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# Racial and ethnic differences in patterns of use and discontinuation of long-acting injectable antipsychotics using Medicaid claims data

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#### **Abstract**

**Introduction:** In general, racial and ethnic differences exist in antipsychotic prescription practices. However, little is known about such differences between individual long-acting injectable (LAI) antipsychotic formulations, specifically. This study's primary objective was to determine racial and ethnic differences among LAI antipsychotic use. Secondary objectives were to identify if discontinuation rates differed between agents and by race or ethnicity.

Methods: International Classification of Diseases, 10th edition (ICD-10) codes were used to identify patients with schizophrenia and related disorders (18-64 years) who received an LAI antipsychotic between 2016 and 2020 using Merative Multi-State Medicaid databases. Using National Drug Code numbers for LAI antipsychotics, pharmacy claims were identified and data analyzed. Cochran-Mantel-Haenszel tests and odds ratio estimators were used to investigate conditional association between race or ethnicity and medication, while controlling for age, sex, health plan, and prescription year. Kaplan-Meier survival curves were examined, and stratified log-rank tests were conducted to compare the time until discontinuation distributions by race or ethnicity.

**Results:** The analysis included 37 712 patients. Blacks received an LAI first-generation antipsychotic more often than Whites (OR: 1.64, 95% CI: [1.56, 1.73], Hispanics (OR: 1.46, 95% CI: [1.21, 1.75]) and others (OR: 1.44, 95% CI: [1.20, 1.73]). Aside from fluphenazine decanoate showing earlier discontinuation rates for Whites over Blacks (P = .02), no significant differences in discontinuation across race or ethnicity were identified.

**Discussion:** Despite no significant differences in second-generation antipsychotic LAI discontinuation rates between Blacks and other racial or ethnic groups, Blacks received second-generation antipsychotic LAIs significantly less often than other groups. Further studies are needed to determine why differences may be occurring.

Keywords: long-acting injectable antipsychotics, schizophrenia, discontinuation, adherence, race, ethnicity

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# Introduction

The prevalence of schizophrenia in the United States may range between 0.25% and 0.50% with diagnosis occurring more likely among Blacks compared with Whites and possibly Hispanics. Schizophrenia is associated with decreased quality of life, stigma, and poorer health outcomes. The effect may be increased in minority populations. Racial and ethnic minority populations are more likely to experience difficulty obtaining pathways to mental health services (eg, treatment for psychosis) ranging from stigma toward diagnosis to fears regarding chronic antipsychotic treatment. 6,7



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Antipsychotic medications have been prescribed as first-line agents for several decades and form the basis of long-term treatment. While antipsychotic medications are effective, adherence is a barrier affecting more than 40% of those receiving prescribed oral antipsychotics. Long-acting injectable (LAI) antipsychotic development and use has increased over the past several years. In particular, second-generation antipsychotic (SGA) LAIs have recently gained popularity because of the potential to optimize outcomes. A recent meta-analysis demonstrated the use of LAI antipsychotics overall improved adherence and clinical outcomes.

While these results seem promising, discontinuation rates between race or ethnicity for these medications have not been elucidated. In general, rates of medication adherence and persistence are often low in underserved minority populations. Medication adherence can be affected by cost, adverse events, patient preference, and stigma. One study found differences in adverse event rates across racial or ethnic groups, including greater weight gain among Black users of oral olanzapine than among Whites. Such differences suggest the possibility of differences in discontinuation rates for LAI antipsychotics by race or ethnicity, but this has yet to be formally investigated. Additionally, studies have suggested differences in LAI preferences either by patients or prescribers.

