ABSTRACT

Objectives: We studied the independent association of adherence to oral hypoglycemic medications with poor glycemic control among a population of adults with type 2 diabetes (T2D), adjusting for demographics, health behaviors, and clinical and treatment characteristics.

Study Design: This was a retrospective cohort design.

Methods: We studied a population of Kaiser Permanente Northwest (KPNW) members with T2D who either had: 1) good glycemic control (glycated hemoglobin [A1C] <8.0%; n = 15,891) or 2) poor glycemic control (A1C >9.0%; n = 3709). The primary independent variable was medication adherence to 1 or more oral hypoglycemic medications. High medication adherence was defined as at least 80% of days covered in the 12 months prior to the A1C test date (yes vs no). Multiple logistic regression was used to analyze the independent association of medication adherence with poor glycemic control, adjusting for demographics, health behaviors, comorbidities, healthcare utilization, receipt of diabetes care management services, and intensity of diabetes treatments. All measures were constructed via KPNW’s electronic health record.

Results: Increased adherence to oral hypoglycemic medications was associated with a lower likelihood (OR, 0.54; 95% CI, 0.50-0.59; P <.0001) of having poor glycemic control after adjusting for demographics, health behaviors, medical comorbidities, healthcare utilization, receipt of diabetes care management services, and intensity of diabetes treatments.

Conclusions: Higher adherence to oral hypoglycemic medications is independently associated with a lower likelihood of having poor glycemic control among an adult population with T2D. Studies of the effects of measures to improve medication adherence on population-level glycemic control are needed.


Type 2 diabetes (T2D) is a chronic, progressive condition characterized by the failure of insulin secretion to compensate for resistance to insulin’s actions, resulting in hyperglycemia. The long-term complications of diabetes contribute to its status as a leading cause of premature illness and mortality. In 2012, 29.1 million individuals in the United States had diabetes (approximately 90% of the patients had T2D), and the prevalence appears to have increased in the past 2 decades. In 2012, diabetes resulted in $245 billion in costs, including $176 billion in direct medical costs and $69 billion in reduced productivity.

The long-term control of hyperglycemia is essential in order to improve health outcomes for populations with diabetes. Poor glycemic control has been associated with microvascular complications and mortality, whereas good control reduces the development of microvascular and long-term cardiovascular complications. Current clinical guidelines to manage glycemic control utilize glycated hemoglobin (A1C) target levels, with adjustment for age and length of illness; however, A1C levels greater than 75 mmol/mol (9.0%) are universally considered to reflect poor control. Of particular concern, according to data from a recent National Health and Nutrition Examination Survey, the proportion of adults with diabetes with poor glycemic control (A1C >9.0%) increased from 17.9% in the 2005-to-2008 period to 21.0% in the 2009-to-2012 period.

Despite clinical evidence of the efficacy of several glucose-lowering medications, adherence levels often remain suboptimal. Moreover, several studies have found that lower medication adherence can be associated with poorer glycemic control outcomes. However, these studies have several limitations, including small sample sizes and analyses not conducted on a population level.

With this background, the primary objective of this study was to analyze the independent association of adherence to oral hypoglycemic medications with poor glycemic control among adults with T2D on a population level. Such research has significant clinical implications—given that medication adherence is a potentially modifiable factor—that may be
Medication Adherence and Glycemic Control

influenced by quality improvement initiatives. A secondary objective was to identify demographics, health behaviors, comorbidities, healthcare utilization, diabetes care management services, and treatment intensity measures associated with poor glycemic control, with an emphasis on factors that were modifiable.

METHODS
The institutional review board of Kaiser Permanente Northwest (KPNW) in Portland, Oregon, approved the study protocol and waived the need for patient consent for data use, as is the protocol for data-only studies.

Study Setting and Data Sources
The study was conducted at KPNW, a nonprofit, group-model healthcare system in northwest Oregon and southwest Washington. The system consists of 15 medical clinics and 2 hospitals that serve more than 500,000 members. KPNW membership demographics (age, sex, race/ethnicity) are similar to the larger population in the geographic area. We used the electronic health record (EHR) (Epic Systems Corporation; Madison, Wisconsin) and administrative data systems to ascertain information on patient membership; demographics; clinical data, including height and weight; laboratory results; and medical healthcare utilization.

