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The Effect of Race-Ethnicity on Clozapine Outcomes among Medicaid Beneficiaries with Schizophrenia

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Abstract

Objective—Effectiveness trials have confirmed the superiority of clozapine in the treatment of schizophrenia, but little is known about whether the drug's superiority holds across racial-ethnic groups. This study examined the effect of race-ethnicity on the effectiveness of clozapine relative to other antipsychotics among patients in maintenance antipsychotic treatment.

Methods—Black, Latino, and white Florida Medicaid beneficiaries with schizophrenia receiving maintenance treatment with clozapine or other antipsychotic medications during 7/1/00–6/30/05 were identified. Cox proportional hazard regression models were used to estimate associations of clozapine, race-ethnicity, and their interaction, with time to discontinuation for any cause, our primary measure of effectiveness.

Results—The study cohort included 20,122 episodes of treatment with clozapine (3.7%) and other antipsychotics (96.3%), with 23% black and 36% Latino. Unadjusted analyses suggested that Latinos continue on clozapine longer than whites, while they and blacks discontinue other antipsychotics sooner than whites. Adjusted analyses using 749 propensity score matched sets of clozapine and other antipsychotic users indicated that risk of discontinuation was lower for clozapine users (RR = .45, 95% CI = .39 – .52), an effect that was *not* moderated by race-ethnicity. Times to discontinuation were longer for clozapine users. Overall risk of antipsychotic discontinuation was higher for blacks (RR = 1.56, CI = 1.27 – 1.91), and Latinos (RR = 1.23, CI = 1.02 – 1.48).

Conclusions—This study confirmed clozapine's superior effectiveness and did not find evidence that race-ethnicity modifies this effect. These findings heighten the need for efforts to increase clozapine use, particularly among minority groups.

Introduction

The atypical antipsychotic clozapine is the only antipsychotic drug with Food and Drug Administration (FDA) approval for the management of treatment-resistant symptoms and recurrent suicidal behavior, two severe complications of schizophrenia (1, 2). Furthermore, among all antipsychotics, clozapine has the lowest rate of suicide-related and all-cause mortality (3, 4). Despite these advantages, clozapine is underused in the routine care of U.S.

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patients with schizophrenia (5–7). Consistent with a body of evidence that suggests that patterns of schizophrenia care are influenced by patients' race-ethnicity (7–9), studies have shown that use of clozapine is lower among minority than white patients (10).

While clozapine's superior efficacy has been long established (11, 12), evidence on its superior effectiveness had lagged behind until the publicly-funded *Clinical Antipsychotic Trials of Intervention Effectiveness* (CATIE) study was published in the mid-2000's (13). The study's primary measure of effectiveness was time to discontinuation for any cause, "a synthesis of clinician and patient judgments" on a drug's efficacy and tolerability (14). Use of time to discontinuation for any cause as a measure of effectiveness is supported by evidence that has shown that longer time to discontinuation is associated with greater clinical and functional improvement (15, 16). Unfortunately, like efficacy researchers before them, CATIE researchers did not report on the effect of race-ethnicity on the effectiveness of clozapine relative to the trial's other antipsychotics. We know of two inpatient studies that assessed whether black and white patients differ in their response to clozapine, one showing no differences and the other showing mixed findings (17, 18), and are unaware of studies that have assessed the effect of Latino ethnicity.

The purpose of this study was to fill this evidentiary gap. Using time to discontinuation for any cause as our measure of effectiveness, we examined the effect of race-ethnicity on the effectiveness of clozapine relative to other antipsychotics among patients in maintenance antipsychotic treatment. The paucity of evidence on racial-ethnic differences in antipsychotic effectiveness precluded us from formulating hypotheses.

Methods

Data Sources and Study Population

We used enrollment files, medical, and pharmacy claims from the Florida Medicaid program for fiscal years 2001–2005 (July 1 2000 through June 30 2005) to construct our study cohort. Cohort members were adults aged 18–64 years who had at least two claims with a diagnosis of schizophrenia (ICD-9 diagnostic codes 295.xx) recorded on two different service dates during each fiscal year (FY), and who had filled at least one prescription for antipsychotic drugs during the study period.

