Risk of New-Onset Diabetes Associated With Concomitant Antidepressant, Inhaled Corticosteroid, and Statin Use Among Medicaid Beneficiaries With COPD

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BACKGROUND

- Multimorbidity, the coexistence of two or more chronic conditions, is highly prevalent among individuals with chronic obstructive pulmonary disease (COPD).
- Use of multiple medications to treat inflammation-related multimorbidity among individuals for COPD has been increasing.2
- Researchers have reported that 98% of patients with COPD received at least one prescription of "nonrespiratory drugs." Specifically, 64% received cardiovascular medication and 8% received depression medication.1
- Use of antidepressants, inhaled corticosteroids (ICS), and statins have been linked with new-onset diabetes.1,3
- No study has specifically examined the relationship between antidepressants, ICS, statins, and new-onset diabetes among patients with newly diagnosed COPD.

OBJECTIVES

- To evaluate the association between commonly used medications (antidepressants, ICS, statins) and new-onset diabetes. The study also evaluated the relationship between long-term use of antidepressants, statins, and new-onset diabetes.

METHODS

Data Source

- We used data from multiple years (2005-2008) and multiple states (California, Illinois, New York, and Texas) from the Medicaid Analytic eXtract (MAX) files. These files contain personal summary (enrollment), inpatient, outpatient, and pharmacy claims.

Study Design

- Using a retrospective longitudinal cohort design, we identified Medicaid beneficiaries with newly diagnosed COPD in a 2-year period (2006-2007).
- First date of COPD diagnosis, as defined below, was considered the index date. Baseline period was defined as 1 year prior to the index date, and follow-up period was defined as 1 year after the index date.

Study Population

- Patients with at least one inpatient or two outpatient visits (14 days apart) for an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis of chronic bronchitis (491.xx), emphysema (492.xx), or unspecified chronic airway obstruction (496.xx) were considered to have COPD.
- The final study population was restricted to fee-for-service Medicaid beneficiaries without Medicare eligibility who were aged 40 to 64 years, had continuous enrollment during the baseline and follow-up periods, had newly diagnosed COPD, and did not have diabetes (as defined below).

Dependent Variables: New-Onset Diabetes

- Any Medicaid beneficiary who had at least one inpatient or two outpatient claims for diabetes based on ICD-9-CM diagnosis (250.xx or 250.xx2) were considered to have new-onset diabetes.

Key Independent Variable: Multiple Medication Use

- Antidepressants, ICS, and statins were identified using National Drug Codes (NDC) recorded in pharmacy claims.
- Antidepressant use (yes/no), ICS use (yes/no), and statin use (yes/no) were defined as receipt of at least one prescription of the respective medications.

Other Independent Variables

- Patient characteristics, including year of diagnosis, demographic characteristics (e.g., age, sex, and race), medical eligibility, number of other clinical conditions, serious mental illness, alcohol abuse, tobacco use, and polypharmacy, were examined. County-level characteristics included variables from the area resource file such as metro status, primary care, and specialist care provider density in the county.

Statistical Analyses

- Bivariate analyses: Chi-square tests of independence were used to determine subgroup differences in multiple medication use categories and new-onset diabetes.
- Multivariate analyses: We used multivariable logistic regression to examine the relationship between any antidepressant, ICS, and statin use and new-onset diabetes after controlling for a comprehensive set of covariates as described in Methods.
- All analyses were conducted using SAS v9.3 (Cary, NC: SAS Institute Inc.; 2011).

RESULTS

Antidepressants, ICS, Statins, and New-Onset Diabetes

- Figure 2 shows the rates of new-onset diabetes by medication type. Table 1 describes the unadjusted and adjusted relationship between any antidepressant, ICS, and statin use and new-onset diabetes.
- Findings from bivariate and multivariate analyses with combined medication categories are presented in Figure 3 and Table 1, respectively.

