Continuous Glucose Monitoring and Intensive Treatment of Type 1 Diabetes

The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group*

ABSTRACT

BACKGROUND
The value of continuous glucose monitoring in the management of type 1 diabetes mellitus has not been determined.

METHODS
In a multicenter clinical trial, we randomly assigned 322 adults and children who were already receiving intensive therapy for type 1 diabetes to a group with continuous glucose monitoring or to a control group performing home monitoring with a blood glucose meter. All the patients were stratified into three groups according to age and had a glycated hemoglobin level of 7.0 to 10.0%. The primary outcome was the change in the glycated hemoglobin level at 26 weeks.

RESULTS
The changes in glycated hemoglobin levels in the two study groups varied markedly according to age group (P=0.003), with a significant difference among patients 25 years of age or older that favored the continuous-monitoring group (mean difference in change, −0.53%; 95% confidence interval [CI], −0.71 to −0.35; P<0.001). The between-group difference was not significant among those who were 15 to 24 years of age (mean difference, 0.08; 95% CI, −0.17 to 0.33; P=0.52) or among those who were 8 to 14 years of age (mean difference, −0.13; 95% CI, −0.38 to 0.11; P=0.29). Secondary glycated hemoglobin outcomes were better in the continuous-monitoring group than in the control group among the oldest and youngest patients but not among those who were 15 to 24 years of age. The use of continuous glucose monitoring averaged 6.0 or more days per week for 83% of patients 25 years of age or older, 30% of those 15 to 24 years of age, and 50% of those 8 to 14 years of age. The rate of severe hypoglycemia was low and did not differ between the two study groups; however, the trial was not powered to detect such a difference.

CONCLUSIONS
Continuous glucose monitoring can be associated with improved glycemic control in adults with type 1 diabetes. Further work is needed to identify barriers to effectiveness of continuous monitoring in children and adolescents. (ClinicalTrials.gov number, NCT00406133.)
Despite the increased use of insulin pumps and multiple-injection regimens and the introduction of insulin analogues, intensive treatment of type 1 diabetes mellitus often does not achieve the target glycated hemoglobin levels recommended by the Diabetes Control and Complications Trial (DCCT) more than 15 years ago. Although self-monitoring of blood glucose plays an important role in achieving target glycated hemoglobin levels, few patients with type 1 diabetes measure glucose levels after meals or overnight. Consequently, postprandial hyperglycemia and asymptomatic nocturnal hypoglycemia are commonly seen, even in patients with well-controlled type 1 diabetes who measure blood glucose meters, and asymptomatic nocturnal hypoglycemia are commonly seen, even in patients with well-controlled type 1 diabetes who measure blood glucose levels recommended by the Diabetes Control and Complications Trial (DCCT) more than 15 years ago.

In many patients, fear of hypoglycemia or development of hypoglycemia-associated autonomic failure hinders the successful implementation of intensive insulin therapy. Although short-term or uncontrolled studies have provided data only for short-term retrospective analysis or were too difficult and uncomfortable for clinical use, although not yet as accurate as blood glucose meters, newer real-time devices for continuous glucose monitoring provide improved accuracy and functionality, such as sounding alarms when the glucose trend projects future hypoglycemia, and are better tolerated by users, although short-term or uncontrolled studies have suggested benefit, whether these systems help to produce a sustained lowering of glycated hemoglobin levels and reduce hypoglycemia in patients with type 1 diabetes has not been established. Therefore, in this randomized, multicenter clinical trial, we evaluated the efficacy and safety of continuous glucose monitoring in adults and children with type 1 diabetes.

Methods

Patients

All eligible patients were 8 years of age or older, had received a diagnosis of type 1 diabetes at least 1 year before randomization, either used an insulin pump or received at least three daily insulin injections, had a glycated hemoglobin level of 7.0 to 10.0%, and had not used continuous glucose monitoring at home in the 6 months leading up to the trial. Patients completed a run-in phase using a continuous glucose monitor that was modified so that the glucose values were recorded in the receiver but were not visible to the patient; we refer to this as a “blinded” continuous glucose monitor. Eligibility required that patients wear a sensor for at least 6 of 7 days before randomization, with a minimum of 96 hours of glucose values including at least 24 hours overnight, and that home blood glucose monitoring be performed at least three times daily.

Study Treatment

Patients meeting these criteria were randomly assigned to receive continuous glucose monitoring (continuous-monitoring group) or home monitoring with a blood glucose meter (control group) with the use of a permuted-block design stratified according to clinical center, age group (≥25 years, 15 to 24 years, and 8 to 14 years), and glycated hemoglobin level (≤8.0% and >8.0%). A total of 23 patients (1 in the ≥25-year group, 8 in the 15-to-24-year group, and 14 in the 8-to-14-year group) were screened for the study but were not enrolled, either because the run-in phase was not successfully completed or because the patient elected not to enter the study after using the blinded continuous glucose monitor.

Patients in the continuous-monitoring group were provided with one of the following devices: the DexCom Seven (DexCom), the MiniMed Paradigm Real-Time Insulin Pump and Continuous Glucose Monitoring System (Medtronic), or the FreeStyle Navigator (Abbott Diabetes Care). Each system consists of a glucose oxidase–based electrochemical sensor, which is placed subcutaneously and replaced every 3 to 7 days (depending on the type of device), along with a receiver to which interstitial glucose measurements are sent wirelessly and stored. Since the purpose of the study was to evaluate a treatment strategy using the technology of continuous glucose monitoring and not a specific device, a device was assigned to each patient by the clinical center on the basis of device features and the patients’ preferences. Patients were instructed to use the device on a daily basis and to verify the accuracy of the glucose measurement with a home blood glucose meter (provided by the study) before making management decisions, according to the regulatory labeling of the devices. Patients in the control group were given blood glucose meters and test strips and asked to
perform home blood glucose monitoring at least four times daily.

