The Diabetes Control and Complications Trial (DCCT) was a multicenter clinical trial conducted between 1983 and 1993. It was designed to determine whether intensive therapy with the aim of maintaining blood glucose and glycosylated hemoglobin concentrations as close to the normal range as possible would prevent or delay long-term complications in patients with type 1 diabetes mellitus. The trial showed that during an average treatment period of 6.5 years, the risk of the development or progression of early microvascular complications of diabetes was substantially lower in the intensive-therapy group than in the conventional-therapy group. At the close of the trial in 1993, patients in the conventional-therapy group were offered intensive therapy and instructed in its use. All patients received subsequent care from their own physicians, and most were enrolled in the Epidemiology of Diabetes Interventions and Complications (EDIC) study, a long-term observational study. One of the objectives of the EDIC study is to compare the long-term effects of the intensive or conventional therapy provided during the DCCT on the development of more advanced retinal and renal complications of diabetes. In this report, we describe the continued differences between the two original treatment groups in the incidence of these complications four years after the close of the DCCT.

**METHODS**

**Patients**

The 1441 patients enrolled in the DCCT between 1983 and 1989 were 13 to 39 years old, had had type 1 diabetes for 1 to 15 years, and were in generally good health. The primary-prevention cohort consisted of 726 patients who had no retinopathy and who had a urinary albumin excretion rate of less than 28 µg per minute (less than 40 mg per 24 hours); the duration of their diabetes ranged from one to five years. The secondary-intervention cohort consisted of 715 patients who had had diabetes for 1 to 15 years and who had minimal-to-moderate nonproliferative retinopathy and a urinary albumin excretion rate of less than 139 µg per minute (less than 200 mg per 24 hours). The patients in the primary-prevention and secondary-intervention cohorts were randomly assigned to receive either intensive therapy, with the goal of achieving blood glucose and glycosylated hemoglobin concentrations as close to the normal range as possible, or conventional therapy. Intensive therapy consisted of at least three daily injections of insulin or treatment with an insulin pump, with the dose adjusted frequently on the basis of self-monitored blood glucose values (at least four measurements per day), diet, and exercise. Conventional therapy consisted of one or two insulin injections per day with one urine or blood glucose test per day. The mean duration of follow-up was 6.5 years.

Address reprint requests to the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group, Box NIDC/EDIC, Bethesda, MD 20892, or at nathan@gec.mgh.harvard.edu. The writing group (John M. Lachin, Sc.D., Saul Gershon, M.D., Patricia Cleary, M.S., Matthew D. Davis, M.D., and David M. Nathan, M.D.) assumes responsibility for the overall content and integrity of the manuscript. Other members of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group are listed in the Appendix.
All surviving patients were evaluated at the close of the trial, between January and April 1993. In 1994, 1375 of the patients in the original cohort, including 688 patients in the former conventional-therapy group and 687 patients in the former intensive-therapy group, volunteered to participate in the EDIC study, which included annual follow-up examinations. During the EDIC study, all therapy was provided by the patients’ own physicians.

### Assessment of Retinopathy, Renal Function, and Glycemic Control

Retinopathy was assessed by fundus photography according to the DCCT-EDIC protocol in 369 patients during EDIC study year 1, 443 patients during year 2, 419 patients during year 3, and 1208 patients during year 4 (1997). All photographs were graded centrally according to the final Early Treatment Diabetic Retinopathy Study (ETDRS) grading scale and DCCT methods; the graders were unaware of the DCCT therapy assignment. The outcomes related to retinopathy included a progression of at least three steps in the grade of retinopathy from the level on enrollment in the DCCT, the presence of severe, nonproliferative diabetic retinopathy or worse, and the development of proliferative retinopathy. Patients who received panretinal scatter-photocoagulation (laser) therapy were thereafter counted as having worse retinopathy for all these outcomes. The presence of clinically significant macular edema was defined according to ETDRS criteria. Patients who underwent focal photocoagulation for macular edema were counted as having macular edema thereafter. The level of retinopathy at the end of the DCCT was classified as no retinopathy (ETDRS grade 10 in both eyes), microaneurysms only (grade 20 in either eye), mild nonproliferative diabetic retinopathy (grade 30 in either eye), moderate or greater nonproliferative diabetic retinopathy (grade 40 or more in either eye), and any previous laser therapy (focal or scatter). Visual acuity was assessed by ETDRS methods.