We selected patients receiving maintenance antipsychotic treatment with clozapine or any of seven antipsychotic drugs (olanzapine, quetiapine, risperidone, ziprasidone, aripiprazole, haloperidol, or perphenazine). We focused on patients in maintenance antipsychotic treatment because drug discontinuation during maintenance-phase treatment is less likely to be influenced by intolerability and patient factors associated with adherence behavior compared to acute-phase treatment. We defined maintenance treatment based on the observation of prescriptions filled for any of the eight study drugs *beyond* an initial 3-month period representing acute-phase treatment. Episodes were excluded if during the 3-month period preceding the date when the antipsychotic drug was first filled, the beneficiary had less than 3 months of continuous fee for service enrollment, or any Health Maintenance Organization (HMO) or Medicare coverage. When more than one qualifying maintenance antipsychotic treatment episode was observed per beneficiary, we selected the first episode. Episodes that were still ongoing by the end of the study period were observed for one additional year.

Outcome Variables

Our primary outcome variable was time to discontinuation for any cause among beneficiaries receiving maintenance treatment with clozapine versus other antipsychotics. We operationalized discontinuation as breaks in prescription fills of 45 or more days. We

selected this interval to allow for dose reductions or short-lived treatment interruptions due to refill delays stemming from less than optimal adherence or other treatment barriers commonly encountered by this population.⁽⁷⁾ We sought to capture a broader set of poor outcomes through a secondary outcome variable that measured time to *either* antipsychotic discontinuation *or* hospitalization for schizophrenia.

Explanatory Variables

Our main explanatory variables were **antipsychotic drug treatment, race-ethnicity, and their interaction**. Antipsychotic drug treatment categories were clozapine versus a group of seven antipsychotic drugs (other antipsychotics). The group of other antipsychotics comprised all then-available atypical antipsychotics (olanzapine, quetiapine, risperidone, ziprasidone, and aripiprazole), as well as two conventional antipsychotics (haloperidol, perphenazine). We included haloperidol because of its dominance in the conventional market and its prominent role in antipsychotic outcomes research, and included perphenazine because it was the conventional drug included in the CATIE trial. Because fewer studies have assessed the comparative effectiveness of clozapine versus other atypicals, we conducted additional analyses that only compared clozapine to the atypicals in the “other antipsychotic” group.

Race-ethnicity was defined as black, Latino, and non-Latino white, and it was assessed at the date when the study drug was first filled. The Florida Medicaid program uses a racial classification that describes beneficiaries as white, black, Hispanic, Oriental, American Indian, or “Other.” We excluded the small proportion of people (less than 1%) otherwise meeting inclusion criteria who during the study period were classified as Oriental or American Indian. While the percent of people who were classified as black or white varied little during the study period, the percent of people classified as “Other” and Hispanic varied dramatically due to changes in data recording. An analysis of beneficiaries present in the data between FYs 2005 and 2006 showed that 92% of persons classified as Hispanic in FY 2006 had been classified as “Other” in FY 2005. Conversely, analyses of individuals classified as “Other” in FY 2005 who were also observed in FY 2006 revealed that 71% were reclassified as Hispanic in FY 2006. Most of the remaining 29% remained “Other,” suggesting that they too were Hispanic. Because a majority of those classified as “Other” during our study period were classified as Hispanic in previous or subsequent years, we reclassified the “Other” group as “Ever Hispanic.” As a result of this decision, we have some minor misclassification in our racial-ethnic groups. Individuals classified as Hispanic or “Ever Hispanic” are referred to as Latinos.

Other explanatory variables included several need-related variables that may impact the decision to use clozapine versus other antipsychotics. These were age (continuous); sex; and four measures of illness severity (psychiatric comorbidity, substance use disorder comorbidity, intensity of use of inpatient services for schizophrenia, and Social Security Insurance [SSI] status, all further described below). Because patients’ physical health status and geographic location may influence prescriber decision-making, additional explanatory variables were metabolic comorbidity and other medical comorbidity, and a geographic variable indicating 11 multi-county areas used by the Florida Medicaid program to administer benefits (<http://www.fdhc.state.fl.us/Medicaid/Areas>).

