Antipsychotic Medication Adherence and Diabetes-Related Hospitalizations Among Medicaid Recipients With Diabetes and Schizophrenia

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Objective: This cross-sectional study examined the relationship between antipsychotic medication adherence and preventable diabetes-related hospitalizations for individuals with diabetes and schizophrenia.

Methods: Hospitalizations related to diabetes, an ambulatory care sensitive condition, were assessed among Medicaid recipients in New York State with comorbid diabetes and schizophrenia (N=14,365) for three levels of antipsychotic medication adherence: very low to no engagement (two or fewer prescriptions or none in first 6 months), moderate to low adherence, and adherent (proportion of days covered \geq 80%).

Results: Rates of preventable diabetes hospitalization were highest among individuals with very low to no engagement in antipsychotic treatment (4.7%), followed by those with moderate to low adherence (3.3%). Diabetes hospitalizations among adherent individuals were comparable with those of the total diabetes population (both 2.0%). The odds of a

preventable diabetes hospitalization were significantly higher among individuals with very low to no engagement in antipsychotic treatment (adjusted odds ratio [AOR]=2.42) and among those with moderate to low adherence (AOR=1.57) than among adherent individuals. Black individuals were also at increased risk of a preventable diabetes hospitalization after the analyses adjusted for antipsychotic adherence and other variables (AOR=1.38).

Conclusions: This study indicates a relationship between antipsychotic adherence and improved diabetes outcomes among individuals with schizophrenia. Engagement in mental health treatment may be a critical path toward improving health disparities for individuals with schizophrenia. Individuals with very low to no engagement were a particularly vulnerable group, and the exclusion of persons with less than two prescriptions from research and quality measures should be revisited.

Psychiatric Services 2020; 71:236-242; doi: 10.1176/appi.ps.201800505

Antipsychotic medication adherence has been linked to critical psychiatric outcomes in schizophrenia. Low adherence to antipsychotic medication among individuals with schizophrenia has been associated with relapse; poor functional outcomes and prognosis; lower quality of life and life satisfaction; and increased emergency room visits, hospitalization, and suicide (1–13). Moreover, relapse and rehospitalization due to low adherence to medication are linked to increased patient cost (1–3).

Although antipsychotic medication is the foundation for pharmacological management of schizophrenia (4, 5), these medications can have significant metabolic side effects, including weight gain, hyperglycemia, and diabetes (6–9). The iatrogenic effects of antipsychotics may compound the risk of diabetes resulting from the onset of schizophrenia itself (10). Antipsychotics may both increase the incidence of diabetes and have adverse impacts on glucose control among those who have diabetes (6, 11). There is also some evidence

HIGHLIGHTS

- Among individuals with schizophrenia and diabetes, those who had the highest level of antipsychotic adherence had the best diabetes outcomes, and those with the lowest level of antipsychotic adherence had the poorest diabetes outcomes.
- Individuals with schizophrenia and diabetes who were antipsychotic adherent had rates of preventable diabetes hospitalization that were comparable to those of the total diabetes population.
- Black individuals were more likely than individuals of other race-ethnicities to have a preventable diabetes hospitalization independent of antipsychotic medication adherence.
- Results of this study suggest that improving engagement in antipsychotic treatment among individuals with schizophrenia and diabetes could reduce preventable diabetes-related hospitalizations.

that individuals with schizophrenia are at increased risk of poor medical outcomes after they develop diabetes. A study of the Nationwide Inpatient Database found that individuals with a comorbid diagnosis of schizophrenia were more likely to have a diabetes-related hospitalization (12).

Alternatively, antipsychotic adherence may have some benefits for general medical outcomes. Although symptoms associated with mental health conditions may impede diabetes self-management (13) and lead to a greater risk of medical rehospitalization (14, 15), antipsychotic adherence is associated with greater psychiatric stability, which may allow individuals to manage their health better. Stability of mental health conditions may be particularly important for diabetes because of the level of self-care required, including careful monitoring of dietary intake, glucose checks, and often complex medication regimens.