The Merative MarketScan Research Databases are a collection of large sample data sets on all health insurance claims, making possible research on medication usage, disease prevalence and incidence, and other epidemiologic topics.<sup>15</sup> Studies using MarketScan data in patients with bipolar disorder and schizophrenia suggested LAI aripiprazole was associated with lower hospitalization rates for both all-cause and psychiatric hospitalizations (eg. 37% to 68% lower in bipolar) compared with LAI haloperidol decanoate and risperidone microsphere. 16,17 Also, patients initiating LAI aripiprazole lauroxil had significant reductions in inpatient admissions (22.4%).<sup>18</sup> While these results appear promising, the study did not compare other LAI antipsychotics and only evaluated a 6-month period. 18 Additionally, there were no comparisons between ethnicities or races. In summary, racial and ethnic differences exist in antipsychotic prescription practices, in general, but limited recent data exist about such differences among specific LAI formulations. Therefore, the primary objective of this study is to determine racial or ethnic differences among LAI antipsychotic use. Secondary objectives were to identify if discontinuation rates differed between agents (ie, individual agent, generation) and by race or ethnicity using more recent real-world data.

# **Methods**

# Study Design and Data Sources

This study used claims data from Merative MarketScan Multi-State Medicaid Databases (referred to hereafter as the

MarketScan Medicaid Database) between January 1, 2016 and December 31, 2020. The MarketScan Medicaid Database contains longitudinal records of inpatient and outpatient services and prescription drug claims for patients covering millions of enrollees. The data provide insight into treatment patterns across diverse patient populations. Medical claims from facilities and providers included International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis codes and health plan information. Drug Code (NDC) numbers for dispensed first-generation antipsychotic (FGA) and SGA LAI medications. University IRB exempt status was obtained.

# Study Population and Cohort Assignment

Patients between the ages of 18 to 64 with a pharmacy claim for a LAI antipsychotic were identified in the MarketScan Medicaid Database. LAI antipsychotics were identified using NDC numbers for all doses using brand or generic names through the NDC list (https://ndclist.com/) and cross referenced with medication package insert through the FDA drug database (www.accessdata.fda.gov), when needed.<sup>20,21</sup> Patients were required to have ≥1 inpatient or >2 outpatient claims with an ICD-10-CM diagnosis code for schizophrenia (F20.x), schizotypal (F21), or schizoaffective (F25.x) prior to or on the index date, which was defined as the first fill for an LAI antipsychotic. A refill date was defined as the fill date plus the coverage period, which varies by medication and formulation type (eg, 2 weeks vs 4 weeks for different risperidone formulations). Based on previous studies using similar methodology, discontinuation was defined as a continuous medication gap of 60 days or greater (>59 days after the refill date). 18,22 Patients were required to be continuously enrolled in their health plans through the month of the date 59 days past the last refill date. Effectively, this requirement excluded change or loss of insurance as the cause of a discontinuation event.

# **Study Variables**

The response variable of primary interest was the number of days from the index date until antipsychotic discontinuation date, defined as the number of days each fill would last according to formulation. Antipsychotic discontinuation rates were measured for FGA LAI (ie, fluphenazine decanoate, haloperidol decanoate) and SGA LAI (ie, risperidone microspheres, risperidone subcutaneous, aripiprazole monohydrate, aripiprazole lauroxil, olanzapine pamoate, paliperidone palmitate 1-month and 3-month formulations). The health plans for this population included exclusive provider organization, HMO, and PPO. Patient demographics (ie, age, sex, race or ethnicity) and health plan were obtained at index date. Age was classified into 5 levels (ie, 18-24, 25-34, 35-44, 45-54,

TABLE: Merative MarketScan Multi-State Medicaid Database (2016-2020) long-acting injectable antipsychotic use

	Sample Size Total	White	Black	Hispanic	Other
First-generation antipsychotic					
Fluphenazine decanoate	1782	706	1007	42	27
Haloperidol decanoate	6686	2532	3924	105	125
FGA total	8468 (22%)	3238	4931	147	152
Second-generation antipsychotic					
Risperidone microsphere (2 week)	3099	1413	1523	80	83
Risperidone subcutaneous (4 week)	78	40	36	1	1
Aripiprazole lauroxil	2111	1197	811	47	56
Aripiprazole monohydrate	5285	2627	2364	145	149
Paliperidone palmitate (1 month)	17 423	8560	8057	402	404
Paliperidone palmitate (3 month)	1170	673	438	37	22
Olanzapine pamoate	78	34	37	1	6
SGA total	29 244 (78%)	14 544	13 266	713	721
Total	37 712	17 782	18 197	860	873

FGA = first-generation antipsychotic; SGA = second-generation antipsychotic.