Patients in the two groups were provided with written instructions on how to use the data provided by continuous glucose monitoring and blood glucose meters to make real-time adjustments of insulin doses and on the use of computer software (for those with a home computer) to retrospectively review the glucose data to alter future insulin doses. The two study groups had the same target premeal glucose values (70 to 130 mg per deciliter [3.9 to 7.2 mmol per liter]), peak post-prandial values (<180 mg per deciliter [10.0 mmol per liter]), and bedtime or overnight values (100 to 150 mg per deciliter [5.6 to 8.3 mmol per liter]). Instructions for the insulin regimen included the determination of a premeal bolus dose on the basis of the glucose level and the patient’s insulin-to-carbohydrate ratio and guidelines for correcting high glucose levels outside the target range at other times. Patients using a continuous glucose monitor received additional instructions for modifying their insulin doses and treatment of hypoglycemia on the basis of the glucose trend.

**FOLLOW-UP**

The number of scheduled contacts with study staff was identical for both study groups. Visits were conducted at 1, 4, 8, 13, 19, and 26 weeks (±1 week), with one telephone contact between each visit, to review glucose data and adjust diabetes management. After the visits at 13 weeks and 26 weeks, the control group used a blinded continuous glucose monitor for 1 week, which was repeated if fewer than 96 hours of glucose values were obtained. Glycated hemoglobin was measured at baseline and at 13 and 26 weeks at a central laboratory. The primary outcome was the change in the mean glycated hemoglobin level from baseline to 26 weeks, as determined by a central laboratory. A sample size of 110 patients in each of three age groups (≥25 years, 15 to 24 years, and 8 to 14 years) was planned to have a power of 90% within each age group to detect a difference in the mean glycated hemoglobin level between study groups, assuming a population difference of 0.5%, a standard deviation of 0.9 at 26 weeks, a correlation between baseline and 26-week values of 0.58, an alpha level of 0.05, and a loss to follow-up of no more than 15%. An interim estimation of sample size that was based on only the observed variance in the change in glycated hemoglobin levels indicated that 86 patients would be needed in each age group to provide sufficient statistical power.

All analyses were performed according to the intention-to-treat principle. The primary analysis was a comparison between the two study groups of the change in the glycated hemoglobin levels from baseline to 26 weeks in analysis of covariance (ANCOVA) models, conducted separately in each of the three age groups and adjusted for the baseline glycated hemoglobin level and clinical center. There was a highly significant interaction between study group and age group (P=0.003) in an ANCOVA model containing an age group–treatment group interaction term, a finding that confirmed the need to analyze outcomes separately for each age group. As a result, a P value of 0.0167 was considered the significance level for the primary analysis in each age group to maintain an overall type I error rate of 0.05.
Within each age group, in addition to the primary ANCOVA analysis, five prespecified binary outcomes for glycated hemoglobin at 26 weeks (a relative decrease of ≥10%, a 26-week level of <7.0%, an absolute decrease of ≥0.5%, a relative increase of ≥10%, and an absolute increase of ≥0.5%) were evaluated in logistic-regression models, adjusted for the baseline glycated hemoglobin level and clinical center. In a post hoc analysis, a binary outcome of a glycated hemoglobin level of less than 7.0% with no severe hypoglycemic events at 26 weeks was similarly analyzed. Prespecified exploratory analyses were conducted to assess the consistency of the treatment effect on the change in the glycated hemoglobin level from baseline to 26 weeks in subgroups that were based on the type of insulin delivery (pump or multiple daily injections) and the baseline glycated hemoglobin level (≤8.0% or >8.0%).

Data regarding continuous glucose monitoring in both groups after the 26-week visit (blinded monitors in the control group and unblinded monitors in the continuous-monitoring group) were used to estimate the amount of time per day the glucose level was hypoglycemic (≤70 mg per deciliter or ≤50 mg per deciliter [≤3.9 or ≤2.8 mmol per liter]), hyperglycemic (>180 mg per deciliter or >250 mg per deciliter [10.0 or 13.9 mmol per liter]), or in the target range (70–180 mg per deciliter or 50–250 mg per deciliter [3.9–10.0 mmol per liter]).

Table 1. Baseline Characteristics of the Patients, According to Age.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>≥25 Yr</th>
<th>15–24 Yr</th>
<th>8–14 Yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex — no. (%)</td>
<td>31 (60)</td>
<td>26 (57)</td>
<td>29 (51)</td>
</tr>
<tr>
<td>Age — yr</td>
<td>41.2±11.2</td>
<td>44.6±12.3</td>
<td>18.8±3.0</td>
</tr>
<tr>
<td>Non-Hispanic white race — no. (%)</td>
<td>52 (100)</td>
<td>41 (89)</td>
<td>47 (82)</td>
</tr>
<tr>
<td>Body-mass index z score — no. (%)‡</td>
<td>Less than −0.5</td>
<td>8 (15)</td>
<td>9 (20)</td>
</tr>
<tr>
<td>−0.5 to 0.5</td>
<td>34 (65)</td>
<td>28 (61)</td>
<td>18 (32)</td>
</tr>
<tr>
<td>&gt;0.5</td>
<td>10 (19)</td>
<td>9 (20)</td>
<td>33 (58)</td>
</tr>
<tr>
<td>Duration of diabetes — yr</td>
<td>23.6±10.6</td>
<td>21.8±10.4</td>
<td>9.5±4.8</td>
</tr>
<tr>
<td>Insulin administration — no. (%)</td>
<td>Pump</td>
<td>43 (83)</td>
<td>39 (85)</td>
</tr>
<tr>
<td>Multiple daily injections</td>
<td>9 (17)</td>
<td>7 (15)</td>
<td>19 (33)</td>
</tr>
<tr>
<td>Glycated hemoglobin — %</td>
<td>7.6±0.5</td>
<td>7.6±0.5</td>
<td>8.0±0.7</td>
</tr>
<tr>
<td>7.0–8.0% — no. (%)</td>
<td>43 (83)</td>
<td>40 (87)</td>
<td>34 (60)</td>
</tr>
<tr>
<td>8.1–8.9% — no. (%)</td>
<td>8 (15)</td>
<td>5 (11)</td>
<td>18 (32)</td>
</tr>
<tr>
<td>≥9.0% — no. (%)§</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>5 (9)</td>
</tr>
<tr>
<td>One or more episodes of severe hypoglycemia during previous 6 mo — no. (%)‡</td>
<td>7 (13)</td>
<td>3 (7)</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Daily home glucose-meter reading — no./day</td>
<td>6.5±2.3</td>
<td>6.6±2.2</td>
<td>5.6±2.0</td>
</tr>
<tr>
<td>College graduate (patient or primary caregiver) — no. (%)</td>
<td>42 (81)</td>
<td>36 (78)</td>
<td>35 (61)</td>
</tr>
</tbody>
</table>

