Glycemic Control in Pharmacist-Managed Insulin Titration Versus Standard Care in an Indigent Population

Jamie M. Pitlick, PharmD, BCPS, and Amie D. Brooks, PharmD, BCPS

Abstract

Purpose. To assess the impact of a pharmacist-managed insulin titration program on achieving clinical goals in an underserved population with diabetes.

Methods. The study included 35 subjects followed in a pharmacist-managed insulin titration and 35 matched control subjects. Control subjects were followed under standard procedures within the same clinic and were matched for age, titration time frame, and insulin regimen. The primary outcome was change in A1C between the two groups at 6 months. Secondary outcomes included change in A1C within groups at 3, 6, 9, and 12 months, as well as the proportion of subjects attaining a goal A1C of < 7% and adhering to preventive care recommendations.

Results. Between-group comparison demonstrated a significant absolute difference in mean change in A1C at 6 months favoring pharmacist management (0.9%, 95% CI 0.2–1.6, P = 0.009). Within-group comparisons demonstrated significant A1C reduction from baseline at 6 months (−1.1%, 95% CI −1.7 to −0.4, P = 0.002), 9 months (−1.4%, 95% CI −2.0 to −0.7, P < 0.001), and 12 months (−1.3%, 95% CI −2.0 to −0.5, P = 0.001) in the pharmacist-managed group with no significant changes observed in the control group.

Conclusion. Pharmacist-managed insulin titration resulted in significant improvement in glycemic control compared to standard care in an indigent population.

Based on evidence of decreased microvascular and macrovascular complications, the current American Diabetes Association (ADA) guidelines recommend as goals an A1C of < 7%, blood pressure of < 130/80 mmHg, and LDL cholesterol of < 100 mg/dl.1 It has been demonstrated that the recommended goals can be achieved with formal education, routine appointments, and close telephone follow-up.2 However, in the current health care environment with time constraints on primary care providers and common patient follow-up intervals of every 3 months, these proven methods are impractical. Thus, attainment of glycemic control in the primary care setting has, historically, been suboptimal.3,4

It has been demonstrated that diabetes-focused pharmacist care can improve outcomes, including reductions in A1C, improvement in lipid parameters, and increased adherence to preventive care guidelines.5–10 There are fewer data evaluating the impact of pharmacist-managed insulin titration.

Achieving glycemic control presents additional unique challenges in low-income minority patient groups. Some barriers encountered in this population include misconceptions about health and food, inability to afford more healthful dietary options, and a low level of health literacy. A recent cross-sectional study11 found that more than half of low-income, minority patients surveyed believed that a normal glucose level

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was ≤ 200 mg/dl. Programs that have demonstrated efficacy in improving outcomes in diabetes for this type of patient population include those that focus on individualization of care and that occur frequently and longitudinally.12,13

In an effort to address these challenges in an evidence-based manner, a pharmacist-run insulin titration program was developed in a primary care clinic serving low-income, minority patients. The community health center serves as a safety net clinic for patients who are uninsured or underinsured with limited income. More than 80% of the health center’s patients are African American.

The objectives of the insulin titration program are to achieve ADA-established goals for A1C, blood pressure, and lipid parameters and improve adherence to preventive care recommendations through frequent, ongoing, individualized patient care provided by clinical pharmacists in collaboration with primary care providers. The purpose of this study was to assess the impact of the pharmacy insulin titration program on achieving these goals compared to standard care.

Study Methods
Study design
The study was a retrospective, matched, case-control design, with data retrieval through a review of electronic health records (EHRs). It was reviewed and approved by an associated institutional review board.

Study population
Intervention subjects were identified through program referrals between August 2007 and August 2008. All referred subjects were included if they interacted with the pharmacy service for initial education and at least two follow-up phone calls. The index date, or baseline, was the date of the initial education session. Subjects were excluded if the referral was for management of hypoglycemia or if a matched control subject could not be identified.