Age, sex, and area of residence were assessed at the date when the antipsychotic drug was first filled. The comorbidity, intensity of inpatient use, and SSI status measures were constructed with data observed during the 3-month period preceding the date when the antipsychotic drug was first filled (i.e., baseline period). The binary comorbidity measures required the observation of 1 or more claims with selected ICD-9 diagnoses. These were major depression, dysthymia, and anxiety disorders (**psychiatric comorbidity**); abuse/

dependence of alcohol or drugs other than tobacco (**substance use disorder comorbidity**); diabetes, dyslipidemias, and obesity (**metabolic comorbidity**); and all chronic medical disorders (**other medical comorbidity**). Intensity of inpatient service use was defined as the total number of **inpatient days** for schizophrenia. **SSI** status, a severity indicator because SSI eligibility suggests a more disabling illness, was operationalized as SSI, Aid for Families with Dependent Children [AFDC], or Other.

To account for possible secular trends, we also created a categorical variable indicating the **quarter** in which the antipsychotic drug was first filled.

Statistical Analysis

Propensity Score Models for Clozapine Use—We used propensity score matching to address potential selection bias in medications received (19). We modeled the log-odds of receiving clozapine versus other antipsychotics as a function of the explanatory variables (age, sex, four comorbidity variables, intensity of inpatient use, and SSI status, area, and quarter). Our propensity score models were estimated separately within each race-ethnicity group. We estimated log-odds of receiving clozapine versus other antipsychotics and compared probabilities between patients who received clozapine and those who received other antipsychotics. We evaluated the comparability of clozapine-treated persons and persons treated with other antipsychotic drugs by assessing the extent to which they overlapped on each variable. Adequate comparability was a priori defined as standardized differences between the groups of 10% or smaller (20). For each clozapine-treated person, we identified two similar persons treated with other antipsychotics of the same race-ethnicity. This resulted in matched sets containing 1 clozapine-treated person and 2 persons treated with other antipsychotics for each racial-ethnic group. Because we a-priori believed that use of clozapine as well as race-ethnicity distributions might vary widely geographically, and medication discontinuation rates might vary over time, we used fine balancing (21) to exactly match clozapine and other antipsychotic users on *when* they had their index prescription (quarter) and *where* they lived (area) at that time.

For each set, we assessed number of days from the start of the antipsychotic episode to four mutually exclusive outcomes, whichever was observed first: antipsychotic discontinuation as defined above; hospitalization for schizophrenia; withdrawal (defined as any discontinuity in Medicaid enrollment or more than one month of HMO or Medicare coverage); and administrative censoring (defined as ongoing use of the study drug by June 1 2006, the end of the additional period of observation).

Discontinuation Models—We first estimated Kaplan-Meier curves of time to antipsychotic discontinuation and considered the other three outcomes (hospitalization for schizophrenia, withdrawal, and administrative censoring) as censored events. We also estimated Kaplan-Meier curves of time to antipsychotic discontinuation or to hospitalization for schizophrenia, and considered withdrawal and administrative censoring as censored events. Final model estimates were based on Cox proportional hazard regression models that accounted for the matched sets and included a clozapine dummy variable, a set of race-ethnicity dummy variables, and a set of interaction terms between antipsychotic drug treatment and race-ethnicity. We assessed differences in risk of discontinuation among the groups (i.e., the proportionality assumption) through graphical summaries of Schoenfeld residuals plotted against log(time), chi-square tests for each covariate (drug treatment, race-ethnicity), and a chi-square global test. Statistical models were estimated using the S-PLUS software system (S-PLUS 8.0, Software International Incorporated, 2007). Statistical significance was set at $p = .05$. We report comparisons in the form of relative risks (RR) and 95% confidence intervals (CI).

Our study was granted exempt status by the University of Pittsburgh IRB because we used data free of personal identifiers (study was initiated when first author was at University of Pittsburgh).