* Plus–minus values are means ±SD.
† Race was self-reported.
‡ The body-mass index z scores were adjusted for age and sex on the basis of scores for a healthy population.
§ A severe episode of hypoglycemia was defined as an event that required assistance from another person to administer carbohydrate, glucagon, or other resuscitative actions.
Table 2. Glycemic Outcomes at 26 Weeks, According to Age.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>≥25 Yr</th>
<th>15–24 Yr</th>
<th>8–14 Yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycated hemoglobin level†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline — %</td>
<td>7.6±0.5</td>
<td>7.6±0.5</td>
<td>8.0±0.7</td>
</tr>
<tr>
<td>Change from baseline to 26 weeks — %‡</td>
<td>−0.50±0.56</td>
<td>0.02±0.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Relative decrease by ≥10% — no. (%)</td>
<td>13 (26)</td>
<td>2 (4)</td>
<td>0.003</td>
</tr>
<tr>
<td>Absolute decrease by ≥0.5% — no. (%)</td>
<td>24 (48)</td>
<td>5 (11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Relative increase ≥10% — no. (%)</td>
<td>0</td>
<td>1 (2)</td>
<td>0.48</td>
</tr>
<tr>
<td>Absolute increase ≥0.5% — no. (%)</td>
<td>0</td>
<td>5 (11)</td>
<td>0.02</td>
</tr>
<tr>
<td>26-week level &lt;7.0% — no. (%)</td>
<td>17 (34)</td>
<td>4 (9)</td>
<td>0.006</td>
</tr>
<tr>
<td>Glucose level§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean min per day in 3 ranges — baseline/26 wk¶</td>
<td>854/986</td>
<td>811/840</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;180 mg/dl</td>
<td>497/834</td>
<td>549/519</td>
<td>0.002</td>
</tr>
<tr>
<td>&gt;250 mg/dl</td>
<td>149/101</td>
<td>181/161</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean mg/dl/min — baseline/26 wk¶</td>
<td>0.73/0.68</td>
<td>0.72/0.74</td>
<td>0.07</td>
</tr>
</tbody>
</table>

* Plus–minus values are means ±SD.
† At 26 weeks, data regarding glycated hemoglobin levels were not available for five patients who dropped out of the study (in the continuous-monitoring group, two patients who were 25 years of age or older and one who was 15 to 24 years of age; in the control group, two who were 15 to 24 years of age).
‡ The between-group difference was significant among patients 25 years of age or older (mean difference, −0.53%; 95% confidence interval [CI], −0.71 to −0.35) but not among those 8 to 14 years of age (mean difference, −0.13; 95% CI, −0.38 to 0.11).
§ Data regarding continuous glucose monitoring were obtained after completion of the 26-week visit with the use of an unblinded device in the continuous-monitoring group and a blinded device in the control group. Data were missing in the continuous-monitoring group for two patients who were 25 years of age or older, seven patients who were 15 to 24 years of age, and two patients who were 8 to 14 years of age; data were missing in the control group for two patients who were 8 to 14 years of age.
¶ This value was the absolute rate of change.
liter), and in the target range (71 to 180 mg per deciliter [3.9 to 10.0 mmol per liter]). Variability in glucose levels was assessed by computing the absolute rate of change. Comparisons between study groups were performed with the use of ANCOVA models based on van der Waerden normal scores and adjusted for the corresponding baseline value, baseline glycated hemoglobin level, clinical center, and type of continuous glucose monitor. In the continuous-monitoring group, the association between age group and the amount of sensor use during the 26-week period was evaluated with the use of the Kruskal–Wallis test. The association between sensor use and the baseline glycated hemoglobin level was evaluated with Spearman’s correlation coefficients.

The proportions of patients who had one or more severe hypoglycemic events in each study group were compared with the use of Fisher’s exact test. Incidences of hypoglycemic events were compared and confidence intervals for the treatment group difference calculated with the use of permutation tests. Similar analyses were performed for the subgroup of hypoglycemic events associated with seizure or coma.

Analyses were conducted with the use of SAS software, version 9.1 (SAS Institute). All P values are two-sided. Adjustment for imbalances between baseline factors and imputation for missing data with the use of Rubin’s method did not alter the results (data not shown). Parallel analyses were performed on data regarding glycated hemoglobin levels and continuous glucose monitoring obtained at 13 weeks.

RESULTS

PATIENTS

In 2007, between February and December, 322 patients underwent randomization, with 165 patients assigned to the continuous-monitoring group and 157 to the control group. Of those patients, 98 patients were 25 years of age or older, 110 patients were 15 to 24 years old, and 114 patients were 8 to 14 years old. The majority of patients were non-Hispanic white, were using insulin pumps, were
measuring glucose levels more than five times per day with a home glucose meter, and had a mean glycated hemoglobin level of 8.0% or less (Table 1).

Across the three age groups, the rate of completion of visits in the two study groups was 95 to 100% (Fig. 1 in the Supplementary Appendix, available with the full text of this article at www.nejm.org). For protocol-specified telephone contacts, the rate was 93 to 98%. The 26-week visit was completed by all but two patients in the continuous-monitoring group who were 25 years of age or older, by all but one patient in the continuous-monitoring group and two patients in the control group who were 15 to 24 years of age, and by all patients who were 8 to 14 years of age. Two patients in the control group (both 8 to 14 years of age) initiated the use of continuous glucose monitoring before completing the 26-week visit.

GLYCEMIC CONTROL
In the primary analysis, a significant between-group difference in the change in glycated hemoglobin levels from baseline to 26 weeks was seen in patients who were 25 years of age or older favoring the continuous-monitoring group (mean difference in change, −0.53%; 95% confidence interval [CI], −0.71 to −0.35; P<0.001) but not in those 15 to 24 years of age (0.08; 95% CI, −0.17 to 0.33; P=0.52) nor in those 8 to 14 years of age (−0.13; 95% CI, −0.38 to 0.11; P=0.29).