Renal function was assessed in 649 patients during year 3 of the EDIC study and in 653 patients during year 4 by the measurement of urinary albumin excretion and creatinine clearance in a four-hour urine specimen. Urinary albumin excretion was expressed in micrograms per minute. Creatinine clearance was also estimated on the basis of the inverse of the serum creatinine concentration (with the equations of Cockcroft and Gault), as follows: 

\[
K = \frac{1004 - \text{age} \text{ (years)}}{72 \times \text{serum creatinine} (\text{mg/dL})} \times \text{weight (kg)}
\]

where \(K\) equals 1 for men and 0.85 for women. Microalbuminuria was defined as a urinary albumin excretion rate of more than 28 µg per minute (40 mg per 24 hours), albuminuria as a urinary albumin excretion rate of more than 208 µg per minute (300 mg per 24 hours), and abnormal glomerular filtration as a creatinine clearance of less than 70 ml per minute per 1.73 m² of body-surface area.

Glycosylated hemoglobin was measured annually in a central laboratory by high-performance liquid chromatography. The total mean glycosylated hemoglobin value was calculated as the time-weighted average during both the DCCT and the EDIC study.

### Statistical Analysis

To test for differences between groups, Wilcoxon rank-sum tests were used for quantitative or ordinal data, and chi-square tests were used for categorical data. Logistic-regression analysis was used to estimate the cumulative incidence of the progression of retinopathy during the EDIC study with the use of all photographs in all patients, including those obtained at one, two, and three years in some patients. All analyses were performed with SAS software.

### RESULTS

The level of retinopathy was evaluated in 1208 patients during year 4 of the EDIC study. The characteristics of these patients on enrollment in the DCCT and at its end are shown in Table 1. The characteristics of the patients at the end of the DCCT were the base-line characteristics for the EDIC study. The groups that had received intensive and conventional treatment did not differ significantly with respect to sex, age, duration of diabetes, or duration of follow-up in the DCCT. However, they did differ with respect to the level of retinopathy at the end of the DCCT and the need for photocoagulation therapy.

### Table 1. Characteristics of the 1208 Patients Enrolled in the EDIC Study Who Were Evaluated After Four Years of Follow-up.*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>DCCT Treatment Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CONVENTIONAL (N=603)</td>
<td>INTENSIVE (N=605)</td>
</tr>
<tr>
<td>At DCCT entry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women (%)</td>
<td>47</td>
<td>48</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>27±7</td>
<td>27±7</td>
</tr>
<tr>
<td>Duration of diabetes (yr)</td>
<td>5.6±4.1</td>
<td>5.9±4.2</td>
</tr>
<tr>
<td>Glycosylated hemoglobin (%)</td>
<td>9.0±1.6</td>
<td>9.0±1.6</td>
</tr>
<tr>
<td>At EDIC entry‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>33±7</td>
<td>34±7</td>
</tr>
<tr>
<td>Duration of diabetes (yr)</td>
<td>11.7±4.8</td>
<td>12.1±4.9</td>
</tr>
<tr>
<td>DCCT follow-up (yr)</td>
<td>6.1±1.7</td>
<td>6.2±1.7</td>
</tr>
<tr>
<td>Glycosylated hemoglobin (%)</td>
<td>9.0±1.2</td>
<td>7.3±0.9</td>
</tr>
<tr>
<td>Level of retinopathy (%)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>18</td>
<td>29</td>
</tr>
<tr>
<td>Microaneurysms only</td>
<td>30</td>
<td>38</td>
</tr>
<tr>
<td>Mild nonproliferative retinopathy</td>
<td>30</td>
<td>22</td>
</tr>
<tr>
<td>Moderate or severe nonproliferative retinopathy</td>
<td>22</td>
<td>11</td>
</tr>
<tr>
<td>Photosoclagulation during DCCT (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scatter, for retinopathy</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Focal, for macular edema</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Nephropathy at EDIC year 3 or 4 (%)‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin excretion &gt;28 µg/min</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>Albumin excretion &gt;208 µg/min</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Creatinine clearance &lt;70 ml/min/1.73 m²</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Treatment at EDIC year 4 (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous subcutaneous insulin infusion (pump) or multiple daily injections</td>
<td>75</td>
<td>95</td>
</tr>
<tr>
<td>Self-monitoring of blood glucose ≥4 times per day</td>
<td>40</td>
<td>45</td>
</tr>
</tbody>
</table>