RESULTS

Characteristics of Study Cohort

Over the entire study period, 41,262 persons met diagnostic, age, and racial-ethnic criteria, and also filled an antipsychotic prescription. Most of them filled any of the eight study drugs (99%, N= 40,725). Further application of our inclusion and exclusion criteria reduced the size of the study cohort to an analytic sample of 20,122 persons, each contributing one episode of maintenance antipsychotic treatment (see Flowchart in online Appendix). The sample included 23% black (N= 4,623), 36% Latino (N= 7,206), and 41% white (N= 8,293) persons (Table 1). Mean age was 42 years, 52% (N= 10,414) were female, and 87% (N= 17,443) had SSI as their eligibility mechanism. Comorbidity rates ranged between 5% (N= 1,027) for substance use disorder comorbidity, and 29% (N= 5,816) for other medical comorbidity. A majority of episodes were observed in area 11, which includes Miami Dade and Monroe counties (41%, N= 8,199), and in the first six quarters of the study period (50%, N= 10,125). Clozapine was used in 3.7% of person-episodes (N= 749), and at lower rates by blacks (2.3%, N= 107) and Latinos (2.1%, N= 149) than whites (5.9%, N= 493). Among the other 19,373 episodes, the index antipsychotic drug was a non-clozapine atypical in 87% of the cases (N= 16,903), with risperidone (28%, N= 5,398) and olanzapine (35%, N= 6,692) the most frequently observed drugs. Based on standardized differences, clozapine users differed from users of other antipsychotic on most of the variables included in our multivariate models. With few exceptions, these differences were also observed within each racial-ethnic group.

Unadjusted Analyses

The overall rate of discontinuation was 72.7% (N= 14,634). Mean and median times to discontinuation were 794 days and 548 days, respectively. Clozapine users had lower rates of discontinuation than other antipsychotic users regardless of race-ethnicity. Latinos had lower rates of discontinuation from clozapine than blacks and whites, but the differences were not statistically significant. Whites had lower rates of discontinuation from other antipsychotics than blacks and Latinos. Times to discontinuation results mirrored the rates results (Table 2).

Adjusted Analyses

We created 749 matched sets containing all clozapine users (N= 749) and twice as many other antipsychotic users (N= 1,498). Our propensity score model generated well balanced groups, as evidenced by the fact that with just one exception, standardized differences for all variables were smaller than 10%. The exception was time and only for the 20th quarter (standardized difference = 10.4%).

Adjusted analyses confirmed most of the unadjusted results (Table 3 and Figure). Clozapine users had a lower risk of discontinuation than users of other antipsychotics (RR = .45, CI = .39 – .52). This effect was not moderated by race-ethnicity. Overall risk of discontinuation, however, was higher for blacks than whites (RR = 1.56, CI = 1.27 – 1.91), and Latinos than whites (RR = 1.23, CI = 1.02 – 1.48). While assessment of the proportionality assumption suggested some non-constant hazards (global chi-square = 953; p = .021), with blacks having a slightly higher overall risk of discontinuation earlier than whites (chi-square = 6.06, p = .014), the (log) hazard ratio was small (<1.0). In keeping with the Cox model results,

clozapine users had longer times to discontinuation than users of other antipsychotics (Table 4 and Figure).

Results did not change when we examined time to discontinuation or hospitalization, or when clozapine was compared only to atypicals (Figures 2 and 3 in online Appendix).

Discussion

In this 5-year study of a Medicaid cohort receiving maintenance treatment for schizophrenia, we did not observe any modifying effect of race-ethnicity on the effectiveness of clozapine relative to other antipsychotics. These findings did not change when we assessed risk of discontinuation or hospitalization, or when the comparator group only included non-clozapine atypicals. This is an important set of results given the paucity of evidence on the effect of race-ethnicity on clozapine outcomes, and on whether comparative effectiveness research findings can be generalized to racial-ethnic minorities.

Our study replicates the findings of the CATIE study, although for a Medicaid population comprised only of people in maintenance antipsychotic treatment, and expands on those findings by evaluating the influence of race-ethnicity on outcomes of clozapine and other antipsychotic treatment. We know of only two studies that have assessed whether clozapine outcomes vary by race, and know of no study that has assessed the effect of Latino ethnicity. An RCT conducted among treatment-refractory hospitalized veterans found that black race was not predictive of differential response to clozapine versus haloperidol, as assessed through standardized assessments and hospital days (18). A study that used a longitudinal statewide dataset comprising all inpatient episodes where clozapine had been used found that blacks experienced more robust early improvements on some but not all the standardized scales used to assess response (17).