At 26 weeks, among patients in the continuous-monitoring group who were 25 years of age or older, there were improvements in virtually all measures of glycemic control, as compared with the control group (Table 2 and Fig. 1 and 2). In the secondary analyses, more patients in the continuous-monitoring group had a relative reduction of 10% or more in the mean glycated hemoglobin level, as compared with baseline (P=0.003), and more achieved the target glycated hemoglobin level of less than 7.0% (P=0.005), as recommended for adults by the American Diabetes Association.21

The frequency of the combined outcome of a 26-week glycated hemoglobin level of less than 7.0% and no severe hypoglycemic events was 30% in both study groups after the 26-week visit, was present for only a small portion of the day and did not differ significantly between the two groups.

Among patients who were 15 to 24 years of age, the mean decrease in glycated hemoglobin levels from baseline to 26 weeks was approximately 0.2% in both study groups. There were no significant differences between groups on any of the secondary glycemic measures.

Among patients who were 8 to 14 years of age, the mean decrease in glycated hemoglobin levels was 0.37% in the continuous-monitoring group, which did not differ significantly from the decrease of 0.22% in the control group. However, secondary indexes of glycemic control were improved in the continuous-monitoring group — namely, more patients had a relative reduction of 10% or more in the glycated hemoglobin level from baseline (P=0.04) and more patients had glycated hemoglobin levels of less than 7.0% (P=0.01) (Table 2 and Fig. 1 and 2). At 26 weeks, there were no significant differences between the two study groups in outcomes as measured by continuous glucose monitoring. Within the three age groups, the 13-week results were similar to the 26-week results (Table 1 in the Supplementary Appendix). At 26 weeks, results were consistent in subgroups based on the type of insulin delivery (pump vs. multiple daily injections) and baseline glycated hemoglobin levels (≤8.0% vs. >8.0%) (Table 2 in the Supplementary Appendix).

HYPOGLYCEMIA AND OTHER ADVERSE EVENTS
Severe hypoglycemic events were infrequent in the two study groups. In the six age-stratified groups, 5 to 10% of patients had at least one severe hypoglycemic event, with no significant differences between the two study groups on the basis of age (Table 3). Likewise, there were no significant differences in the incidence of severe hypoglycemic events between study groups according to age. One patient in the continuous-monitoring group who was 30 years of age had six events involving either seizure or coma during a period in which he reported not using any long-acting insulin; for four of the six events, he reported that he had not used short-acting insulin on the day of the event.

Biochemical hypoglycemia (blood glucose, ≤70 mg per deciliter), which was evaluated by collecting data from continuous glucose monitoring in both study groups after the 26-week visit, was present for only a small portion of the day and did not differ significantly between the two groups.
Figure 2. Cumulative Distribution of Glycated Hemoglobin Levels, According to Age.

Shown are glycated hemoglobin levels for patients 25 years of age or older (Panel A), 15 to 24 years (Panel B), and 8 to 14 years (Panel C). The vertical dotted line represents the American Diabetes Association target of 7.0%.
Table 3. Hypoglycemia and Other Adverse Events, According to Age.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age Group</th>
<th>Continuous-Monitoring Group (N = 52)</th>
<th>Control Group (N = 46)</th>
<th>P Value†</th>
<th>Continuous-Monitoring Group (N = 57)</th>
<th>Control Group (N = 53)</th>
<th>P Value†</th>
<th>Continuous-Monitoring Group (N = 56)</th>
<th>Control Group (N = 58)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe hypoglycemic event‡</td>
<td>≥25 Yr</td>
<td>47 (90)</td>
<td>42 (91)</td>
<td></td>
<td>54 (95)</td>
<td>48 (91)</td>
<td></td>
<td>52 (93)</td>
<td>52 (90)</td>
<td></td>
</tr>
<tr>
<td>No. per patient — no. of patients (%)</td>
<td>1 event</td>
<td>3 (6)</td>
<td>3 (7)</td>
<td></td>
<td>1 (2)</td>
<td>4 (8)</td>
<td></td>
<td>3 (5)</td>
<td>5 (9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 events</td>
<td>1 (2)</td>
<td>0</td>
<td></td>
<td>2 (4)</td>
<td>1 (2)</td>
<td></td>
<td>1 (2)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 events</td>
<td>0</td>
<td>1 (2)</td>
<td></td>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 events</td>
<td>1 (2)</td>
<td>0</td>
<td></td>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Patients with ≥1 event — no. of patients (%)</td>
<td>≤10 events</td>
<td>5 (10)</td>
<td>4 (9)</td>
<td>1.0</td>
<td>3 (5)</td>
<td>5 (9)</td>
<td>0.48</td>
<td>4 (7)</td>
<td>6 (10)</td>
<td>0.74</td>
</tr>
<tr>
<td>Events per 100 person-yr — no.</td>
<td>43.4§</td>
<td>26.3</td>
<td>0.66</td>
<td>17.9</td>
<td>23.9</td>
<td>0.64</td>
<td>17.9</td>
<td>24.4</td>
<td>0.64</td>
<td></td>
</tr>
<tr>
<td>Glucose level‖</td>
<td>Mean min per day in 2 ranges — baseline/26 wk</td>
<td>≤70 mg/dl</td>
<td>89/60</td>
<td>80/81</td>
<td>0.41</td>
<td>99/88</td>
<td>102/88</td>
<td>0.79</td>
<td>49/47</td>
<td>59/59</td>
</tr>
<tr>
<td></td>
<td>≤50 mg/dl</td>
<td>32/11</td>
<td>22/23</td>
<td>0.10</td>
<td>37/29</td>
<td>42/31</td>
<td>0.99</td>
<td>17/10</td>
<td>18/13</td>
<td>0.50</td>
</tr>
</tbody>
</table>
Other adverse events — no. of patients