55-64), and sex classified as male or female. Race or ethnicity was defined as White, Black, Hispanic, or other.

#### **Statistical Analysis**

Descriptive statistics were used to determine demographic characteristics across our cohorts. Cochran-Mantel-Haenszel tests and odds ratio estimators (95% CI; P < .05) were used to investigate conditional association between race or ethnicity (ie, White, Black, Hispanic, other) and generation of LAI antipsychotic (ie, first, second), while controlling for age, sex, health plan, and the year the medication was first prescribed. Kaplan-Meier survival curves were examined, and stratified log-rank tests were conducted to compare the time until discontinuation distributions across racial or ethnic groups and LAI antipsychotics (ie, generation, individual).

# **Results**

A total of 42 922 patients taking a LAI antipsychotic met the initial selection criteria in the MarketScan Medicaid Database. After exclusion of patients without listed race or ethnicity (n = 5199) and health plan (n = 11) there were 37 712 patients in the final analysis. From these, 22% (n = 8468) received an FGA, and 78% (n = 29 244) received an SGA. The mean age was 39.4  $\pm$  12.74 with 62% male. The racial and ethnic distribution included ~47% White (n = 17 782), ~48% Black (n = 18 197), ~2% Hispanic (n = 860), and ~2% other (n = 873). There were no significant differences between age, sex, and health plans and the generation (ie, first, second) of LAI antipsychotics. The most commonly used LAI antipsychotics included paliperidone palmitate (1 month), haloperidol decanoate, and

aripiprazole monohydrate (Table). Blacks were more likely to receive a FGA LAI (as opposed to a SGA) than Whites (OR: 1.64, 95% CI: [1.56, 1.73], Hispanics (OR: 1.46, 95% CI: [1.21, 1.75]), and others (OR: 1.44, 95% CI: [1.20, 1.73]). Aside from fluphenazine decanoate showing earlier discontinuation rates for Whites over Blacks (P = .02), no significant differences in discontinuation across race or ethnicity were found (Figures 1 through 3).

# **Discussion**

Even though there were no significant differences in SGA LAI discontinuation rates between Blacks and other racial or ethnic groups, Blacks received an SGA LAI significantly less often than any other group. Further exploration is needed to determine the basis of a racial disparity in access to SGA LAI antipsychotics (eg, prescriber bias, patient preference). However, in the absence of a clinically justifiable basis for different prescription practices by race for these medications, reducing or eliminating the racial disparity should be a psychiatric health care goal to achieve better health outcomes for black patients.

Barriers may exist when transitioning from oral to LAI antipsychotic regimen. Despite the potential advantages LAI antipsychotics offer, it is currently unknown if transitioning from oral to LAI antipsychotics are similar across diverse populations. For example, studies focusing on adherence and cost savings of LAI antipsychotic use demonstrate benefits.<sup>23</sup> However, there is limited discussion regarding differences between race or ethnicity. Older studies suggest Blacks were more likely to receive LAI antipsychotics compared with Whites.<sup>24-26</sup> Interestingly, the data are from approximately 30 years ago and before SGA