Time to discontinuation for any cause is influenced by the drug's efficacy, tolerability, patient adherence behavior, and also prescriber behavior (22). It is therefore notable that we did not find racial differences in clozapine's effectiveness relative to other antipsychotics given evidence that clozapine-treated blacks receive lower doses (17), experience more weight gain (23), and have a higher likelihood of having clozapine unnecessarily discontinued by their physicians (17, 24, 25).

Our finding that blacks and Latinos had higher risk of discontinuing maintenance antipsychotic treatment than whites is in keeping with a study of California Medicaid beneficiaries that found that black race was associated with time to antipsychotic discontinuation (three non-clozapine atypicals and a conventional drug) (26). What may underlie this result? Although there may be racial-ethnic differences in antipsychotic efficacy (27), there is no RCT evidence to support this possibility. There is evidence that racial-ethnic minorities may be more prone to certain side effects (28), a phenomenon that may be driven by inadequate drug choice or excessive dosing (29). Lastly, some (e.g., (30–33) but not all (34) adherence studies have found that blacks and Latinos are more likely to exhibit poor adherence to antipsychotics.

Consistent with other evidence, a small fraction of patients in our study were on maintenance treatment with clozapine. Although all major schizophrenia guidelines call for the use of clozapine to manage severe presentations (35), rates of any use of clozapine remain low in the U.S. (5–7). Although it has been posited that underuse stems from patients' aversion to needles, psychiatrists' safety concerns, or the higher burden associated with clozapine prescribing, these factors are unlikely to fully explain the underuse phenomenon (36, 37). Multiple studies have found that the likelihood of any use of clozapine is even lower for blacks (7, 17) and Latinos (10, 38). The factors driving the lower

use of clozapine among racial-ethnic minorities are not well understood. It has been suggested that lower use of clozapine among blacks may stem from providers' expectation that blacks will have lower response rates, their perception of blacks as less treatment-adherent, and their unfounded concern that agranulocytosis may be more likely among blacks (24).

Our study needs to be considered in light of some limitations. First, because of the non-experimental nature of our study design, there may be unmeasured differences between users of clozapine and users of other antipsychotics. In particular, we were unable to select patients based on their treatment response status, an important confounder. However, this limitation may have worked to attenuate our findings by comparing clozapine-treated persons, all of them very likely to be treatment non-responders, to persons with higher degrees of treatment responsiveness receiving treatment with other antipsychotics. Second, unlike CATIE researchers, we were unable to differentiate between discontinuation due to lack of efficacy, intolerability, and patient factors associated with adherence behavior. However, we think that by assessing discontinuation among people in maintenance treatment, thus selecting a population that had already shed many of those most likely to discontinue because of intolerability or proclivity to not adhere to treatment, our *discontinuation for any cause* results are closest to discontinuation due to lack of efficacy. Additionally, we evaluated incidence of concurrent antipsychotic polypharmacy because polypharmacy can lead to discontinuation of the entire drug regimen due to higher incidence of side-effects. Our analyses showed that rates of polypharmacy were similar for clozapine and other antipsychotic users for all racial-ethnic groups combined and for whites (Results not shown). Although for blacks and Latinos, rates of polypharmacy were higher for clozapine users than for users of other antipsychotics, if at all impactful, these differences may have worked to attenuate our findings by increasing the likelihood of discontinuing clozapine among minority groups. Third, we may have been under-powered to detect the racial-ethnic differences in the comparative effectiveness of clozapine and other antipsychotics suggested by the unadjusted analyses. Last, the generalizability of our study is limited by the fact that Florida differs from other state Medicaid programs because of its racial-ethnic diversity and restrictive eligibility requirements.