*Plus–minus values are means ±SD. EDIC denotes Epidemiology of Diabetes Interventions and Complications, and DCCT Diabetes Control and Complications Trial.

†The base-line data in the EDIC study were the same as the data at the end of the DCCT.

‡The results for nephropathy include 1302 EDIC participants (649 from the former conventional-therapy group and 653 from the former intensive-therapy group).
during the DCCT. These differences reflect the benefit of intensive therapy as compared with conventional therapy during the trial.

Among the 1302 patients in whom renal function was evaluated during year 3 or 4 of the EDIC study, the proportion with microalbuminuria at the end of the DCCT was nearly twice as high in the group of patients who had received conventional therapy as in the group of patients who had received intensive therapy (Table 1). The prevalence of urinary albumin values above 208 µg per minute and creatinine clearance values under 70 ml per minute per 1.73 m² was low and did not differ significantly between the treatment groups at the end of the DCCT.

During the 6.5 years of treatment in the DCCT, the patients in the intensive-therapy group used their assigned therapy (at least three insulin injections per day or continuous infusion of insulin with an external pump) 98 percent of the time, and the patients in the conventional-therapy group gave themselves one or two insulin injections per day 97 percent of the time. During year 4 of the EDIC study, 95 percent of the patients in the former intensive-therapy group continued treatment with multiple daily injections of insulin or an insulin infusion pump, as compared with 75 percent of the patients in the former conventional-therapy group (P<0.001). Less than half the patients in each group were performing self-monitoring of blood glucose four or more times per day.

At the time of enrollment in the DCCT, the mean glycosylated hemoglobin value in each group was about 9 percent (Table 1). The distribution of glycosylated hemoglobin values during the DCCT and during the EDIC study for the 1208 patients who had an eye evaluation during year 4 of the EDIC study is shown in Figure 1. Over the average of 6.5 years of follow-up in the DCCT, the median glycosylated hemoglobin value was 7.2 percent in the intensive-therapy group and 9.1 percent in the conventional-therapy group. By the end of year 1 in the EDIC study, the glycosylated hemoglobin values in the two groups had almost converged; the median value was 8.1 percent in the conventional-therapy group and 7.7 percent in the intensive-therapy group. Thereafter, the difference continued to narrow. During the four-year follow-up period in the EDIC study, the median glycosylated hemoglobin values were 8.2 percent in the conventional-therapy group and 7.9 percent in the intensive-therapy group (P<0.001). The correlation coefficient for the mean glycosylated hemoglobin value during the EDIC study and that during the DCCT was 0.58 in the conventional-therapy group and 0.67 in the intensive-therapy group.

Ophthalmologic Outcomes

The rates of prevalence of various levels of retinopathy and of clinically important macular edema were significantly lower in the former intensive-therapy group than in the former conventional-therapy group during year 4 of the EDIC study, as was the case in the same 1208 patients at the end of the DCCT (Fig. 2). With respect to the principal DCCT outcome, the likelihood (odds) of an increase in retinopathy of three or more steps from base line was...
Conventional-–R therapy
Intensive-–R therapy