In a study of Medicaid beneficiaries with schizophrenia, individuals who adhered to their antipsychotic medication had fewer medical and psychiatric hospitalizations and, consequently, lower costs of care (16). A national study in Taiwan found that individuals with schizophrenia and type 2 diabetes who regularly used antipsychotic medication were less likely to have diabetes-related complications than those with no antipsychotic medication treatment (17). However, because of conflicting reports in the literature, the relationship between antipsychotic adherence and health outcomes remains unclear. Antipsychotic medications have been linked to increased risk of premature mortality (18), with some contested studies finding the opposite effect (19–22).

A better understanding of the relationship between antipsychotic adherence and diabetes outcomes for individuals with schizophrenia is needed to guide patient education and clinical decision making. Moreover, an examination of adherence and preventable diabetes hospitalizations may inform the development of successful adherence interventions. In the current study, we used a national measure of quality developed by the Agency for Healthcare Research and Quality to identify diabetes-related hospitalizations that may have been prevented given adequate primary care in the community. We examined the risk of preventable diabetes-related hospitalizations among individuals with schizophrenia, by the level of antipsychotic medication adherence, in a large state Medicaid program.

METHODS

Data Source

The data source was New York State (NYS) Medicaid inpatient, outpatient, and pharmacy claim and encounter records extracted from the Office of Health Insurance Programs Medicaid DataMart. Data extraction and analysis were conducted from 2013 to 2016. Medicaid claims and encounters are administrative data; no medical record review was conducted for this study. Approval for this study was granted by the NYS Department of Health Institutional Review Board; this study was exempt from obtaining informed consent. Demographic characteristics are available for almost all NYS Medicaid recipients because such information is collected at the time of enrollment; status changes, such as those for payer and aid category, are updated frequently. Claim and encounter records include primary and up to 25 additional diagnoses classified by *ICD-9-CM* code; primary and up to 25 additional procedure codes; primary and up to five additional revenue codes; state-specific rate codes; and prescription drug codes classified by National Drug Codes (NDCs).

Study Population

Individuals included in our study population were ages 18-64 with prevalent diabetes mellitus (type 1 or type 2) and schizophrenia and were continuously enrolled in Medicaid for the calendar year 2012. Diabetes was defined according to the 2013 Healthcare Effectiveness Data and Information Set (HEDIS) criteria, which specifies that an enrollee must have had one inpatient visit, or two outpatient visits, with a diagnosis of diabetes or pharmacy claims for drugs used to treat diabetes during the measurement year (2012) or the year prior (2011) (23). Individuals were identified as having schizophrenia if they had an Episode Diagnostic Category indicating schizophrenia during the measurement year (2012) (24, 25). To identify prevalent cases in which an individual had both diabetes and schizophrenia, individuals had to meet criteria for diabetes and schizophrenia diagnoses in the measurement year as well as the year prior to the measurement year (2011 and 2012). Our continuous Medicaid enrollment criteria allowed for up to a 1-month gap in enrollment during the measurement year. We excluded individuals who had Medicare at any point in the year.

More than 219,651 Medicaid recipients were identified as having diabetes in 2012, and of those, 191,521 were identified with prevalent diabetes (87.2%). Among those with prevalent diabetes, 14,365 individuals with prevalent schizophrenia were identified for this investigation.

Study Variables

The proportion of individuals with one or more preventable diabetes-related hospitalizations was the primary outcome. The Agency for Healthcare Research and Quality created a set of prevention quality indicators, including four diabetes-related measures, to identify hospitalizations that may have been prevented with adequate primary care in the community (26). All four diabetes-related prevention measures were used to create our composite outcome measure, including short-term diabetes complications, long-term diabetes complications, uncontrolled diabetes, and lower extremity amputation (26). Individuals met criteria for the outcome composite variable if they had one or more preventable diabetes-related hospitalizations during the calendar year 2012.