Conclusions

We have found that race-ethnicity does not modify the superior effectiveness of clozapine relative to other antipsychotics in a population of Medicaid beneficiaries with schizophrenia. We have thus confirmed and expanded CATIE's findings, heightening the need for efforts aimed at understanding factors underlying the underuse of clozapine and at increasing its use, particularly among minority groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Clozapine versus Other Antipsychotics (n = 749 matched sets)

Figure.
Survival Curve for Risk of Discontinuation, by Antipsychotic Drug Treatment and Race-ethnicity

Table 1

Cohort Characteristics

Variable #	ALL (N= 20,122)		Clozapine (n= 749)		Other Antipsychotics (N= 19,373)		Standardized difference*
	N	% [^]	N	% [^]	N	% [^]	
Black	4,623	23.0	107	14.3	4,516	23.3	-23.3
Latino	7,206	35.8	149	19.9	7,057	36.4	-37.4
White	8,293	41.0	493	65.8	7,800	40.3	53.0
Age (mean, SD)	42.4	11.1	38.7	10.8	42.6	11.2	-.4
Female	10,414	51.8	325	43.4	10,089	52.1	17.5
Inpatient days (mean, SD)	.71	3.7	.79	3.9	.72	3.7	.02
Psychiatric comorbidity	3,854	19.2	53	7.1	3,801	19.6	-37.5
Substance use disorder comorbidity	1,027	5.1	20	2.7	1,007	5.2	-13.0
Metabolic comorbidity	2,706	13.5	39	5.2	2,667	13.8	-29.5
Other medical comorbidity	5,816	28.9	75	10.0	5,741	29.6	-37.5
SSI status	17,443	86.7	632	84.4	16,811	86.8	-6.8

Variable	ALL (N= 20,122)		Clozapine (n= 749)		Other Antipsychotics (N= 19,373)		Standardized difference**
	N	% [*]	N	% [*]	N	% [*]	
Geographic Area ^{***1}	659	3.3	29	3.9	630	3.3	3.4
2	764	3.8	18	2.4	746	3.9	-8.3
3	1,413	7.0	36	4.8	1,377	7.1	-9.7
4	1,815	9.0	118	15.8	1,697	8.8	21.4
5	1,519	7.5	101	13.5	1,418	7.3	20.3
6	942	4.7	47	6.3	895	4.6	7.3
7	1,290	6.4	77	10.3	1,213	6.3	14.6
8	635	3.2	58	7.7	577	3.0	21.3
9	1,131	5.6	64	8.5	1,067	5.5	11.9
10	1,755	8.7	71	9.5	1,684	8.7	2.7
11	8,199	40.7	130	17.4	8,069	41.7	-55.3

Variable	ALL (N= 20,122)		Clozapine (n= 749)		Other Antipsychotics (N= 19,373)		Standardized difference**
	N	%*	N	%*	N	%*	
Quarter 1 (Jul-Sep '00)	5,188	25.8	475	63.4	4,713	24.3	85.7
2 (Oct-Dec '00)	1,351	6.7	39	5.2	1,312	6.8	-6.6
3 (Jan-Mar '01)	1,055	5.2	38	5.1	1,017	5.3	-.8
4 (Apr-Jun '01)	828	4.1	24	3.2	804	4.2	-5.0

Variable	ALL (N= 20,122)		Clozapine (n= 749)		Other Antipsychotics (N= 19,373)		Standardized difference**
	N	%*	N	%*	N	%*	
Quarter 5 (Jul-Sep '01)	919	4.6	12	1.6	907	4.7	-17.7
6 (Oct-Dec '01)	784	3.9	13	1.7	771	4.0	-13.5
7 (Jan-Mar '02)	771	3.8	14	1.9	757	3.9	-12.2
8 (Apr-Jun '02)	765	3.8	13	1.7	752	3.9	-13.0
9 (Jul-Sep '02)	765	3.8	21	1.9	744	3.8	-5.8
10 (Oct-Dec '02)	748	3.7	8	1.1	740	3.8	-17.9
11 (Jan-Mar '03)	862	4.3	11	1.5	850	4.4	-17.4
12 (Apr-Jun '03)	785	3.9	12	1.6	773	4.0	-14.5
13 (Jul-Sep '03)	752	3.7	16	2.1	736	3.8	-9.8
14 (Oct-Dec '03)	690	3.4	12	1.6	678	3.5	-12.1
15 (Jan-Mar '04)	721	3.6	10	1.3	711	3.7	-15.0
16 (Apr-Jun '04)	646	3.2	6	.8	640	3.3	-17.7
17 (Jul-Sep '04)	679	3.4	8	1.1	671	3.5	-16.1
18 (Oct-Dec '04)	632	3.1	8	1.1	624	3.2	-14.9
19 (Jan-Mar '05)	649	3.2	5	.7	644	3.3	-19.1
20 (Apr-Jun '05)	533	2.6	4	.5	529	2.7	-17.4