The control group included subjects on insulin therapy followed by the same group of primary care providers. Control subjects were identified by pharmacy claims for insulin and were matched to intervention subjects based on age and insulin regimen (basal only, bolus only, or basal-bolus). The index date for this group was defined as the date of an office visit for diabetes within 3 months of the matched intervention subject’s index date. Subjects were excluded from this group if they had any interaction with the clinical pharmacy.

Subjects were excluded from the analysis if they had a diagnosis of type 1 or gestational diabetes, were seen by an outside endocrinologist, or had no laboratory measurements in the past 2 years, or if a matched control subject could not be identified.

Study interventions
The pharmacist-run insulin titration program consists of an initial educational session, frequent telephone follow-up, physician collaboration, and monitoring. Patients are enrolled through primary care provider referral. An initial session includes chart review to determine the need for medication initiation, adjustment, or discontinuation; laboratory monitoring; or referral for specialty exams. Recommendations are communicated to referring providers through entry of notes in patients’ EHRs. Education provided in the initial session includes general diabetes, medication, self-monitoring of blood glucose (SMBG), insulin administration, and program enrollment.

The first session is followed by weekly to bimonthly follow-up, generally via telephone. Each interaction includes review of SMBG readings, discussion of any occurrence of hypoglycemia, and preventive care measures. Based on this information, the clinical pharmacist provides any necessary education and adjusts insulin doses in collaboration with patients’ primary care physician.

Titration of basal insulin is based on the titration schedule for the Treat-to-Target trial,14 and bolus insulin is adjusted based on clinical judgment. Dose adjustments are individualized taking into consideration patients’ previous responses and history of hypoglycemia. Dose adjustments are communicated to patients or their caregivers and, when refills are needed, to patients’ pharmacy.

Although the pharmacist’s scope of practice does not allow autonomous medication adjustment for hyperlipidemia, blood pressure, and other comorbidities, pharmacist recommendations are communicated promptly to primary care providers in person or via the EHR and are frequently implemented. Patients receive laboratory monitoring at regular intervals on the recommendation of the clinical pharmacy team in collaboration with referring providers.

Outcome measurements
The primary outcome evaluated was change in A1C at 6 months between subjects in the intervention (pharmacist-run insulin titration) and control (standard primary care) groups. Other between-group comparisons included change in A1C at 3, 9, and 12 months; attainment of ADA goals for A1C, blood pressure, and LDL cholesterol; prevalence of ADA-recommended medications on patient profile, change in fasting plasma glucose (FPG), lipid parameters (total, LDL, and HDL cholesterol and triglycerides), frequency of smoking cessation (if applicable), and hypoglycemia events. Hypoglycemia events were defined as documented events of symptomatic hypoglycemia in a provider chart note.

Statistical analysis
A sample size of 60 subjects—30 per group—was calculated to provide 80% power to detect a difference in A1C of 1.5% (standard deviation 2, effect size 0.75) between the groups using a two-sided t test with an α of 0.05.

Data were analyzed using SPSS 16.0 software (IBM, Armonk, NY). Primary and secondary outcomes were analyzed using an intention to treat, last observation carried forward method. Two a priori sub-analyses of the primary outcome were completed. The first (time analysis) excludes subjects who interacted with the pharmacy team for < 6 months (either because they withdrew from the program or were lost to follow-up). The other (laboratory analysis) excluded subjects who had only baseline laboratory
data. For continuous variables, the student’s $t$ test was used for between-group comparisons, and paired $t$ tests were used for within-group comparisons of continuous data. To analyze differences for nominal data, researchers used $\chi^2$ and Fisher’s exact tests.

**Study Results**

**Patient characteristics**

Forty-eight patients were referred to the pharmacist-managed insulin titration program between August 2007 and August 2008, and 70 subjects were included in the study (intervention $n = 35$, control $n = 35$) (Figure 1). The average subject was 51.2 ($\pm$ 9.7) years of age and 224.4 ($\pm$ 56.2) lb, with a BMI of 36.2 ($\pm$ 8.8) kg/m$^2$ and an A1C $> 7\%$.