In this study, the demographic characteristics of interest included age, race, Medicaid payer type, and receipt of Supplemental Security Income (SSI). Age group and race categories were dichotomized. Age groups were divided into those younger than age 45 and those age 45 and older. Raceethnicity was dichotomized into black and non-black categories because of small cell sizes. The non-black category included members identified as American Indian-Alaska Native, Asian-Pacific Islander, Hispanic, white, and other race-ethnicity. The Medicaid payer and disability status categories were also dichotomized into Medicaid managed care and fee-for-service and those who received SSI and those who did not (non-SSI), respectively.

Our primary exposure variable, adherence to antipsychotic medications, was constructed as three categories based on examination of claims data: adherent, moderate to low adherence, and very low to not engaged in antipsychotic treatment. Adherence group definitions were based on HEDIS specifications for the Antipsychotic Medication Adherence for Persons With Schizophrenia measure (23). In brief, Medicaid claims and encounter data were used to identify antipsychotic prescriptions, dispense date, and days' supply for all antipsychotic prescriptions filled. For long-acting injectable antipsychotics, medication-specific standard days' supply was used, consistent with HEDIS specifications (23). The proportion of days covered (PDC) by an antipsychotic was calculated from the date of the first filled outpatient antipsychotic prescription during the year of observation through the end of the year.

Adherent individuals were defined as those with schizophrenia who had a PDC of \geq 80%, and the first prescription filled must have been within the first 180 days of the year. Individuals with moderate to low adherence were defined as those with an antipsychotic PDC of <80%, but who had a minimum of two prescriptions, with one or more filled during the first 180 days of the year. Individuals with very low to no engagement were defined as those with less than two antipsychotic prescriptions filled during the measurement year, or with no antipsychotic prescriptions filled in the first 180 days of the measurement year. Although these individuals did not meet minimum inclusion criteria for the HEDIS measure, they were included in this study as the group with the lowest level of antipsychotic adherence.

Data Analysis

We performed a cross-sectional analysis of our study population during the calendar year 2012. Bivariate analyses were conducted to examine differences in demographic characteristics among the three groups (adherent, moderate to low adherence, and very low to no engagement) in our study population. Demographic variables significantly associated with antipsychotic adherence or preventable diabetes-related hospitalizations in the bivariate analyses (p<0.05) were included in the multivariable models. In addition, although the chi-square p value for payer (fee-for-service or Medicaid managed care) was not significant, we believe that there are meaningful differences between these two sub-populations, and therefore, we opted to include the variable in the adjusted logistic regression model.

We estimated the likelihood of a preventable diabetesrelated hospitalization given the level of adherence to antipsychotic medication among individuals with diabetes and schizophrenia. A corresponding model among the same population adjusted for age (younger than age 45 or age 45 and older), race-ethnicity (black or non-black), sex (male or female), and payer (fee-for-service or Medicaid managed care) was also run by using logistic regression. Aid category (SSI or non-SSI) was considered for this model but was excluded because of small cell sizes. We used SAS, version 9.4, for all statistical analyses (27).

RESULTS

In our study population of individuals with prevalent schizophrenia and diabetes, 33.3% were younger than age 45, 56.6% were female, 31.6% were black, 78.5% were enrolled in a Medicaid-managed care plan, and 79.2% were receiving SSI benefits (Table 1). One-third (33%, N=4,747) of the study population was classified as antipsychotic adherent, 13% (N=1,914) as having moderate to low adherence, and more than half (54%, N=7,704) as having very low or no engagement in antipsychotic treatment.

All three groups of individuals within our study population (adherent, moderate to low adherence, or very low to no engagement in antipsychotic treatment) were significantly different from one another across all demographic categories (p<0.001; Table 1). Medication-adherent individuals with schizophrenia had a diabetes-related hospitalization rate similar to the total prevalent diabetes population (both 2.0%), whereas proportions were elevated for both the moderate- to low-adherence group and the very low- to no-engagement group (3.3% and 4.7%), respectively.