<table>
<thead>
<tr>
<th>Event</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>Group 5</th>
<th>Group 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic ketoacidosis</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cellulitis related to sensor use</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness during blood draw</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Anxiety and depression</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Kidney laceration</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Seizure not caused by hypoglycemia</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* NA denotes not applicable.
† Fisher’s exact test was used to compare the percentages of patients in each study group who had at least one hypoglycemic event; permutation tests were used to compare the incidence rates and compute the confidence intervals.
‡ The between-group difference was 17.1 (95% CI, −37.4 to 73.5) for patients who were 25 years of age or older, −6.0 (95% CI, −35.8 to 23.7) for those who were 15 to 24 years of age, and −6.5 (95% CI, −33.4 to 20.6) for those who were 8 to 14 years of age.
§ One patient in the continuous-monitoring group who was 25 years of age or older had six episodes of seizure or coma. During this period, he reported that he had not used any long-acting insulin; for four of the six episodes, he reported that he had not used a short-acting insulin on the day of the event. With the exclusion of data from this patient, the incidence rate for severe hypoglycemia was 20.0 per 100 person-years, and the incidence rate for seizure or coma was 0.
¶ The between-group difference was 19.3 (95% CI, −12.8 to 56.3) for patients who were 25 years of age or older and −8.3 (95% CI, −23.4 to 7.0) for those who were 15 to 24 years of age. For patients who were 8 to 14 years of age, there were no events.
‖ Data were obtained from continuous glucose monitoring after completion of the 26-week visit with the use of an unblinded device in the continuous-monitoring group and a blinded device in the control group. Data were missing in the continuous-monitoring group for two patients who were 25 years of age or older, seven patients who were 15 to 24 years of age, and two patients who were 8 to 14 years of age; data were missing in the control group for two patients who were 8 to 14 years of age.

In this randomized, controlled trial, we observed that the benefit associated with continuous glucose monitoring was strongly related to age. A significant difference in the primary analysis of the change in glycated hemoglobin levels from baseline to 26 weeks was seen in the predefined group of patients who were 25 years of age or older but not in the two younger age groups. In the continuous-monitoring group, there was a greater decrease in glycated hemoglobin levels and sensor glucose results with continuous glucose monitoring than in the control group, indicating a higher glycemic control in both glycated hemoglobin levels and sensor glucose results with continuous glucose monitoring than in the control group.

In contrast, comparisons between study groups showed less benefit of continuous glucose monitoring among patients who were 8 to 14 years of age and no benefit among those who were 15 to 24 years of age. Among those 8 to 14 years of age, the between-group difference in mean glycated hemoglobin levels was 17.0% (95% CI, −2.1 to 46.2), with a higher mean glycated hemoglobin level in the control group than in the continuous-monitoring group.

At least 60 days of sensor use per week was the average for 83% of patients who were 25 years of age or older, 70% of patients who were 15 to 24 years of age, and 66% of patients who were 8 to 14 years of age. Sensor use was not associated with the baseline glycated hemoglobin level (Spearman’s correlation coefficients, 0.08, −0.02, and 0.03 in the three groups, respectively).

In the continuous-monitoring group, the use of continuous glucose monitoring before completing the 26-week visit was the average for 93% of patients who were 25 years of age or older, 80% of patients who were 15 to 24 years of age, and 90% of patients who were 8 to 14 years of age.Sensor use was not associated with the baseline glycated hemoglobin level (Spearman’s correlation coefficients, 0.08, −0.02, and 0.03 in the three groups, respectively).
cated hemoglobin levels did not achieve statistical significance. However, in this age group, in secondary analyses, more patients in the continuous-monitoring group than in the control group had glycated hemoglobin levels of less than 7.0% and more had a relative reduction of 10% or more in glycated hemoglobin levels from baseline values. The latter observation is important, since the DCCT showed that a relative reduction of 10% in glycated hemoglobin levels is associated with a reduction of more than 40% in the rate of development and progression of early diabetic retinopathy.\textsuperscript{22,23}

The observed age effect may be related to substantially greater use of sensors in the adults than in patients in the two younger groups. Imperfect adherence with many aspects of diabetes management has long been recognized as an obstacle to successful intensive treatment in adolescents and young adults with type 1 diabetes.\textsuperscript{24-27} Greater parental involvement could be the reason that patients in the continuous-monitoring group between the ages of 8 and 14 years had greater sensor use than the patients between the ages of 15 and 24 years. In adolescents, the transition from parental assistance with management of diabetes to patient-only management is often accompanied by deterioration of glycemic control.\textsuperscript{25,28}

Severe hypoglycemic events were infrequent and did not differ significantly according to study group. This finding must be interpreted with caution, since the trial was not powered to detect a between-group difference in such events. In the two groups, the rate of severe hypoglycemia was much lower than that reported in the DCCT.\textsuperscript{1,29}

The use of a blinded continuous glucose monitor in the control group also provided the opportunity to compare the exposure of the two groups to biochemical hypoglycemia, which is often asymptomatic. In this regard, among patients 25 years of age or older, it was noteworthy that the decrease in glycated hemoglobin levels was not associated with an increase in hypoglycemia. This finding is in direct contrast to that of the DCCT, which showed that the rate of hypoglycemic events increased in patients who lowered their glycated hemoglobin levels.\textsuperscript{1,29}
Continuous Glucose Monitoring in Type 1 Diabetes

With respect to the generalizability of the results, it is important to recognize that before the study, patients were receiving intensive insulin therapy with either an insulin pump or multiple daily injections and frequent home blood glucose monitoring, and most had better-than-average glycated hemoglobin levels. In addition, to be eligible for the study, patients needed to show the ability to wear a sensor and insert a new sensor at home. Therefore, the results do not shed light on the use of such devices in a less well controlled, less motivated population of patients with type 1 diabetes. Although the results in patients using multiple daily injections were similar to the results in those using an insulin pump, the number of patients using multiple daily injections was too small for a definitive assessment.

The results of this study indicate that continuous glucose monitoring improves glycated hemoglobin levels and may enhance the management of type 1 diabetes in adults who have the motivation to use this technology and the capability to incorporate it into their own daily diabetes management. Further work is needed to identify and address the lack of effectiveness of continuous glucose monitoring in children and adolescents.