Baseline characteristics of study subjects are shown in Table 1. A1C and total daily dose (TDD) of insulin were the only characteristics that differed significantly at baseline. In the intervention group, 63.9% ($n = 23$) were on insulin before enrollment, and the average baseline TDD of insulin was 23 units. In the control group, 94.3% ($n = 33$) were on insulin before the index date, and the average baseline TDD of insulin was 50 units.

For the time sub-analysis, 14 subjects in the intervention group were excluded, leaving 21 subjects and their matched control subjects. The mean baseline A1C for the primary intervention and standard groups were 9.8 and 9%, respectively. Seven subjects were excluded from the primary intervention group for laboratory analysis, leaving 28 subjects and their matched control subjects. The mean baseline A1C for the laboratory analysis intervention and standard groups were 10.2 and 9.1%, respectively.

**Efficacy analysis**

Within-group comparisons demonstrated significant A1C reduction from baseline at 6, 9, and 12 months in the pharmacist-managed group with no significant changes observed in the control group (Figure 2). The primary outcome of mean change in A1C at 6 months between groups (Figure 3) demonstrated a significant difference favoring pharmacist management at 6 months (1.0%, 95% CI 0.2–1.6, $P = 0.009$). Secondary time and laboratory analyses showed similar trends.

Attainment of ADA-recommended goals for A1C, blood pressure, and LDL cholesterol improved from baseline to 12 months for both intervention and control groups, although there was no statistical difference for either group from baseline to 12 months or between the groups at any time point. Medication utilization is illustrated in Figure 4.

The only significant difference in medication utilization was that more
Despite the change over time seen in FPG from baseline at any time point. There were no recorded episodes of severe hypoglycemia, defined as blood glucose < 40 mg/dl and/or requiring assistance, for either group.

### Discussion

Many successful pharmacist-led diabetes-management strategies have been documented in the literature in recent years, including one focused on insulin titration. To our knowledge, this is the first available evaluation specific to pharmacist-led insulin titration in a medically underserved, low-income, minority population.

It has been suggested that low-income, African-American patients respond differently from other populations to diabetes management programs. Interventions that have demonstrated efficacy in socially disadvantaged populations with diabetes include those that are longitudinal (> 6 months’ duration), frequent (> 10 contact times), and inclusive of one-on-one care that is individualized.

Our clinical pharmacist-managed insulin titration program includes all of these characteristics. Therapy plans are individualized and take patient-specific social and medical factors into consideration. In general, patients are followed on a weekly basis either via telephone or in person. Although the majority of our follow-up is accomplished via phone rather than in person, this tele-management is necessary in our patient population to allow for frequent follow-up because of the regularity of transportation difficulties, financial constraints, and other barriers to frequent clinic visits.

The results of this study will be used to improve the pharmacist-managed insulin titration service. Specifically, although the improvements demonstrated in glycemic control were significant, the authors were disappointed in the lack of statistical improvement observed in preventive care measures. In an effort to improve, the clinical service will now utilize shadow files for enrolled patients with a flow sheet that...

#### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n = 36)</th>
<th>Control (n = 35)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.3 ± 9.8</td>
<td>51.2 ± 9.8</td>
<td>0.87</td>
</tr>
<tr>
<td>Female (%)</td>
<td>21 (60.0)</td>
<td>22 (62.9)</td>
<td>1.00</td>
</tr>
<tr>
<td>Weight (lb)</td>
<td>234 ± 59.4</td>
<td>214.8 ± 51.8</td>
<td>0.14</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>37.1 ± 8.7</td>
<td>35.0 ± 9.6</td>
<td>0.41</td>
</tr>
<tr>
<td>A1C (%)</td>
<td>10.1 ± 2.2</td>
<td>9.0 ± 2.1</td>
<td>0.03</td>
</tr>
<tr>
<td>FPG (mg/dl)</td>
<td>207.6 ± 104.7</td>
<td>168.4 ± 89.1</td>
<td>0.11</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>185.2 ± 41.9</td>
<td>181.3 ± 43.4</td>
<td>0.71</td>
</tr>
<tr>
<td>LDL</td>
<td>103.4 ± 36.5</td>
<td>103.6 ± 40.8</td>
<td>0.95</td>
</tr>
<tr>
<td>HDL</td>
<td>52.9 ± 13.8</td>
<td>48.0 ± 17.6</td>
<td>0.33</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>178.2 ± 277.1</td>
<td>198.8 ± 322.1</td>
<td>0.85</td>
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<tr>
<td>Blood pressure (mmHg)</td>
<td></td>
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<tr>
<td>Systolic</td>
<td>139.0 ± 22.3</td>
<td>140.3 ± 24.9</td>
<td>0.79</td>
</tr>
<tr>
<td>Diastolic</td>
<td>77.1 ± 13.0</td>
<td>76.5 ± 14.6</td>
<td>0.83</td>
</tr>
<tr>
<td>Current smoker (n [%])</td>
<td>13 (36.1)</td>
<td>8 (22.9)</td>
<td>0.98</td>
</tr>
<tr>
<td>Coronary artery disease (n [%])</td>
<td>7 (19.4)</td>
<td>5 (14.3)</td>
<td>0.56</td>
</tr>
<tr>
<td>Basal/bolus insulin therapy (n [%])</td>
<td>13 (37.1)</td>
<td>13 (37.1)</td>
<td>0.14</td>
</tr>
<tr>
<td>TDD of insulin (units [SD])</td>
<td>22.9 (24.9)</td>
<td>50.5 (38.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Aspirin (n [%])</td>
<td>21 (60.0)</td>
<td>10 (28.6)</td>
<td>0.11</td>
</tr>
<tr>
<td>ACE inhibitor therapy (n [%])</td>
<td>25 (69.4)</td>
<td>13 (37.1)</td>
<td>0.49</td>
</tr>
<tr>
<td>Angiotensin receptor blocker therapy (n [%])</td>
<td>8 (22.2)</td>
<td>10 (28.6)</td>
<td>0.80</td>
</tr>
<tr>
<td>Statin therapy (n [%])</td>
<td>24 (68.6)</td>
<td>20 (57.1)</td>
<td>0.72</td>
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</table>

*α = 0.05 for two-sided statistical analysis

Twenty-four episodes of hypoglycemia were documented during the study period (intervention n = 13, control n = 9, P = 1.00). There was no consistent trend in any lipid parameter either between or within the groups at any time point (Table 2). FPG decreased significantly from baseline at 6-, 9-, and 12-month time points for the intervention group (Table 2). In contrast, the control group did not experience a significant change in FPG from baseline at any time point. Despite the change over time seen in the intervention group, no consistent trend was demonstrated between the two groups over time.

Thirteen subjects (36.1%) in the intervention group were classified as smokers at baseline. By the end of the study, 10 (27.8%) remained smokers (P = 0.25). The control group had eight subjects who smoked, and none were able to successfully quit by the end of the study. There was no statistical difference in number of smokers (P = 0.79) or number of successfully quit smokers (intervention 23.1%, control 0%, P = 0.26) between the two groups at the end of the study.
prompts the clinician to follow up on preventive care attainment.

Additionally, the authors were surprised to see that significant improvement in glycemic control was not observed at the 3-, 9-, and 12-month time points. This could be because many patients do not have follow-up data at the 3-month time point. We have incorporated into the shadow file and the service protocol a mechanism to remind providers to order A1C tests 3 months after patients are enrolled in the service.

Two potential reasons have been identified for the lack of significant improvement at the 9- and 12-month intervals. First, a large number of subjects enrolled in the study did not have complete data for evaluation at 9 and 12 months because of referral late in the index period. Second, patients have historically been discharged from the service once their A1C goal has been met. To address this as a potential reason for lack of continued clinical improvement, we have revised our service protocol to continue following patients at a less frequent (monthly) interval once they have achieved their A1C goal.