Population Selection
We conducted a retrospective cohort of KPNW members who met all the following inclusion criteria: 1) had an A1C test between July 1, 2014, and June 30, 2015; 2) were 18 years or older on the A1C test date; 3) were on the KPNW diabetes registry with a T2D indication at the time of the A1C test; and 4) had continuous health plan enrollment for 12 or more months prior to the A1C test date, which was defined as the index date. If the results of multiple A1C tests were available between July 1, 2014, and June 30, 2015, the latest value was used in the analysis.

KPNW members enter the diabetes registry through any of 3 ways: 1) receipt of treatment with oral hypoglycemic medications, 2) 2 or more abnormal fasting or nonfasting glucose test results in the previous 3 years (eg, fasting glucose >125 mg/dL, nonfasting glucose >200 mg/dL), or 3) 1 or more elevated A1C test results (>6.5%). In addition, those with T2D had an International Classification of Diseases, Ninth Revision (ICD-9)-related encounter (in any medical setting) as far back as membership existed. T2D ICD-9 codes include any of the following: 250.00, 250.02, 250.12, 250.20, 250.22, 250.30, 250.32, 250.40, 250.42, 250.52, 250.60, 250.62, 250.70, 250.72, 250.80, 250.82, 250.90, and 250.02.

Uncontrolled and Good Glycemic Control Groups
The process flow describing the study population is shown in the FIGURE. We identified 37,514 members who met the initial inclusion criteria. Of this population, 4759 members had an A1C value greater than 9.0% and formed the poor glycemic control group, while 27,514 had an A1C value less than 8.0% and made up the good glycemic control group. Another 5250 members with A1C values between 8.0% and 9.0% were not included in the analysis. The final analytic population (n = 19,600) included poor (3709) and good (15,891) glycemic control populations that received 1 or

PRACTICAL IMPLICATIONS
Among a population of adult patients with type 2 diabetes, higher adherence to oral hypoglycemic medications was independently associated with a lower likelihood of having poor glycemic control.

- These findings have clinical significance, given that medication adherence is a potentially modifiable factor.
- More research is needed to understand: 1) which interventions are most successful in improving medication adherence, and 2) whether subsequent improvements in medication adherence result in an improvement in glycemic control.

A1C indicates glycated hemoglobin.
more oral hypoglycemic medications in the 12 months prior to the A1C test. Generally, adherence to oral hypoglycemic medications and other study covariates was measured in the year prior to the A1C test date, for a complete study period between July 1, 2013, and June 30, 2015.

**Study Variables**

**Dependent variable.** The primary dependent variable was poor glycemic control (A1C >9.0%) versus good glycemic control (A1C <8.0%).

**Medication adherence.** Adherence to oral hypoglycemic medications was the primary independent variable in the analysis. We used the proportion of days covered (PDC) to construct medication adherence—a measure well described in the literature and considered to be more consistent than another adherence measure commonly used with electronic pharmacy information, such as the medication possession ratio. The denominator included the total number of days between the first hypoglycemic medication fill and the end of the 365-day observation period, prior to the A1C test date. The numerator included total days covered by prescription fills during the denominator period. High medication adherence was defined as 80% or more days covered during the denominator period. If multiple medications were prescribed, a measure of total average days covered was constructed. No insulin use was included in the adherence measure.

**Covariate measures.** We identified 6 groups of covariate measures: demographics, health behaviors, comorbidities, healthcare utilization, use of diabetes care management services, and diabetes treatment-intensity measures. The rationale for selecting these measures was 2-fold. First, they are important factors previously associated with poor glycemic control in the literature. Second, adjusting for these measures on a population level increased the ability to better assess the independent association of medication adherence with poor glycemic control.

**Demographics.** Using KPNW’s EHR, we measured age (continuous: assessed upon A1C test date), sex (female vs male), race/ethnicity, and primary language status (non–English speaker: yes vs no).

**Health behaviors.** Two health behavior measures were included. The first, current tobacco use (yes vs no), was assessed at the time closest to the A1C test, with a 1-year look-back period. Second, current physical activity status—whether an individual exercised 4 or more times per week (yes vs no)—was the most recent measurement assessed closest to the A1C test date. This information, systematically assessed at routine KPNW office visits and asked in person by clinic staff, was the most recent update in the member’s EHR.