Duration of Antidepressant and Statin Use and New-Onset Diabetes

- Duration of antidepressant use did not have a statistically significant association with new-onset diabetes. Adults with both long-term use (AOR = 1.44; 95% CI, 1.22-1.70) and short-term statin use (AOR = 1.58; 95% CI, 1.25-1.99) were more likely to have new-onset diabetes than those without any statin use.

Secondary Analysis: Controlling for Selection Bias in Statin Use

- To control for selection bias in statin use, we conducted secondary analyses with instrumental variable regression. We used county-level variables obtained from the area resource file, including poverty status (categorized into quartiles) and density of pulmonologists.
- The instrumental variable approach revealed that statin use was not associated with new-onset diabetes (parameter estimate = 0.15; P = 0.613).

DISCUSSION AND CONCLUSIONS

- After controlling for baseline characteristics, we did not observe a statistically significant association between antidepressant use and new-onset diabetes. These results are consistent with findings using data from the general population (not specific to COPD).1,5,10
- Our primary analyses revealed that adults who had any statin use were more likely to have new-onset diabetes compared with those without statins. However, once we controlled for selection bias, the statistically significant association disappeared.
- We did not find an association between ICS and new-onset diabetes when we combined all three medications and derived a combination variable.
- Use of multiple medications is not associated with risk of new-onset diabetes; further studies should evaluate long-term effects of medication use among patients with COPD.

REFERENCES

Please see handout for complete reference list.

CONTACT INFORMATION

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Table 1. Association Between Medication Use and New-Onset Diabetes

<table>
<thead>
<tr>
<th>Medication Use</th>
<th>N</th>
<th>Row %</th>
<th>OR 95% CI</th>
<th>P Value</th>
<th>AOR 95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any antidepressant use</td>
<td>475</td>
<td>6.5</td>
<td>1.06</td>
<td>0.93-1.20</td>
<td>0.098</td>
<td>0.91</td>
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<td>No</td>
<td>492</td>
<td>9.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Any ICS use</td>
<td>488</td>
<td>7.4</td>
<td>1.39</td>
<td>1.22-1.58</td>
<td>&lt; 0.001</td>
<td>1.23</td>
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<tr>
<td>No</td>
<td>478</td>
<td>5.5</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Any statin use</td>
<td>344</td>
<td>9.2</td>
<td>1.79</td>
<td>1.56-2.05</td>
<td>&lt; 0.001</td>
<td>1.48</td>
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<tr>
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<td>623</td>
<td>5.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Medication use categories</td>
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<tr>
<td>All three</td>
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<td>10.0</td>
<td>2.17</td>
<td>1.68-2.77</td>
<td>&lt; 0.001</td>
<td>1.56</td>
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<td>Any statin</td>
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<td>7.9</td>
<td>1.97</td>
<td>1.67-2.39</td>
<td>&lt; 0.001</td>
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<td>ADICS</td>
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<td>6.3</td>
<td>1.31</td>
<td>1.05-1.63</td>
<td>0.002</td>
<td>1.09</td>
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<td>Statin/ICS</td>
<td>90</td>
<td>12.4</td>
<td>2.74</td>
<td>2.13-3.57</td>
<td>&lt; 0.001</td>
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<tr>
<td>IC only</td>
<td>140</td>
<td>4.9</td>
<td>0.93</td>
<td>0.79-1.24</td>
<td>0.752</td>
<td>0.90</td>
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<tr>
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<td>68</td>
<td>7.3</td>
<td>1.54</td>
<td>1.15-2.04</td>
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<tr>
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<tr>
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<td>192</td>
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</tr>
</tbody>
</table>

AD = antidepressant; AOR = adjusted odds ratio; CI = confidence interval; ICS = inhaled corticosteroid; OR = odds ratio.

Note: Based on 15,287 Medicaid beneficiaries with newly diagnosed COPD who were diabetes-free during the baseline period, obtained from MAX files observed during 2006-2008.