This study had some limitations that should be acknowledged. Inclusion in the study required patients to be enrolled in the pharmacy service within the indexed 1-year timeframe. Thus, a full 12 months’ worth of data may not have been available for subjects referred to the program late in the reference period. This could have resulted in underestimation of the impact of the pharmacy service.

Including subjects only if they had at least two follow-up phone calls was necessary to ensure evaluation of the pharmacy service. However, it may have led to a selection bias, including subjects who are more motivated to improve diabetes care.

Additionally, subjects with Medicare Part D insurance were excluded. This was necessary because these subjects would not be

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**Table 2. Changes in Lipid and FPG Levels**

<table>
<thead>
<tr>
<th></th>
<th>Treatment (Change [95% CI; P value])</th>
<th>Control (Change [95% CI; P value])</th>
<th>Between Groups (Change [95% CI; P value])</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total cholesterol (mg/dl)</strong></td>
<td></td>
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</tr>
<tr>
<td>3 months</td>
<td>-11.4 (-22.3 to -0.5; 0.04)</td>
<td>-2.3 (-6.3 to 1.8; 0.26)</td>
<td>-11.2 (-23.4 to 1.1; 0.07)</td>
</tr>
<tr>
<td>6 months</td>
<td>-10.9 (-26.0 to 4.2; 0.15)</td>
<td>-2.2 (-7.2 to 2.9; 0.39)</td>
<td>-12.6 (-31.1 to 5.8; 0.17)</td>
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<tr>
<td>9 months</td>
<td>-2.7 (-15.4 to 10.0; 0.67)</td>
<td>-0.2 (-7.8 to 7.4; 0.96)</td>
<td>-6.0 (-21.9 to 9.9; 0.45)</td>
</tr>
<tr>
<td>12 months</td>
<td>-9.7 (-22.3 to 2.9; 0.13)</td>
<td>10.4 (-5.8 to 26.7; 0.20)</td>
<td>-24.7 (-46.4 to -3.0; 0.03)</td>
</tr>
<tr>
<td><strong>LDL cholesterol (mg/dl)</strong></td>
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<tr>
<td>3 months</td>
<td>-11.8 (-22.7 to -0.9; 0.03)</td>
<td>-1.4 (-4.0 to 1.2; 0.27)</td>
<td>-12.8 (-26.3 to 0.8; 0.06)</td>
</tr>
<tr>
<td>6 months</td>
<td>-9.4 (-23.8 to 4.9; 0.19)</td>
<td>-1.8 (-5.1 to 1.4; 0.26)</td>
<td>-4.8 (-13.3 to 22.8; 0.59)</td>
</tr>
<tr>
<td>9 months</td>
<td>-1.5 (-13.3 to 10.4; 0.80)</td>
<td>1.7 (-5.4 to 8.7; 0.63)</td>
<td>1.9 (-12.8 to 16.6; 0.79)</td>
</tr>
<tr>
<td>12 months</td>
<td>-6.8 (-18.6 to 4.9; 0.24)</td>
<td>13.9 (-4.9 to 32.6; 0.14)</td>
<td>-18.0 (-41.3 to 5.3; 0.13)</td>
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<tr>
<td><strong>HDL cholesterol (mg/dl)</strong></td>
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<tr>
<td>3 months</td>
<td>-0.5 (-2.2 to 1.3; 0.58)</td>
<td>0.8 (-0.4 to 2.0; 0.18)</td>
<td>-1.1 (-3.5 to 1.3; 0.36)</td>
</tr>
<tr>
<td>6 months</td>
<td>-1.8 (-4.4 to 0.9; 0.18)</td>
<td>0.3 (-1.4 to 2.1; 0.70)</td>
<td>-1.8 (-5.3 to 1.6; 0.29)</td>
</tr>
<tr>
<td>9 months</td>
<td>-0.7 (-3.2 to 1.8; 0.58)</td>
<td>0.4 (-1.4 to 2.2; 0.63)</td>
<td>-0.8 (-3.8 to 2.2; 0.61)</td>
</tr>
<tr>
<td>12 months</td>
<td>-1.4 (-4.0 to 1.1; 0.26)</td>
<td>-0.5 (-4.8 to 3.7; 0.81)</td>
<td>0.2 (-4.4 to 4.9; 0.92)</td>
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<tr>
<td><strong>Triglycerides (mg/dl)</strong></td>
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<td></td>
<td></td>
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<tr>
<td>3 months</td>
<td>3.5 (-8.3 to 15.2; 0.85)</td>
<td>-7.6 (-23.2 to 8.1; 0.33)</td>
<td>4.6 (-11.3 to 20.4; 0.56)</td>
</tr>
<tr>
<td>6 months</td>
<td>2.4 (-14.2 to 19.0; 0.77)</td>
<td>-2.5 (-20.0 to 14.9; 0.77)</td>
<td>-3.9 (-24.2 to 16.4; 0.70)</td>
</tr>
<tr>
<td>9 months</td>
<td>-0.5 (-16.8 to 15.7; 0.95)</td>
<td>-14.8 (-38.9 to 9.4; 0.22)</td>
<td>5.5 (-21.2 to 32.2; 0.68)</td>
</tr>
<tr>
<td>12 months</td>
<td>-5.0 (-21.7 to 11.6; 0.54)</td>
<td>-7.7 (-33.9 to 18.6; 0.56)</td>
<td>-2.2 (-39.0 to 18.9; 0.48)</td>
</tr>
<tr>
<td><strong>FPG (mg/dl)</strong></td>
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</tr>
<tr>
<td>3 months</td>
<td>-18.9 (-38.0 to 0.3; 0.05)</td>
<td>-9.7 (-26.9 to 7.5; 0.26)</td>
<td>-9.2 (-35.0 to 16.6; 0.48)</td>
</tr>
<tr>
<td>6 months</td>
<td>-43.4 (-75.8 to -11.1; 0.01)</td>
<td>-6.0 (-21.1 to 9.1; 0.42)</td>
<td>-37.4 (-73.4 to -1.5; 0.04)</td>
</tr>
<tr>
<td>9 months</td>
<td>-54.8 (-86.4 to -23.2; 0.001)</td>
<td>-17.8 (-43.8 to 8.2; 0.17)</td>
<td>-37.0 (-80.2 to 6.2; 0.09)</td>
</tr>
<tr>
<td>12 months</td>
<td>-54.5 (-85.5 to -23.6; 0.001)</td>
<td>-13.7 (-42.7 to 15.2; 0.34)</td>
<td>-34.6 (-84.0 to 2.5; 0.06)</td>
</tr>
</tbody>
</table>
eligible for the pharmacy benefits program provided by the indigent clinic, which was the method used to identify the control group. This subsequently resulted in a population that was younger than the total intervention population, and this may have decreased the study’s external validity.