**Comorbidities.** Four comorbidity measures were analyzed. The first was obesity, as reflected by a body mass index (BMI) of 30 or higher (yes vs no) if height and weight were available, using the most recent assessment with a look-back period of 60 months (5 years). The Charlson Comorbidity Index (CCI) score was used to assess patient-level comorbidities. CCI score (continuous), an established risk of mortality score in the medical literature, was constructed using utilization of inpatient and outpatient services in the year prior to the A1C test date. The duration of diabetes was assessed by measuring months on the diabetes registry (continuous) as far back as membership existed.

**Healthcare utilization.** Four dichotomous (yes vs no) variables assessed healthcare utilization in the year prior to the A1C assessment date: 1) primary care visits (1 or more visits vs none), 2) specialty care visits (excluding visits to internal medicine, family practices or pediatrics: 1 or more visits vs none), 3) hospital admission (1 or more admissions vs none), and 4) emergency department (ED) utilization (1 or more visits vs none).

**Diabetes care management services.** Enrollment in diabetes care management services was assessed by any contact with a diabetes care management program (yes vs no) in the year prior to the A1C assessment date.

**Diabetes treatment intensity measures.** Two diabetes treatment measures were assessed in the year prior to the A1C test date: 1) use of oral hypoglycemic medications (1 medication vs 2 or more medications) and 2) use of insulin (any use vs no use).

**Statistical Analysis**

We first examined the association of adherence to oral hypoglycemic medications and other covariate measures with poor glycemic control using $\chi^2$ analysis. Variables that were significant in the bivariate analysis ($P < .05$) were included in a final logistic regression model. The model examined the independent association of adherence to oral hypoglycemic medications and other covariate measures with poor glycemic control. Odds ratios (ORs) and 95% confidence intervals (CIs) were constructed for medication adherence and each covariate measure. The final logistic regression model included all covariate measures with the exception of: 1) ED utilization, which was not significant in the bivariate analysis, and 2) proteinuria. The proteinuria measure, although significant in the bivariate analysis, was dropped from the final logistic regression model because of a high level of missing information. The final model included the following variables: age (continuous), sex (female vs male [reference group]), and race/ethnicity (Hispanic, African American, Asian American/Pacific Islander, other race
RESULTS

Bivariate results are presented in Table 1 and multivariate results are in Table 2. Significant multivariate results are presented below.

Adherence to Oral Hypoglycemic Medications

Those with high adherence to oral hypoglycemic medications were less likely to have poor glycemic control (OR, 0.54; 95% CI, 0.50-0.59) compared with those with low medication adherence, adjusting for other study covariates.

Association of Covariate Measures With Poor Glycemic Control

Demographics. Of the demographic factors, age, sex, and race/ethnicity were significantly associated with poor glycemic control. Specifically, younger age (OR, 0.96; 95% CI, 0.95-0.96) was associated with poorer glycemic control, while women (OR, 0.88; 95% CI, 0.81-0.96) were less likely to have poor glycemic control than men. Lastly, African Americans (OR, 1.40; 95% CI, 1.16-1.69), Hispanics (OR, 1.62; 95% CI, 1.40-1.87), Asian Americans/Pacific Islanders (OR, 1.31; 95% CI, 1.11-1.55), and those of other race (OR, 1.44; 95% CI, 1.17-1.77) were more likely to have poor glycemic control compared with non-Hispanic whites.

Health behaviors. One of 2 health behaviors, exercise status was significantly associated with glycemic control in the multivariate analysis. Those who exercised 4 or more times per week were less likely to have poor glycemic control (OR, 0.75; 95% CI, 0.68-0.82) compared with those who exercised 3 or fewer times per week.

Comorbidities. Two comorbidity measures were associated with poor glycemic control. Specifically, those with a BMI of 30 or greater (OR, 1.18; 95% CI, 1.05-1.07) was associated with increased likelihood of having poor glycemic control.