Within our study population, individuals with moderate to low adherence and those with very low or no engagement in antipsychotic treatment during the measurement year were significantly more likely to experience a preventable diabetes-related hospitalization compared with those who were adherent to their antipsychotic medications (Table 2). These relationships to antipsychotic adherence persisted after the analyses controlled for age, sex, race, and payer (Table 2). We also found that black individuals were significantly more likely than other racial-ethnic groups to experience a preventable diabetes-related hospitalization, even after the analyses adjusted for antipsychotic adherence and other factors (Table 2). Younger adults (<45) were more likely than older adults to have a preventable diabetesrelated hospitalization, but age was no longer statistically significant after the analyses controlled for lower antipsychotic adherence in this group and other factors.

DISCUSSION

Consistent with previous research, in the current study, individuals with comorbid schizophrenia and diabetes had a higher prevalence of preventable diabetes hospitalizations TABLE 1. Characteristics of Medicaid recipients with diabetes only or diabetes and comorbid schizophrenia (study population), by adherence to antipsychotics^a

Characteristic				Study population (diabetes and schizophrenia)							
	Diabetes population (N=191,521)		Total (N=14,365)		Adherent (N=4,747)		Moderate to low adherence (N=1,914)		Very low to no engagement (N=7,704)		
	Ν	%	Ν	%	Ν	%	Ν	%	Ν	%	pb
Age group											<.001
<45	43,449	22.7	4,778	33.3	1,064	22.4	515	26.9	3,199	41.5	
≥45	148,072	77.3	9,587	66.7	3,683	77.6	1,399	73.1	4,505	58.5	
Sex											<.001
Female	109,476	57.2	8,129	56.6	2,468	52.0	949	49.6	4,712	61.2	
Male	82,045	42.8	6,236	43.4	2,279	48.0	965	50.4	2,992	38.8	
Race-ethnicity											.001
Black	39,489	20.6	4,545	31.6	1,592	33.5	853	44.6	2,100	27.3	
Non-black	152,032	79.4	9,820	68.4	3,155	66.5	1,061	55.4	5,604	72.7	
Payer											.901
FFS ^c	17,710	9.3	3,090	21.5	1,024	21.6	322	16.8	1,744	22.6	
MMC ^d	173,811	90.8	11,275	78.5	3,723	78.4	1,592	83.2	5,960	77.4	
Aid category ^e											<.001
Non-SSI	120,361	62.8	2,993	20.8	335	7.1	256	13.4	2,402	31.2	
SSI	71,160	37.2	11,327	78.9	4,412	92.9	1,658	86.6	5,302	68.8	
Preventable diabetes	3,881	2.0	525	3.7	97	2.0	63	3.3	365	4.7	<.001

^a The study population included individuals ages 18–64 who were diagnosed as having prevalent diabetes mellitus (type 1 or type 2) and schizophrenia and who were continuously enrolled in Medicaid in New York State for the calendar year 2012. The diabetes population met criteria for diabetes in 2011 or 2012.
^b Reflects difference in the study population by adherence level (chi-square test).

^c Fee for service.

^d Medicaid managed care.

^e SSI, Supplemental Security Income.

than the total Medicaid population with diabetes (12, 28, 29). Our findings extend previous research in two important ways. First, we identified an inverse relationship between antipsychotic adherence and risk of a preventable diabetes hospitalization: individuals with the lowest level of antipsychotic adherence had the highest prevalence of diabetes hospitalizations, followed by individuals with moderate to low adherence. The hospitalization rate among individuals who were adherent to their antipsychotic treatment, on the other hand, was comparable to that of the total diabetes population. Second, the individuals with schizophrenia and diabetes with very low to no engagement in antipsychotic treatment, and therefore who did not meet inclusion criteria for measures of antipsychotic adherence used nationally for quality measurement (23), represented more than half of the study sample and had the highest rates of preventable diabetes-related hospitalizations.