A1C differed between the intervention and control groups at baseline. Although this was not a surprise given that patients are referred to the service in an effort to improve glycemic control, it does make comparisons more difficult because a more pronounced decrease in A1C would be expected in those with a higher baseline value. However, an evaluation of A1C results using the percentage of change instead of raw numerical decreases yielded similar findings with the intervention group, demonstrating a 10.9% change in A1C at 6 months and a 13.9% change at 9 months compared to 1.1 and 5.6% changes at 6 and 9 months, respectively, in the control group. These results continue to demonstrate clinical significance.

Finally, the observational design of the study cannot conclusively prove causation.

The primary strength of this study is that it is practice-based, and the clinical service provided could be implemented in other varied ambulatory care sites. As the health care system continues to investigate alternative, effective means for improving outcomes in patients with diabetes, inclusion of a pharmacist in the patient care team should be considered.

Acknowledgments
The results of this study were presented at the 2009 American College of Clinical Pharmacy annual meeting in Anaheim, Calif., and were published in abstract form.16

References

Figure 3. Change in A1C. Comparison between groups.

Figure 4. Preventive care measures.


California Medi-Cal Type 2 Diabetes Study Group: Closing the gap: effect of diabetes case management on glycemic control among low-income ethnic minority populations. Diabetes Care 27:95–103, 2004


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