Inpatient days for schizophrenia, comorbidity variables, and SSI status were assessed over the 3-month period preceding the first filled antipsychotic prescription

^a Column percents

** Standardized differences for [clozapine versus other antipsychotics] comparisons: differences larger than 10% are statistically significant (positive if mean/rate is higher for clozapine users)

* Column percents

** Differences larger than 10% are statistically significant
 *** Counties shown in online Appendix
 * Column percents
 ** Differences larger than 10% are statistically significant

Unadjusted Effectiveness Results: Median Days and Rates of Discontinuation by Antipsychotic Treatment, for All and by Race-Ethnicity (N= 20,122)

Table 2

Antipsychotic Treatment ⁰⁰¹ ^	Discontinuation for Any Cause				P-Value for Rates
	ALL (N= 749)	Blacks (N= 107)	Latinos (N= 149)	Whites (N= 493)	
Clozapine					
Median days to discontinuation	740	646	789	736	
Rate (%)	53.3	55.1	48.3	54.4	.397
Other antipsychotics					
	ALL (N= 19,373)	Blacks (N= 4,516)	Latinos (N= 7,057)	Whites (N= 7,800)	
Median days to discontinuation	282	248	281	304	
Rate (%)	73.5	75.5	74.0	71.9	<.001 *

^ All clozapine vs. other antipsychotic rate comparisons are significant (<.001)

* Per Tukey's test, blacks-white and Latino-white differences were statistically significant at the .05 level

Table 3

Effectiveness Results ^{*}(Risk of Discontinuation for Any Cause), by Antipsychotic Drug Treatment and Race-Ethnicity, 749 matched sets

Model Covariate	Discontinuation for Any Cause	
	Relative Risk	95% CI
Main analyses		
Antipsychotic Treatment ^{**}		
Clozapine	.45	.39 – .52
Other Antipsychotics	1.00	–
Race-Ethnicity ^{**}		
Blacks	1.56	1.27 – 1.91
Latinos	1.23	1.02 – 1.48
Whites	1.00	–
Interactions (Antipsychotic Drug Treatment [Clozapine] and Race-Ethnicity)		
Blacks	.77	.53 – 1.12
Latinos	.83	.59 – 1.16
Whites	1.00	–

^{*} Adjusted through matching by age, sex, inpatient days for schizophrenia, four measures of comorbidity (psychiatric, substance use disorder, metabolic, and other medical comorbidity), SSI status, geographic area, and quarter

^{**} Estimates generated by the model without interaction terms.

Table 4

Adjusted Effectiveness Results* (Days to Discontinuation for Any Cause), by Antipsychotic Drug Treatment and Race-Ethnicity, 749 matched sets

Racial-Ethnic Group	N	Days to Discontinuation for Any Cause	
		Median Days to Outcome	95% CI
Clozapine			
Blacks	107	1422	961– 1840
Latinos	149	1659	1299 – 2052
Whites	493	1228	1070 – 1593
Other Antipsychotics			
Blacks	214	459	364 – 694
Latinos	298	566	426 – 754
Whites	986	639	584 – 701
Overall (All Antipsychotics Combined)			
Blacks	321	720	569 – 937
Latinos	447	895	754 – 1038
Whites	1479	812	742 – 883

* Adjusted through matching by age, sex, inpatient days for schizophrenia, four measures of comorbidity (psychiatric, substance use disorder, metabolic, and other medical comorbidity), SSI status, geographic area, and quarter; estimates generated by the model without interaction terms.