Healthcare utilization. Three of 4 utilization variables were significantly associated with glycemic control. Having a primary care visit (OR, 0.95; 95% CI, 0.94-0.97) or specialty care visit (OR, 0.98; 95% CI, 0.98-0.99) was associated with a lower likelihood of poor glycemic control compared with no primary or specialty care utilization. Interestingly,

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Poor Glycemic Control: A1C &gt;9.0% (n = 3709)</th>
<th>Good Glycemic Control: A1C &lt;8.0% (n = 15,891)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication adherence</td>
<td>High adherence (≥80% days covered) 1275 (34.4%)</td>
<td>8448 (53.2%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Demographics</td>
<td>Age, years: mean ± SD 57.5 ± 12.5</td>
<td>64.5 +/- 12.0</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td>Female, n (%) 1734 (46.8%)</td>
<td>7740 (48.7%)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td></td>
<td>Race ethnicity, n (%)</td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td>White 2601 (70.1%)</td>
<td>12,872 (81.0%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hispanic 471 (12.7%)</td>
<td>970 (6.1%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>African American 204 (5.5%)</td>
<td>564 (3.6%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asian American/Pacific Islander 267 (7.2%)</td>
<td>1005 (6.3%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other race (Native American/Aleutian/Eskimo) 166 (4.5%)</td>
<td>480 (3.0%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-English speaker, n (%)</td>
<td>148 (4.0%)</td>
<td>447 (2.8%)</td>
</tr>
<tr>
<td>Health behaviors</td>
<td>Tobacco user, n (%)</td>
<td>380 (10.3%)</td>
<td>1367 (8.7%)</td>
</tr>
<tr>
<td></td>
<td>Exercise ≥4 times/week, n (%)</td>
<td>862 (23.6%)</td>
<td>4537 (28.8%)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>BMI ≥30, n (%)</td>
<td>2766 (74.6%)</td>
<td>10,437 (65.8%)</td>
</tr>
<tr>
<td></td>
<td>CCI score, mean ± SD</td>
<td>2.04 +/- 1.7</td>
<td>2.32 +/- 1.9</td>
</tr>
<tr>
<td></td>
<td>Months on KPNW diabetes registry, mean ± SD</td>
<td>102.8 +/- 71.9</td>
<td>93.4 +/- 70.5</td>
</tr>
<tr>
<td></td>
<td>Proteinuria, n (%)</td>
<td>821 (36.7%)</td>
<td>2463 (26.9%)</td>
</tr>
<tr>
<td>Healthcare utilization</td>
<td>≥1 primary care visits, n (%)</td>
<td>3407 (91.9%)</td>
<td>15,038 (94.6%)</td>
</tr>
<tr>
<td></td>
<td>≥1 specialty care visits, n (%)</td>
<td>3198 (86.2%)</td>
<td>14,496 (91.2%)</td>
</tr>
<tr>
<td></td>
<td>≥1 hospital admissions, n (%)</td>
<td>370 (10.0%)</td>
<td>2089 (13.2%)</td>
</tr>
<tr>
<td></td>
<td>≥1 ED visits, n (%)</td>
<td>990 (26.7%)</td>
<td>4125 (26.0%)</td>
</tr>
<tr>
<td>Diabetes care management</td>
<td>≥1 contacts with diabetes care management services</td>
<td>1729 (46.6%)</td>
<td>2761 (17.4%)</td>
</tr>
<tr>
<td>Diabetes Treatment</td>
<td>Number of hypoglycemic meds</td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1824 (49.2%)</td>
<td>10,894 (68.6%)</td>
</tr>
<tr>
<td></td>
<td>≥2</td>
<td>1885 (50.8%)</td>
<td>4997 (31.5%)</td>
</tr>
<tr>
<td></td>
<td>Any insulin use</td>
<td>1493 (40.3%)</td>
<td>2865 (18.0%)</td>
</tr>
</tbody>
</table>

A1C indicates glycated hemoglobin; BMI, body mass index; CCI, Charlson Comorbidity Index; ED, emergency department; KPNW, Kaiser Permanente Northwest; SD, standard deviation.

Sample limited to those with proteinuria tests (N = 11,389; 2240 uncontrolled, 9149 controlled)
those with 1 or more hospital admissions were less likely to have poor glycemic control (OR, 0.85; 95% CI, 0.79-0.92) compared with those with no hospital admissions, adjusting for patient-level covariates.