This study suggests that for individuals with schizophrenia and diabetes, antipsychotic adherence improves diabetes outcomes despite the well-established association between antipsychotic medications and increased risk of metabolic concerns, including diabetes (6, 30, 31). This finding is particularly promising given that individuals with serious mental illness have higher medical morbidity and mortality than the general population, with worse outcomes for diabetes and other chronic medical conditions (32, 33). Several interventions have been developed to improve diabetes outcomes for individuals with serious mental illness (34–36). The current study suggests that antipsychotic adherence may be a modifiable risk factor for preventable diabetes hospitalization for individuals with schizophrenia; however, additional study is needed to explore these results further and to inform interventions.

A logic model may be useful to summarize a possible explanation for the relationship between antipsychotic adherence and preventable diabetes hospitalizations and can create a framework for future study. Among individuals with schizophrenia, antipsychotic adherence leads to better control of psychiatric symptoms, which may create the capacity for improved diabetes self-care and better engagement in diabetes treatment, leading to improved diabetes outcomes including decreased risk of preventable hospitalization. Antipsychotic adherence is associated with reduced psychiatric symptoms and lower relapse rates for schizophrenia (37); it stands to reason that uncontrolled psychotic symptoms would make it more challenging for individuals to engage in the complex self-care routines required for management of diabetes, including managing the timing and content of meals, testing blood sugars, and adjusting medication.

It is possible that the findings are due in part to the "healthy adherer effect," in which adherence to any medication may be an indicator of other healthy behaviors (38).

		Recipients with at least 1 diabetes-related hospitalization							
Variable	Recipients (N)	N	N per 10,000 population	OR	95% CI	р	AOR ^a	95% CI	р
Antipsychotic adherence Adherent (reference) Moderate to low adherence	4,747 1,914	97 63	204 329	1.63	1.18-2.25	.003	1.57	1.14-2.17	.006
Age group <45 ≥45 (reference)	4,778 9.587	200 325	474 419 339	1.25	1.04-1.49	.001	1.11	.93-1.34	.250
Sex Female Male (reference)	8,129 6,236	285 240	351 385	.91	.76-1.08	.278	.85	.71–1.01	.071
Race-ethnicity Black Non-black (reference)	4,545 9,820	195 330	429 336	1.29	1.08-1.54	.006	1.38	1.15–1.66	.001
Payer MMC ^b FFS (reference) ^c	11,275 3,090	394 131	349 424	.82	.67–1.00	.051	.84	.69–1.03	.097

TABLE 2. Association between characteristics of 14,365 Medicaid recipients with diabetes and schizophrenia and likelihood of a preventable diabetes-related hospitalization

^a Adjusted odds ratio.

^b Medicaid managed care.

^c Fee for service.

Further research is needed to examine the relationship between antipsychotic adherence and adherence to diabetes medication and treatment and, most important, whether changes in antipsychotic adherence over time are associated with changes in diabetes treatment engagement and preventable diabetes hospitalization. In addition, understanding whether these relationships persist for individuals with different levels of disease severity, such as those with prior diabetes hospitalizations or more severe complications, may help inform future interventions. It is also worth exploring whether antipsychotic adherence in schizophrenia is associated with improved health outcomes for other ambulatory care sensitive conditions (32, 33). Engagement in mental health treatment may be a critical path toward improving health disparities for individuals with schizophrenia.

Among individuals with prevalent schizophrenia and diabetes, we found that those with very low to no engagement in antipsychotic treatment were the largest group and had the highest risk of a diabetes-related hospitalization. This work extends a previous report that examined diabetes complications in Taiwan using individuals with no antipsychotic medications (medication possession ratio=0) as the reference group (17). These individuals have been overlooked in assessments of medication adherence in schizophrenia that require a minimum of two prescriptions filled (23), including the HEDIS measure of adherence to antipsychotic medications for individuals with schizophrenia. Given that this group had the worst outcomes, research and quality studies need to focus on, rather than exclude, this population.