Progression of Retinopathy

End of DCCT EDIC Year 4A

Odds reduction, 76%
(95% CI, 67–82%)
P<0.001

Adjusted odds reduction, 75%
(95% CI, 67–81%)
P<0.001

Percentage of Patients

Conventional therapy
Intensive therapy

Proliferative or Severe Nonproliferative Retinopathy

End of DCCT EDIC Year 4

Odds reduction, 68%
(95% CI, 45–82%)
P<0.001

Adjusted odds reduction, 69%
(95% CI, 48–82%)
P<0.001

Percentage of Patients

Conventional therapy
Intensive therapy

Macular Edema

End of DCCT EDIC Year 4

Odds reduction, 46%
(95% CI, 9–68%)
P=0.03

Adjusted odds reduction, 58%
(95% CI, 31–74%)
P<0.001

Percentage of Patients

Conventional therapy
Intensive therapy
76 percent lower in the intensive-therapy group than in the conventional-therapy group at the end of the DCCT. After four years of follow-up in the EDIC study, 49 percent of the patients in the conventional-therapy group had had a progression in retinopathy of three or more steps from the DCCT base line, compared with 18 percent of the patients in the intensive-therapy group. Logistic-regression analysis with adjustment for the level of retinopathy at the end of the DCCT showed a 75 percent reduction in the likelihood of progression (P<0.001). For each outcome included in Figure 2, there was a significantly lower risk in the intensive-therapy group after adjustment for group differences at the end of the DCCT.

To describe better the persistence of the effect of therapy received in the DCCT during the subsequent four years of the EDIC study, we analyzed the incidence of further progression of retinopathy, defined as an increase of at least three steps from the level of retinopathy at the end of the DCCT (Table 2). Overall, 21 percent of the 581 patients in the conventional-therapy group had progression of retinopathy, as compared with 6 percent of the 596 patients in the intensive-therapy group, for an unadjusted reduction in the odds of this outcome of 75 percent. When the results were analyzed separately for each of the levels of retinopathy at the end of the DCCT, the incidence of progression was significantly lower in the intensive-therapy group. The adjusted reduction in the odds of progression of retinopathy of three or more steps, averaged over all levels of retinopathy at the end of the DCCT, was 72 percent (P<0.001).

An interval-censored life-table analysis (Fig. 3) that included assessments of the level of retinopathy in approximately 25 percent of the cohort at years 1, 2, and 3 of the EDIC study showed that the difference in cumulative incidence of progressive retinopathy between groups increased steadily each year. By year 4, the cumulative incidence in the intensive-therapy group was significantly (70 percent) lower than that in the conventional-therapy group (95 percent confidence interval, 58 percent to 78 percent; P<0.001).

The incidence of worsening of retinopathy at four years in the EDIC study among patients who had been free of each outcome at the end of the DCCT
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is shown in Table 3. Severe nonproliferative retinopathy, or worse, was detected in 10 percent of the 556 patients in the conventional-therapy group and in 2 percent of the 589 patients in the intensive-therapy group, representing a 76 percent reduction in the odds of this outcome, after adjustment for the level of retinopathy at the end of the DCCT. Among the patients in the conventional-therapy group, 6 percent required laser therapy for the first time during the first four years of the EDIC study, as compared with only 1 percent of the patients in the intensive-therapy group. Among the patients in the intensive-therapy group, five had visual acuity that was worse than 20/100 in one eye, three of whom had visual acuity that was worse than 20/200 in one eye; none had visual acuity worse than 20/200 in both eyes. No patient in the intensive-therapy group had visual acuity that was worse than 20/100 in either eye.

Renal Outcomes

During year 3 or 4 of the EDIC study, microalbuminuria was detected for the first time in 11 percent of 573 patients in the former conventional-therapy group, as compared with 5 percent of 601 patients in the former intensive-therapy group (Table 4), representing a 53 percent odds reduction. Likewise, the risk of new albuminuria was reduced by 86 percent in the intensive-therapy group, with similar reductions for patients with normal albumin excretion (no more than 28 µg per minute) and those with microalbuminuria (29 to 208 µg per minute) at the end of the DCCT. Very few patients in either group had a decrease in creatinine clearance, and the adjusted risk of a decrease was similar in the two groups.