Supported by grants (22-2006-1107, 22-2006-1117, 22-2006-1112, 22-2006-1112, and 01-2006-8031) from the Juvenile Diabetes Research Foundation.

Dr. Tamborlane reports receiving consulting fees from Abbott Diabetes Care and Lifecare and consulting and lecture fees and grant support from Medtronic; Dr. Bode, receiving consulting and lecture fees, travel reimbursement, and grant support from Abbott Diabetes Care and Medtronic; and Dr. Fox, receiving supplies for research from Abbott Diabetes Care and Medtronic.

The results of our study indicate that continuous glucose monitoring improves glycated hemoglobin levels and may enhance the management of type 1 diabetes in adults who have the motivation to use this technology and the capability to incorporate it into their own daily diabetes management. Further work is needed to identify and address the lack of effectiveness of continuous glucose monitoring in children and adolescents.

Supported by grants (22-2006-1107, 22-2006-1117, 22-2006-1112, 22-2006-1112, and 01-2006-8031) from the Juvenile Diabetes Research Foundation.

Dr. Tamborlane reports receiving consulting fees from Abbott Diabetes Care and Lifespan and consulting and lecture fees and grant support from Medtronic; Dr. Bode, receiving consulting and lecture fees, travel reimbursement, and grant support from Abbott Diabetes Care and Medtronic; Dr. Fox, receiving supplies for research from Abbott Diabetes Care; Dr. Hirsch, receiving consulting fees and travel reimbursement from Abbott Diabetes Care and grant support from Medtronic; Dr. Laffel, receiving consulting fees from Lifespan and Roche, consulting and lecture fees from Abbott Diabetes Care, consulting fees and grant support from Medtronic, and grant support from the Charles Hood Foundation; Dr. Mauers, receiving grant support from AstraZeneca; Dr. Weininger, receiving lecture fees and travel reimbursement from Medtronic; Dr. Wilson, receiving equipment and software from Abbott Diabetes Care and Medtronic and grant support from Medtronic; and Dr. Wolpert, receiving consulting fees from Abbott Diabetes Care and grant support from Medtronic. No other potential conflict of interest relevant to this article was reported.

**APPENDIX**

The members of the writing committee and study investigators are listed in order according to the number of patients enrolled at each clinical center: **Clinical Center: Barbara Davis Center for Childhood Diabetes, University of Colorado, Denver:** H.P. Chase (principal investigator), R. Fiallo-Scharer, L. Messer, V. Gage, P. Burdick; **Pediatric Adolescent, and Young Adult Section, Joslin Diabetes Center, Boston:** L. Laffel (principal investigator), K. Milaszewski, K. Pratt, E. Bismuth, J. Ready, M. Lawlor; **Stanford University, Stanford, CA:** B. Buckingham (principal investigator), D.M. Wilson, J. Block, K. Benassi; **University of Iowa Carver College of Medicine, Iowa City:** T. Saltsikin (principal investigator), M. Tansey, D. Kucera, J. Coffey, J. Cabbage; **Adult Section, Joslin Diabetes Center, Boston:** H. Wolpert (principal investigator), G. Shetty, A. Atakow-Castillo, J. Giusti, S. O’Donnell, S. Ghilioni; **University of Washington, Seattle:** I.B. Hirsch (principal investigator), L.K. Gilliam, K. Fitzpatrick, D. Khakpour; **Nemours Children’s Clinic, Jacksonville, FL:** T. Wysocki (coprincipal investigator), L.A. Fox (coprincipal investigator), N. Mauers, K. Engert, L. Permuzy, **Atlanta Diabetes Associates, Atlanta:** B.W. Bode (principal investigator), K. O’Neil, L. Tolbert; **Kaiser Permanente, San Diego, CA:** J.M. Lawrence (coprincipal investigator), R. Clemons (coprincipal investigator), M. Mewe, B. Sattler; **Yale University School of Medicine, New Haven, CT:** S. Weinzimer (principal investigator), W.V. Tamborlane, B. Hayes, J. Bosson-Heenan. **Coordinating Center: Julie Center for Health Research, Tampa, FL:** R.W. Beck, K.J. Ruedy, C. Kollman, D. Xing, J. Jackson. **Central Laboratory: University of Minnesota Central Laboratory:** M. Steffenes, J.M. Buecksa, M.L. Nowicki, C. Van Hale, V. Malky. **Cost-Effectiveness Investigators:** National Opinion Research Center, University of Chicago, Chicago: M. O’Grady, E. Huang, A. Basu, D.O. Meltzer, L. Zhao; University of Michigan: J. Lee. **Juvenile Diabetes Research Foundation:** A.J. Kowalski. **Operations Committee:** L. Laffel (cochair), W.V. Tamborlane (cochair), R.W. Beck, A.J. Kowalski, K.J. Ruedy. **Data and Safety Monitoring Board:** R.S. Weinstock (chair), B.J. Anderson, D. Kruger, L. LaVange, H. Rodriguez.

**REFERENCES**


9. Wilson DM, Beck RW, Tamborlane WV.连续葡萄糖监视器在1型糖尿病上的应用
Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

**Supplemental Table 1. Study Outcomes at 13 Weeks by Treatment Group According to Age Group**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>CGM</th>
<th>Control</th>
<th>P value</th>
<th>CGM</th>
<th>Control</th>
<th>P value</th>
<th>CGM</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥25 Years</td>
<td>N=52</td>
<td>N=46</td>
<td></td>
<td>N=57</td>
<td>N=53</td>
<td></td>
<td>N=56</td>
<td>N=58</td>
<td></td>
</tr>
<tr>
<td>15 to 24 Years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 to 14 Years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Glycated hemoglobin level**

- **Baseline (%)**
  - mean ± SD
  - CGM: 7.6 ± 0.5, Control: 7.6 ± 0.5, CGM: 8.0 ± 0.7, Control: 7.9 ± 0.8, CGM: 8.0 ± 0.7, Control: 7.9 ± 0.6

- **Change from baseline (%)**
  - mean ± SD
  - CGM: -0.49 ± 0.50, Control: -0.20 ± 0.45
  - CGM: -0.38 ± 0.56, Control: -0.16 ± 0.60
  - CGM: -0.38 ± 0.56, Control: -0.16 ± 0.60