Our findings also indicate that black individuals were more likely than non-black individuals to have a preventable diabetes-related hospitalization, even after the analyses controlled for engagement in antipsychotic treatment. Our results build on prior research, which suggests that in the general population, black individuals have significantly higher rates of preventable diabetes-related hospitalizations compared with non-Hispanic whites (39). Mangurian and colleagues (40) described the double vulnerability for diabetes among black individuals who have schizophrenia and other serious mental illnesses, calling for increased screening and interventions for this population. The current study suggests that although addressing antipsychotic adherence may reduce preventable diabetes hospitalizations, it will not eliminate the health disparity observed for black individuals. Further research is required and needs to consider the multifactorial and long-standing nature of health disparities for this population, including the quality of care delivered, the impact of discrimination, and other social determinants of health (41-44).

Overall, this study suggests that improving engagement in mental health treatment may reduce preventable diabetes hospitalizations and therefore has the potential to yield cost savings. The estimated average cost of a preventable diabetes-related hospitalization in 2010 was \$13,200 (26, 45). Individuals with schizophrenia with very low or no engagement in antipsychotic treatment were 2.42 times more likely to have a preventable diabetes-related hospitalization than those who were adherent. Engaging individuals with very low or no engagement in antipsychotic treatment may have the potential to avert an estimated 57% of preventable diabetes-related hospitalizations and associated costs for this subpopulation. In a time when U.S. health care expenditures continue to grow yearly (46), identifying ways to reduce health care costs while improving outcomes is increasingly important.

There were limitations to this work. First, this study was conducted in a large state Medicaid program and may not be generalizable to other populations. Antipsychotic adherence was calculated by using claims and encounter data; any medications not paid by Medicaid (e.g., paid out of pocket or medication samples) were not included. We did not consider hospitalizations in adherence calculations, which may result in an underestimate of adherence for individuals with hospitalizations. This study included both type 1 and type 2 diabetes; further study is needed to investigate the relationship between antipsychotic adherence and preventable diabetes hospitalization by disease type. Finally, this cross-sectional study design identified a relationship between antipsychotic adherence and fewer diabetes-related hospitalizations, but future study is needed to understand causal and temporal relationships, if any, between antipsychotic adherence and preventable diabetes-related hospitalizations.

CONCLUSIONS

Among individuals with diabetes and schizophrenia, those who were not adherent to antipsychotic medications were at increased risk of preventable diabetes hospitalizations compared with individuals who were adherent to antipsychotics. However, among those who were antipsychotic adherent, the percentage with a preventable diabetes hospitalization was similar to that of the total diabetes population. An inverse relationship was observed in which preventable hospitalizations were highest among individuals with very low to no antipsychotic engagement (4.7%), followed by those with low to moderate adherence (3.3%) and antipsychotic adherent individuals (2.0%) were comparable with those among the total diabetes population (both 2.0%). Findings also indicated that black individuals in the study population were significantly more likely than individuals of other racial-ethnic minority groups to experience a diabetesrelated hospitalization independent of antipsychotic medication adherence.

These results suggest that interventions targeted at improving engagement in mental health treatment for schizophrenia may reduce preventable diabetes hospitalizations. Further research is needed to understand the impact of race-ethnicity on health outcomes among individuals with comorbid diabetes and schizophrenia. Research is also needed to examine the specific mechanisms by which antipsychotic adherence affects health outcomes among individuals with comorbid diabetes and schizophrenia.

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Institutional support for this study was provided by the New York State Department of Health and the New York State Office of Mental Health. The authors thank Deborah Layman, M.A., and Katrina Vega, M.S.W. These views represent the opinions of the authors and not necessarily those of the New York State Department of Health or the New York State Office of Mental Health. Examples of analysis performed within this article are only examples and should not be used in real-world analytic products.

The authors report no financial relationships with commercial interests.

Received November 8, 2018; revision received August 12, 2019; accepted August 23, 2019; published online November 20, 2019.

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