Relation of Progression of Retinopathy to Hyperglycemia

Within each former therapy group, the likelihood of further progression of retinopathy during the EDIC study increased as the mean glycosylated hemoglobin values during the DCCT and the EDIC study increased, after adjustment for other factors, including the level of retinopathy at the end of the DCCT. In the conventional-therapy group, the risk of a progression of retinopathy was multiplied by 2.8 for every 1 percent increase in the glycosylated hemoglobin.
value during the DCCT and the EDIC study (95 percent confidence interval, 2.2 to 3.8; P<0.001). In
the intensive-therapy group, the risk of a progression of retinopathy was multiplied by 2.6 for every 1 per-
cent increase in the glycosylated hemoglobin value
during the DCCT and the EDIC study (95 percent confidence interval, 1.7 to 3.9; P<0.001). No other
variables, including blood pressure and serum lipid
concentrations, had a substantial effect on these com-
lications, perhaps because patients with hypertension
or hyperlipidemia had been excluded from the DCCT.

**DISCUSSION**

During four years of follow-up in the EDIC study,
the levels of glycemic control converged for the group
of patients who had received intensive therapy and
the group that had received conventional therapy
during the DCCT. On the basis of previous epidemi-
ologic assessments, the small difference in glycosy-
lated hemoglobin values between the two treatment
groups would be expected to reduce the benefit of in-
tensive therapy that was observed during the DCCT.
To the contrary, however, the frequencies of progres-
sive retinopathy, microalbuminuria, and albuminuria
remained markedly lower in the former intensive-ther-
apy group than in the former conventional-therapy
group. These lower frequencies were not merely a re-
flection of the differences between the two groups at

![Figure 3. Cumulative Incidence of Further Progression of Reti-
opathy (an Increase of at Least Three Steps from the Level at the
End of the Diabetes Control and Complications Trial [DCCT]) in
the Former Conventional-Therapy and Intensive-Therapy Groups.
The data are based on regression analysis adjusted for the level
of retinopathy at the end of the DCCT, whether patients received
therapy as primary prevention or secondary intervention, and
both the duration of diabetes and the glycosylated hemoglobin
value on enrollment in the DCCT. Patients who underwent scatter
photocoagulation during the DCCT were excluded from the
analysis (22 in the conventional-therapy group and 9 in the in-
tensive-therapy group). Bars denote 95 percent confidence in-
tervals.](image-url)

<table>
<thead>
<tr>
<th>RETINAL CHANGE†</th>
<th>NO. OF PATIENTS‡</th>
<th>PROGRESSION OF RETINOPATHY</th>
<th>ADJUSTED ODDS REDUCTION (95% CI)§</th>
<th>P VALUE¶</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe nonproliferative retinopathy or worse</td>
<td>76 (52–88)</td>
<td>76 (52–88)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Conventional therapy</td>
<td>556</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive therapy</td>
<td>589</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proliferative retinopathy</td>
<td>564</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional therapy</td>
<td>564</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive therapy</td>
<td>590</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically significant macular edema</td>
<td>564</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional therapy</td>
<td>564</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive therapy</td>
<td>582</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laser therapy (focal or scatter)</td>
<td>544</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional therapy</td>
<td>544</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive therapy</td>
<td>575</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*DCCT denotes Diabetes Control and Complications Trial, EDIC Epidemiology of Diabetes In-
tervention and Complications, and CI confidence interval.
† Patients who underwent scatter photocoagulation after the DCCT were counted as having a pro-
gression of retinopathy; those who underwent focal photocoagulation were counted as having clini-
cally significant macular edema.
‡ The numbers of patients free of each specific type of worsening at the end of the DCCT are given.
§ The odds reduction is for former intensive therapy as compared with former conventional therapy
on the basis of a logistic-regression analysis with adjustment for the level of severity of retinopathy
at the end of the DCCT according to the Early Treatment Diabetic Retinopathy Study categories
shown in Table 2, plus any previous laser therapy (focal or scatter).
¶ P values were calculated by the likelihood-ratio test.
the end of the DCCT (the beginning of the EDIC study), since the reductions in the risk of progressive retinopathy and of nephropathy persisted after adjustment for the differences in the frequency of complications between the two treatment groups at the end of the DCCT.

In the intensive-therapy group, the risks of progressive retinopathy and nephropathy remained low, despite an increase in the median glycosylated hemoglobin value from 7.2 percent during the DCCT to 7.9 percent during the EDIC study. Thus, after four additional years of follow-up, the rate of worsening of complications did not increase in the intensive-therapy group. In contrast, in the former conventional-therapy group, the risk of a progression of retinopathy during the first four years of the EDIC study remained elevated and about the same as during the first four years of the DCCT.\(^\text{15}\) The increased risk of progression of retinopathy persisted in the conventional-therapy group, despite a decrease in the median glycosylated hemoglobin value from 9.1 percent during the DCCT to 8.2 percent during the EDIC study.

