Factors Associated with Secondary Nonadherence to Oral Anti-hyperglycemic Agents Among Patients with T2DM
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Abstract
Glycemic control in patients with T2DM remains sub-optimal. A major contributor to poor goal achievement is medication nonadherence. This study aimed to examine secondary nonadherence to oral anti-hyperglycemic agents (AHA) among T2DM patients and to assess its association with community- and individual-level characteristics. Using claims and electronic medical records in Geisinger Health System from 2003 to 2015, this retrospective cohort study included adults with newly diagnosed T2DM who filled their first order of secondary AHA. Secondary nonadherence was determined when patients did not fill the second oral AHA prescription within 30 days after the first fill supply ended. Among 2,413 patients who filled the first order, 764 (31.7%) were not adherent to the second prescription. Younger age, non-white (vs. white) and chronic kidney disease were associated with higher odds of nonadherence. Patients with higher baseline HbA1c when ≤ 10% were associated with lower odds of nonadherence, while those with higher baseline HbA1c when >10% were more likely to be non-adherent. Community-level characteristics were not found to be associated with nonadherence. Nearly one-third of patients did not complete a second fill of their oral AHA. This study identified patient characteristics associated with secondary nonadherence that may provide intervention points for improving medication adherence in diabetes management.

Background
According to the National Diabetes Statistics Report 2017 (1), more than 30 million (12.2%) US adults had diabetes in 2015. Diabetes prevalence increased with age — 25.2% of those 65 years old or older had diabetes. Asian, non-Hispanic blacks, and Hispanics had higher prevalence of diabetes compared to non-Hispanic whites. American Indian/Alaska Natives had the highest prevalence of diagnosed diabetes. Socioeconomic status was associated with prevalence of diabetes: 12.6% of adults with less than high school education were diagnosed with diabetes, 9.5% of those with high school diploma, and 7.2% of those with more than high school education. In an examination of county-level prevalence of diagnosed diabetes, prevalence ranged from 3.8% to 20%.

ADA Recommendations
The American Diabetes Association (ADA) recommends oral therapy, including metformin, in addition to lifestyle management for patients with mild to moderately uncontrolled type 2 diabetes (2). Oral therapy with one or more agents can reduce HbA1c values by over 2%; however, the proportion of patients reaching target HbA1c control (i.e., ≤ 7%) remains below 50%. A major contributor to this poor goal achievement is medication nonadherence (3-5). Rates of adherence to oral anti-diabetic medications are reported to range from 65% to 85% for patients on treatment 6-24 months (6).

Review of Literature on Nonadherence
One study found that approximately 15% of patients prescribed new oral antidiabetic agents never filled their first prescription. And those with higher HbA1c (≥9%) and lower copayments (<$10) were more likely to fill their first prescription (7). In a recent randomized controlled study, researchers found that despite outreach by nurses to those not filling after 14 days, rates of first fill are only marginally improved, and not as different from no intervention (8). Individuals characterized as loyal to a specific pharmacy were more likely to be adherent to their medication orders when compared to ‘non-adherent’ patients (9). Review of Literature on Nonadherence

This Research
We examined individual and community-level characteristics, using data extracted from electronic health records in Geisinger Health to identify traits associated with secondary nonadherence (no second refill) to oral anti-hyperglycemics. Specifically we were interested in:

- demographics
- health status, including comorbidity and co-occurring conditions
- health care utilization, and
- social determinants at the community level

Statistical Analysis
Secondary non-adherence was defined as filling the second prescription within 30 days following the initial fill (7). Baseline variables were selected using mean and standard deviations for those measured continuously, and frequency and percentage for those collected as categorical. Comparisons between groups was accomplished using the 2-sample t-test, Wilcoxon Rank Sum, or Chi-Square tests, as appropriate. A logistic regression model was then fit that included all variables found to be different between adherent and non-adherent at a p-value < 0.20. Variables were removed from the model if they were not significant at p<0.20. The proportion of patients on each agent at baseline was compared across the subgroups of adherence using a chi-square test, as appropriate.

Logistic Regression of Secondary Nonadherence to Oral Anti-Hyperglycemic Agents

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.99 (0.98, 0.99)</td>
<td>0.0152</td>
</tr>
<tr>
<td>White</td>
<td>0.50 (0.35, 0.74)</td>
<td>0.0001</td>
</tr>
<tr>
<td>BMI ≤ 18.5</td>
<td>0.78 (0.59, 1.05)</td>
<td>0.0628</td>
</tr>
<tr>
<td>BMI 18.5–24.9</td>
<td>1.27 (0.98, 1.64)</td>
<td>8.03 (0.67, 1.03)</td>
</tr>
<tr>
<td>BMI ≥ 25</td>
<td>1.57 (1.03, 3.67)</td>
<td>0.0441</td>
</tr>
</tbody>
</table>

Conclusion
There are differences in likelihood of filling diabetes medication like metformin a second time by demographic and clinical characteristics. Secondary nonadherence is perhaps a more important indicator of long-term adaptation to diabetes management and requires thoughtful intervention in observed nonadherence. Interventions to promote adherence to diabetes management may require differentiated approaches for patients in subgroups. It is important to understand the values and resources of patients in order to develop diabetes management strategies that are appealing and deemed important by patients.

Further research is necessary to characterize those values and resources in order to improve the development of patient-engaged diabetes-management strategies.

Limitations
- Prescription refill information is available only on patients who have Geisinger health care coverage. It is unclear if the same characteristics would emerge for patients with different coverage or for those who had no coverage during the portion of the study period.
- The study period covers both pre- and post-ACA. It may be important to better understand the implications of this timing, since there was a significant increase in the proportion of the population covered, and those with newly acquired insurance may have been more likely to begin filling prescriptions.
- Some of the patients identified as non-adherent for the second fill may have had a clinical indication that caused their provider to change the medication, e.g., chronic kidney disease.
- There is no patient-reported data regarding barriers to taking medication.

References