told of having diabetes-related eye changes or disease by a health care provider. Further, weighting for participation probability based on baseline characteristics of the original cohort of 589 showed that prevalence estimates changed very little from original results.

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References