When examined in relation to the glycosylated hemoglobin values, the likelihood of progressive retinopathy in both groups was strongly associated with the mean glycosylated hemoglobin value during the DCCT and the EDIC study combined. The value during the DCCT appeared to be the stronger determinant of the risk of progression. Similarly, in the Stockholm Diabetes Intervention Study, the prevalence of severe retinopathy after 7.5 years of follow-up was related to the mean glycosylated hemoglobin value during the first 5 years of follow-up.\(^\text{16}\)

During the DCCT, the beneficial effects of intensive therapy on the onset and progression of retinopathy and nephropathy were not evident until after three or four years of therapy. In the current study, we found that the marked reduction in the risk of progressive retinopathy in the intensive-therapy group during the DCCT persisted for at least four years despite rising glycosylated hemoglobin values. These findings strongly suggest that intensive therapy that maintains near-normal glycosylated hemoglobin concentrations has a beneficial effect on the long-term complications of diabetes that persists long after the actual period of such therapy. However, the results of the DCCT and the EDIC study should not be interpreted to mean that intensive therapy needs to be administered for only a limited period of time.

The risk of microvascular complications does not appear to be affected in the short term by the prevailing level of hyperglycemia. Instead, these risks are as-

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**Table 4. Incidence of Worsening of Nephropathy Between the End of the DCCT and After Four Years of the EDIC Study.**

<table>
<thead>
<tr>
<th>Renal Complication during EDIC</th>
<th>No. of Patients</th>
<th>Worsening Nephropathy</th>
<th>Adjusted Odds Reduction (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microalbuminuria (urinary albumin excretion rate &gt;28 µg/min)</td>
<td>53 (26–70)</td>
<td>0.002</td>
<td>5</td>
<td>6 (26–70)</td>
</tr>
<tr>
<td>Intensive therapy</td>
<td>601</td>
<td>11</td>
<td>0</td>
<td>601</td>
</tr>
<tr>
<td>All patients</td>
<td>637</td>
<td>5</td>
<td>639</td>
<td>1</td>
</tr>
<tr>
<td>Conventional therapy</td>
<td>639</td>
<td>1</td>
<td>92 (39–99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intensive therapy</td>
<td>573</td>
<td>2</td>
<td>601</td>
<td>0</td>
</tr>
<tr>
<td>Urinary albumin excretion rate &gt;208 µg/min at end of DCCT</td>
<td>86 (60–95)</td>
<td>&lt;0.001</td>
<td>80 (27–95)</td>
<td>0.006</td>
</tr>
<tr>
<td>Conventional therapy</td>
<td>64</td>
<td>31</td>
<td>38</td>
<td>8</td>
</tr>
<tr>
<td>Intensive therapy</td>
<td>38</td>
<td>8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*DCCT denotes Diabetes Control and Complications Trial, EDIC Epidemiology of Diabetes Intervention and Complications, and CI confidence interval.

†Measurements were performed in year 3 or 4 of the EDIC study (in approximately 50 percent of patients each year).

‡The numbers of patients free of each specific type of worsening at the end of the DCCT are given.

§The odds reduction is for former intensive therapy as compared with former conventional therapy on the basis of a logistic-regression analysis with adjustment for the albumin excretion rate at the end of the DCCT.