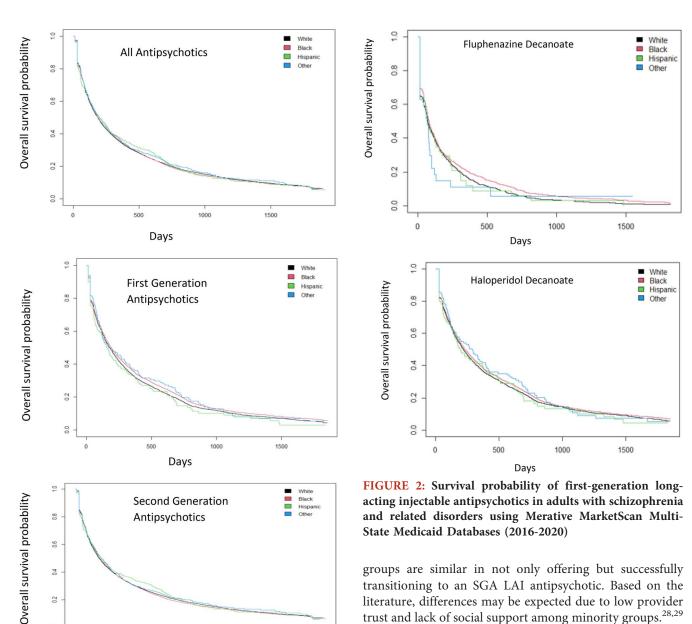


FIGURE 1: Survival probability of long-acting injectable antipsychotics (all and by generation) in adults with schizophrenia and related disorders using Merative Market-Scan Multi-State Medicaid Databases (2016-2020)

Days

1500

0.2

0.0

LAI were readily available. This current study suggests that despite the introduction of SGA LAI in the market, Blacks continue to more frequently receive FGA LAI than any other group even when controlling for health plan.

While FGAs and SGAs serve as first-line agents, data suggest SGA possibly offer better tolerability.<sup>27</sup> Nevertheless, how often minority populations are offered to transition to SGA LAI treatment has not been clearly elucidated. It is also unknown if rates between ethnic groups are similar in not only offering but successfully transitioning to an SGA LAI antipsychotic. Based on the literature, differences may be expected due to low provider trust and lack of social support among minority groups. 28,29

Another barrier associated with differences in use could be prescriber bias. Data suggest minority populations have poorer experiences than Whites when discussing prescribed medications.<sup>30</sup> The transition to any LAI antipsychotic must be accompanied with an open discussion with the patient regarding stigma, preferences, and potential benefits over oral antipsychotics (eg, adherence, less side effects).<sup>31</sup> Additionally, there needs to be better communication with prescribers. For example, clinicians report using LAI antipsychotics in less than 10% of their patients and have not discussed the use with approximately 66%.32 However, there is hope. Data show while only 33% of initial LAI antipsychotic medication recommendations were accepted by patients, the rate increased to more than 95% after a post-visit interview that provided a tailored approach to patient's ambivalence or concerns (eg, discuss benefits vs injection procedure, patient positive experience vs opposition).<sup>33</sup>