- **Relative decrease by >10% no. (%)**
  - CGM: 13 (25), Control: 6 (13)
  - CGM: 13 (24), Control: 6 (12)
  - CGM: 17 (31), Control: 7 (12)

- **Absolute decrease by >0.5% no. (%)**
  - CGM: 24 (47), Control: 10 (22)
  - CGM: 25 (46), Control: 16 (32)
  - CGM: 26 (47), Control: 16 (28)

- **Relative increase >10% no. (%)**
  - CGM: 0, Control: 0
  - CGM: 2 (4), Control: 3 (6)
  - CGM: 2 (4), Control: 0

- **Absolute increase >0.5% no. (%)**
  - CGM: 0, Control: 2 (4)
  - CGM: 5 (9), Control: 6 (12)
  - CGM: 6 (11), Control: 1 (2)

- **13-week level <7.0% no. (%)**
  - CGM: 22 (43), Control: 6 (13)
  - CGM: 10 (19), Control: 4 (8)
  - CGM: 14 (25), Control: 4 (7)

**CGM Glucose Data**

**Glucose Level mean minutes/day**

- **Baseline: 13 weeks**
  - 71-180 mg/dL: 854:972, 811:866, 0.02, 691:807, 697:727, 0.02, 646:764, 710:707, 0.04
  - >180 mg/dL: 497:401, 549:486, 0.09, 650:557, 641:622, 0.05, 745:635, 671:681, 0.09
<table>
<thead>
<tr>
<th>Range</th>
<th>Min-Max</th>
<th>Mean</th>
<th>Min-Max</th>
<th>Mean</th>
<th>Min-Max</th>
<th>Mean</th>
<th>Min-Max</th>
<th>Mean</th>
<th>Min-Max</th>
<th>Mean</th>
<th>Min-Max</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;250 mg/dL</td>
<td>149:94</td>
<td>0.03</td>
<td>271:209</td>
<td>0.03</td>
<td>343:235</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤70 mg/dL</td>
<td>89:67</td>
<td>0.34</td>
<td>99:76</td>
<td>0.53</td>
<td>49:41</td>
<td>0.43</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤50 mg/dL</td>
<td>32:13</td>
<td>0.56</td>
<td>37:23</td>
<td>0.24</td>
<td>17:8</td>
<td>0.17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Absolute rate of change

**mean mg/dL/min**

Baseline: 26 weeks  

0.73:0.72  0.72:0.70  0.59  0.85:0.84  0.86:0.87  0.36  0.84:0.82  0.83:0.84  0.24

*13-week glycated hemoglobin data were not available for four subjects who dropped out of the study and five subjects who missed the 13-week visit (see Supplemental Figure 1)

†CGM glucose data were obtained following completion of the 13 week visit with the CGM group using an unblinded device and the control group using a blinded device. Data were missing in the CGM group for four subjects in the 15 to 24 age group and one in the 8 to 14 age group and in the control group for two subjects in the ≥25 age group, five in the 15 to 24 age group and seven in the 8 to 14 age group. To convert glucose in mg/dL to mmol/liter, multiply by 0.0555.
**Supplemental Table 2. Glycated Hemoglobin Outcome at 26 Weeks by Treatment Group According to Age Group in Subgroups Based on Insulin Modality and Baseline Glycated Hemoglobin**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>CGM</th>
<th>Control</th>
<th>CGM</th>
<th>Control</th>
<th>CGM</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥25 Years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Insulin Modality: Pump</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=43</td>
<td>N=39</td>
<td>N=38</td>
<td>N=40</td>
<td>N=47</td>
<td>N=49</td>
<td></td>
</tr>
<tr>
<td>Baseline Glycated Hemoglobin (%) mean ± SD</td>
<td>7.5 ± 0.4</td>
<td>7.7 ± 0.5</td>
<td>7.9 ± 0.6</td>
<td>7.9 ± 0.8</td>
<td>8.0 ± 0.7</td>
<td>7.9 ± 0.6</td>
</tr>
<tr>
<td>Change from baseline (%) mean ± SD</td>
<td>−0.50 ± 0.51</td>
<td>+0.02 ± 0.47</td>
<td>−0.19 ± 0.69</td>
<td>−0.26 ± 0.63</td>
<td>−0.39 ± 0.92</td>
<td>−0.25 ± 0.55</td>
</tr>
<tr>
<td><strong>Insulin Modality: Multiple Daily Injections</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=9</td>
<td>N=7</td>
<td>N=19</td>
<td>N=13</td>
<td>N=9</td>
<td>N=9</td>
<td></td>
</tr>
<tr>
<td>Baseline Glycated Hemoglobin (%) mean ± SD</td>
<td>7.9 ± 0.6</td>
<td>7.3 ± 0.4</td>
<td>8.2 ± 0.9</td>
<td>8.1 ± 0.9</td>
<td>8.1 ± 0.6</td>
<td>8.1 ± 0.7</td>
</tr>
<tr>
<td>Change from baseline (%) mean ± SD</td>
<td>−0.54 ± 0.85</td>
<td>+0.04 ± 0.34</td>
<td>−0.16 ± 0.60</td>
<td>−0.08 ± 0.55</td>
<td>−0.30 ± 0.85</td>
<td>−0.08 ± 0.51</td>
</tr>
<tr>
<td><strong>Baseline Glycated Hemoglobin: &lt;8.0%</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=43</td>
<td>N=40</td>
<td>N=34</td>
<td>N=36</td>
<td>N=32</td>
<td>N=34</td>
<td></td>
</tr>
<tr>
<td>Baseline Glycated Hemoglobin (%) mean ± SD</td>
<td>7.4 ± 0.3</td>
<td>7.5 ± 0.3</td>
<td>7.5 ± 0.3</td>
<td>7.5 ± 0.3</td>
<td>7.5 ± 0.3</td>
<td>7.4 ± 0.3</td>
</tr>
<tr>
<td>Change from baseline (%) mean ± SD</td>
<td>−0.44 ± 0.44</td>
<td>+0.09 ± 0.35</td>
<td>−0.17 ± 0.63</td>
<td>−0.12 ± 0.62</td>
<td>−0.05 ± 0.74</td>
<td>−0.10 ± 0.41</td>
</tr>
<tr>
<td><strong>Baseline Glycated Hemoglobin: &gt;8.0%</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=9</td>
<td>N=6</td>
<td>N=23</td>
<td>N=17</td>
<td>N=24</td>
<td>N=24</td>
<td></td>
</tr>
<tr>
<td>Baseline Glycated Hemoglobin (%) mean ± SD</td>
<td>8.4 ± 0.4</td>
<td>8.6 ± 0.4</td>
<td>8.7 ± 0.6</td>
<td>8.9 ± 0.6</td>
<td>8.6 ± 0.5</td>
<td>8.5 ± 0.3</td>
</tr>
<tr>
<td>Change from baseline (%) mean ± SD</td>
<td>−0.86 ± 0.95</td>
<td>−0.43 ± 0.72</td>
<td>−0.20 ± 0.70</td>
<td>−0.40 ± 0.56</td>
<td>−0.80 ± 0.93</td>
<td>−0.40 ± 0.66</td>
</tr>
</tbody>
</table>
Supplemental Figure 1. Flow chart indicating visit and study completion in each treatment group according to age group: A: ≥25 years age group. B: 15 to 24 years age group. C: 8 to 14 years age group.
Figure 1A