¶P values were calculated by the likelihood-ratio test.
The following investigators participated in the DCCT and the EDIC Research Group: Albert Einstein College of Medicine — H. Shamoones and H. Duffy; Case Western Reserve University — W. Dahms and L. Mayer; Cornell University Medical Center — D. Brillton and M. Lackaye; Henry Ford Health System — F. Whitehouse and D. Kruger; International Diabetes Center — R. Bergenstal and M. Johnson; Joslin Diabetes Center — A. Jacobson, J. Doyle, and D. Soroko; Massachusetts General Hospital — D. Nathan, S. Fritz, J. Godine, and C. McKitrick; Mayo Foundation — A. Jacobson, J. Doyle, and D. Soroko; Massachusetts General Hospital Laboratory (University of Minnesota) — M. Steffes, J. Bucksa, and B. Geithman, J. Brickbauer, L. Kastorff, and M. Neider; Central Biochemistry Laboratory (Washington University) — M. Davis, J. Backlund, and L. Van Ottingham; Central Fundus Photograph Reading Center (University of Wisconsin) — M. Davis, L. Hubbard, P. Geithman, J. Brickbauer, J. Kastorff, and M. Neider; Central Biochemistry Laboratory (University of Minnesota) — M. Steffes, J. Backlund, and B. Geithman; External Advisory Committee — G. Weir (chair), C. Clark, R. D’Agostino, M. Espeland, R. Klein, H. Jacobson, T. Manolio, L. Rand, D. Singer, and M. Stern; Study Chairs — S. Genuith and D. Nathan; Editor for DCCT/EDIC Publications — D. Nathan.

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APPENDIX

The following investigators participated in the DCCT and the EDIC Research Group: Albert Einstein College of Medicine — H. Shamoones and H. Duffy; Case Western Reserve University — W. Dahms and L. Mayer; Cornell University Medical Center — D. Brillton and M. Lackaye; Henry Ford Health System — F. Whitehouse and D. Kruger; International Diabetes Center — R. Bergenstal and M. Johnson; Joslin Diabetes Center — A. Jacobson, J. Doyle, and D. Soroko; Massachusetts General Hospital — D. Nathan, S. Fritz, J. Godine, and C. McKitrick; Mayo Foundation — J. Service and G. Ziegler; Medical University of South Carolina — J. Colwell, D. Wood, R. Mayfield, T. Garvey, T. Lyons, J. Smith, and K. Hermer; Northwestern University — M. Mollitch and B. Schafer; University of California at San Diego — O. Kollerman and G. Lorenzi; University of Iowa — W. Steir and M. Bayless; University of Maryland School of Medicine — D. Counts, A. Kowarski (former), and D. Ostrowski; University of Michigan — D. Greene, C. Martin, and W. Herman; University of Minnesota — J. Bantle and B. Rugness; University of Missouri — D. Goldstein and S. Hitt; University of New Mexico — D. Schade and D. Hornbeck; University of Pennsylvania — S. Schwartz and B. Jaun Melakas; Carey; University of Pittsburgh — T. Orchard, N. Silvers, and T. Songer; University of South Florida — J. Malone and H. Wetz; University of Tennessee — A. Kutbichi, H. Lambech, and M.B. Murphy; University of Texas Southwestern Medical Center — P. Raskin and S. Stowog; University of Toronto — B. Zinman and A. Barnie; University of Washington — J. Palmier and L. Van Ottingham; University of Western Ontario — J. Dupre and J. Harth; Vanderbilt University — M. May, R. Lorenz (former), and J. Lips; Washington University, St. Louis — N. White, J. Santiago (deceased), and L. Levandowski; Yale University School of Medicine — W. Tamborlane and P. Gutten; Clinical Coordinating Center (Case Western Reserve University) — B. Dahms, P. Corcoran, and J. Quinn; Data Coordinating Center (George Washington University, Biostatistics Center) — J. Lachin, P. Clear, D. Kenny, J. Backlund, L. Diminick, A. Henry, and D. Lamas; National Institute of Diabetes and Digestive and Kidney Diseases Program Office; C. Cowie and R. Eastman; Central Fundus Photograph Reading Center (University of Wisconsin) — M. Davis, L. Hubbard, P. Geithman, J. Brickbauer, J. Kastorff, and M. Neider; Central Biochemistry Laboratory (University of Minnesota) — M. Steffes, J. Backlund, and B. Geither; External Advisory Committee — G. Weir (chair), C. Clark, R. D’Agostino, M. Espeland, R. Klein, H. Jacobson, T. Manolio, L. Rand, D. Singer, and M. Stern; Study Chairs — S. Genuith and D. Nathan; Editor for DCCT/EDIC Publications — D. Nathan.

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