**Diabetes care management services and treatment.** Perhaps serving as a proxy for disease severity, those with 1 or more diabetes care management visits (OR, 2.80; 95% CI, 2.55-3.07) were more likely to have poor glycemic control compared with those with no contact. Similarly, those using more than 1 oral hypoglycemic medication (OR, 2.09; 95% CI, 1.93-2.27) and any insulin (OR, 2.31; 95% CI, 2.09-2.55) were more likely to have poor glycemic control compared with those using 1 oral hypoglycemic medication and no insulin, respectively.

**DISCUSSION**

Improving glycemic control is a central goal of contemporary diabetes management. Nevertheless, many patients with diabetes do not succeed in reaching goal A1C levels. This can be a source of significant frustration for patients and clinicians and portends a greater disease burden upon health systems. Although a range of demographic, behavioral, and clinical factors were associated with poorer glycemic control, we found that medication adherence, as reflected by PDC of at least 80%, was the most significant factor associated with satisfactory glycemic control. In our study, we found that those with high adherence to oral hypoglycemic medications were 46% less likely to have poor glycemic control compared with those with low adherence. Our study results are unique, given that we found this relationship among a population of adults with T2D receiving care in an integrated system (serving more than 500,000 individuals) after adjusting for a comprehensive set of patient-level covariate measures.

Surprisingly, receipt of diabetes care management services was associated with poor glycemic control. Rather than showing the potential ineffectiveness of care management services, the receipt of these services is likely a marker for higher disease severity. Similar results were found for insulin use and higher use of oral hypoglycemic medications.

Our findings are consistent with other recent research findings that examined medication adherence and glycemic control. A study by Feldman and colleagues of the EHRs of more than 200,000 adults with diabetes in Israel found that lower medication adherence was associated with a greater likelihood of having poor glycemic control (A1C >9%). Similarly, a retrospective cohort study by Farmer and colleagues using the Clinical Practice Research Datalink found that reduced medication adherence was associated with smaller reductions in A1C values compared with greater medication adherence.

Our results have direct applicability to clinical practice, given that medication adherence is a modifiable factor that could improve. A recent study by de Vries McClintock and colleagues found that a brief in-person and telephone-based intervention program improved adherence to diabetes medications, which was associated with a subsequent improvement in glycemic control. Our results, coupled with previous research findings, provide a focus for quality improvement opportunities to improve medication adherence.

We also found interesting relationships between several covariate measures and glycemic control that have direct
applicability to clinical care. First, we found that African Americans and other ethnic minorities were more likely to have poor glycemic control compared with non-Hispanic whites, even after adjusting for medication adherence and other patient-level covariates. These results are similar to research findings from Lafata and colleagues\(^{13}\) that found that African American–Caucasian differences in glycemic control could not be explained by medication adherence. These results give the larger KPNW delivery system an opportunity to develop quality improvement interventions to further address racial disparities in glycemic control.

In addition, 2 potentially modifiable factors were found to be associated with glycemic control. First, we found that increased exercise (4 or more times per week vs 3 or fewer times) was independently associated with a lower likelihood of having poor glycemic control after adjusting for medication adherence and other study covariates. Second, a BMI of 30 or higher (vs BMI <30) was associated with a greater likelihood of poor glycemic control. These results reinforce the importance of lifestyle interventions to improve glycemic control and identify another important quality improvement opportunity, specifically, interventions that target weight loss and improvement in medication adherence for adults with T2D.

**Limitations**

Our study has some important limitations. First, the T2D population was identified using electronic databases; thus, they may not be completely accurate and may misclassify some patients. Similarly, medication adherence was constructed from pharmacy dispensing information and may not reflect the medications that were actually taken by the patients observed in the study. Third, given that the study occurred in a group-model health maintenance organization (HMO) setting in the Pacific Northwest, the results cannot be generalized beyond this setting.

**CONCLUSIONS**

Future research should examine which system-level interventions are most successful in improving medication adherence and whether such improvement is associated with subsequent improvements in glycemic control. Such interventions should be pragmatic clinical trials or rigorous observational studies that can be implemented in real-world delivery systems with high levels of generalizability to clinical practice.

Among a population of patients with T2D in a group-model HMO care delivery system, we found that higher adherence to oral hypoglycemic medications was independently associated with a lower likelihood of having poor glycemic control. This finding remained significant, even after adjusting for patient-level demographics, health behaviors, comorbidities, healthcare utilization, use of diabetes care management services, and diabetes treatment measures.

**REFERENCES**