Randomized
N=98

CGM
N= 52

Missed visit=0

Completed 52 (100%)

Dropped= 1

Completed 51 (98%)

Control
N= 46

Completed 46 (100%)

Completed 46 (100%)

Missed visit=0

Missed visit=0

Completed 51 (98%)

Missed visit=0

Completed 46 (100%)

Missed visit=0

Missed visit=0

Completed 46 (100%)

Missed visit=0

Completed 51 (98%)

Completed 46 (100%)

Missed visit=0

Completed 50 (96%)

Missed visit=0

Completed 46 (100%)

Missed visit=0

Completed 50 (96%)

Missed visit=0

Completed 46 (100%)

Missed visit=0

Completed 50 (96%)

Total Dropped=2

Total Dropped= 0
Figure 1B

Randomized
N=110

CGM
N=57

Completed
57 (100%)

Missed
visit=0

Completed
56 (98%)

Missed
visit=1

Completed
54 (95%)

Missed
visit=2

Completed
55 (96%)

Missed
visit=1

Completed
56 (98%)

Total Dropped=1

Control
N=53

Completed
50 (94%)

Missed
visit=1

Completed
48 (91%)

Missed
visit=3

Completed
50 (94%)

Missed
visit=1

Completed
51 (96%)

Missed
visit=0

Completed
51 (96%)

Total Dropped=2

Dropped= 1

1 week visit

4 week visit

8 week visit

13 week visit

19 week visit

26 week visit

Missing visit=3

Dropped=2

Total N=110

N=57

N=53

Missed visit=0

Completed 55 (96%)

Completed 51 (96%)

Dropped=2

Completed 50 (94%)

Completed 48 (91%)

Completed 50 (94%)

Completed 51 (96%)

Completed 55 (96%)

Completed 56 (96%)

Completed 56 (98%)

Completed 51 (96%)

Missed visit=1

Missed visit=0

Missed visit=0

Missed visit=0

Missed visit=1

Missed visit=1

Missed visit=1

Missed visit=3

Missed visit=1

Missed visit=1

Missed visit=1

N=57

Completed 55 (96%)

Completed 56 (96%)

N=53

Completed 50 (94%)

Completed 48 (91%)

Completed 50 (94%)

Completed 51 (96%)

Completed 55 (96%)

Completed 56 (98%)

Total Dropped=1

Total Dropped=2

N=110

Completed 55 (96%)

Completed 50 (94%)

Completed 56 (98%)

Total Dropped=1

Total Dropped=2

N=57

N=53

Completed 56 (98%)

Completed 51 (96%)

Completed 50 (94%)

Completed 48 (91%)

Completed 50 (94%)

Completed 51 (96%)

Completed 55 (96%)

Completed 56 (98%)

Total Dropped=1

Total Dropped=2

N=110

Completed 55 (96%)

Completed 50 (94%)

Completed 56 (98%)

Total Dropped=1

Total Dropped=2

N=57

N=53

Completed 56 (98%)

Completed 51 (96%)

Completed 50 (94%)

Completed 48 (91%)

Completed 50 (94%)

Completed 51 (96%)

Completed 55 (96%)

Completed 56 (98%)

Total Dropped=1

Total Dropped=2

N=110

Completed 55 (96%)

Completed 50 (94%)

Completed 56 (98%)

Total Dropped=1

Total Dropped=2

N=57

N=53

Completed 56 (98%)

Completed 51 (96%)

Completed 50 (94%)

Completed 48 (91%)

Completed 50 (94%)

Completed 51 (96%)

Completed 55 (96%)

Completed 56 (98%)

Total Dropped=1

Total Dropped=2

N=110

Completed 55 (96%)

Completed 50 (94%)

Completed 56 (98%)

Total Dropped=1

Total Dropped=2

N=57

N=53

Completed 56 (98%)

Completed 51 (96%)

Completed 50 (94%)

Completed 48 (91%)

Completed 50 (94%)

Completed 51 (96%)

Completed 55 (96%)

Completed 56 (98%)

Total Dropped=1

Total Dropped=2
**Figure 1C**

Randomized
N=114

CGM
N= 56

Completed
56 (100%)

Completed
56 (97%)

Control
N= 58

Completed
56 (97%)

Completed
58 (100%)

Missed
visit=0

Missed
visit=0

Missed
visit=0

Completed
54 (96%)

Completed
57 (98%)

Completed
58 (100%)

Missed
visit=2

Missed
visit=1

Missed
visit=2

Completed
55 (98%)

Completed
57 (98%)

Completed
57 (98%)

Missed
visit=1

Missed
visit=1

Missed
visit=0

Completed
55 (98%)

Completed
57 (98%)

Completed
57 (98%)

Total Dropped=0

Total Dropped= 0

Completed
56 (100%)

Completed
58 (100%)

1 week visit

4 week visit

8 week visit

13 week visit

19 week visit

26 week visit