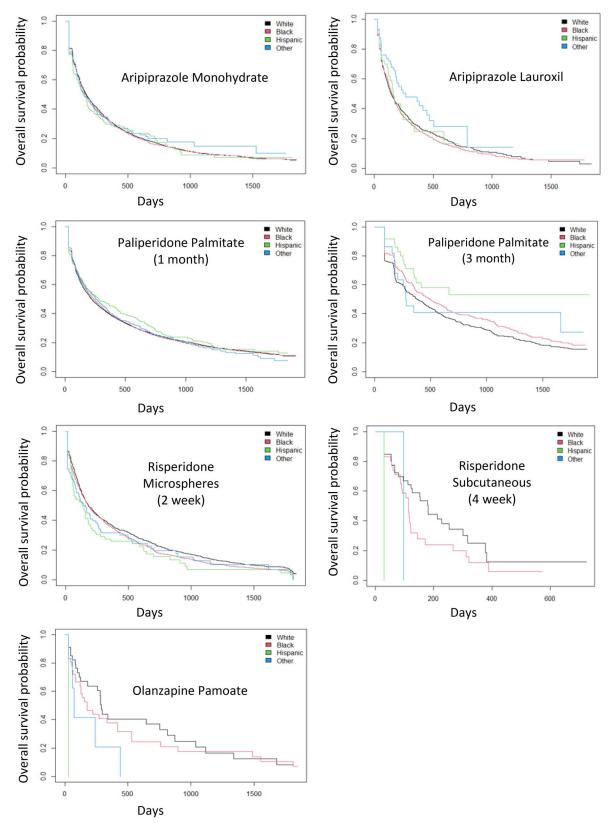


FIGURE 3: Survival probability of second-generation long-acting injectable antipsychotics in adults with schizophrenia and related disorders using Merative MarketScan Multi-State Medicaid Databases (2016-2020)

Approaches to improve the shared decision making process among minority groups have been described in the literature.34 A recent approach used among minority groups included the DECIDE interventions, which focus on deciding the problem, exploring questions, using closed and open ended follow-up questions, identifying the who, why, and how of the problem, directing questions to your health care professional, and enjoying a shared solution.<sup>35</sup> Results of this study suggest that while the DECIDE model is promising, prescribers may need improved coaching to optimize results in minority populations. These may include audiotaped or videotaped sessions before and after coaching to improve their metacognitive skills and provide insight of how they can improve their communication with patients. While such approaches to engage patients (eg, to transition to LAI antipsychotics) seem promising, none have focused on LAI antipsychotics in minority populations. Tailoring of counseling sessions specific to the needs of the patient have been defined as precision counseling in the literature.<sup>36</sup> Precision counseling is the approach for disease management that evaluates social factors (eg, stigma), environmental stressors, treatment side effects, and lifestyle affecting medication adherence for each patient. Therefore, future studies evaluating and tailoring these approaches to minority populations with LAI antipsychotics may be warranted.

Of note, the largest differences noted in our study was with fluphenazine decanoate, which Whites discontinued faster than Blacks. In this cohort, we hypothesized that Whites may be discontinuing at a higher rate because of switching to an SGA LAI at a higher rate than Blacks. A post-hoc analysis comparing agent switched to in this cohort showed this was not the case. Additionally, our study showed different results with paliperidone palmitate than a previous study. One study indicated Hispanics had greater adherence to paliperidone palmitate (1-month LAI) compared with other antipsychotics.<sup>37</sup> However, the study mixed oral and other LAI antipsychotics into one group, thereby limiting the results as oral and LAI agents may carry different adherence rates.

#### Limitations

Even though this study used a large, comprehensive data source, there are some limitations. Coding errors (eg, omission, commission) and reporting bias may affect the results. Diagnoses were obtained from billing codes and therefore cannot be validated nor severity of schizophrenia identified. Discontinuation was determined based on the administration schedule recommended in each LAI antipsychotic prescribing information (ie, package insert); therefore, adherence may have been misclassified if prescribing patterns differ from these guidelines. We do not know the reasons for discontinuation of treatment because of the retrospective nature of the data. These

reasons may differ between population groups and between LAI antipsychotics. Although we controlled for demographic factors it is possible that other confounding factors may bias the data. Finally, some LAI antipsychotics (ie, olanzapine pamoate, risperidone 4-week) have smaller sample sizes (<100) relative to other agents to draw significant conclusions within the specific medication. However, these data are the first to be reported and suggest future studies focus on these agents as well.

# **Conclusion**

Overall, it appears using a LAI antipsychotic in minority populations may mitigate the gap of adherence between racial and ethnic groups to oral antipsychotic treatment and promote better health outcomes. The results from this study demonstrate Blacks received FGA LAI more often than any other racial or ethnic group. Therefore, if discontinuation rates are similar between SGA LAI, prescribers may need to be aware that these agents are a viable option for Blacks. Further education may be warranted to providers on bridging the gap in prescribing rates. However, it is also important to understand the critical barriers to developing a strong health care providerpatient relationship focused on trust and openness. The ability to provide precision counseling may optimize the ability to transition from oral to LAI formulations especially among minority populations.

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