Evaluating Antipsychotic Adherence Patterns Among Medicaid-Enrolled Hospital-Discharged Patients With Schizophrenia

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BACKGROUND

- Schizophrenia patients typically require lifelong antipsychotic medication use to manage the condition and lower the risk of relapse.
- Given the chronic nature of schizophrenia, adherence to the prescribed antipsychotic regimen is important.
  - Several studies have reported an association between nonadherence to antipsychotic therapy and an increased likelihood of hospitalization among patients with schizophrenia.
- Hospitalization leads to significant burden on the health care system.
  - Hospital-discharged schizophrenia patients also face challenges transitioning to the community and are at an increased risk of rehospitalization.[1-3]
- Decreasing the risk of initial hospitalization may in turn reduce the risk of rehospitalization and the associated downstream costs, and thus, information on antipsychotic adherence patterns at various clinically relevant preadmission periods may help in the identification of the high-risk population.
- However, to the best of our knowlege, studies have not evaluated antipsychotic adherence patterns at various clinically relevant preadmission periods, which may help with designing interventions, specifically to target this high-risk population.

OBJECTIVE

- The objective of this study was to evaluate antipsychotic adherence patterns and health care costs across preadmission periods (182-121, 120-61, and 60-0 days and overall 6 months) and postdischarge periods (0-60, 61-120, and 121-182 days and overall 6 months) among schizophrenia patients.

METHODS

Study Design and Data Source

- Retrospective longitudinal cohort analysis of the MarketScan Multi-State Medicaid Database for the period January 1, 2004, to December 31, 2008.
- The database contains information on:
  - Patient characteristics, including demographic details (e.g., age, sex, health coverage, and race), eligibility information, service and provider type, diagnoses
  - Detailed information about hospitalizations, inpatient and outpatient physician services, prescription drug use, and associated costs.
- Data elements included in the database are recorded in accordance with the Health Insurance Portability and Accountability Act (HIPAA) definition for limited-use datasets.
- The conduct of this study was approved by the institutional review board at RTI International.

Study Cohort

The study cohort was selected using the following inclusion and exclusion criteria.

Inclusion Criteria

- Schizophrenia-related inpatient admission (i.e., primary diagnosis) between July 1, 2004, and December 31, 2007, and associated hospital discharge on or before December 31, 2007

- Continuous Medicaid enrollment during the preindex period, the index inpatient admission, and the postindex period
  - Index admission date: date of the first observed inpatient admission
  - Index discharge date: date of discharge associated with the index admission
  - Preindex period: 6-month period prior to the index admission
  - Postindex period: 6-month period following the index discharge date
- One or more outpatient or physician office visits, or two or more visits with primary schizophrenia diagnosis or prescription claims for first- or second-generation antipsychotic medications during the 6-month period prior to the index admission date or the 12-month period after the index discharge date

Exclusion Criteria

- Schizophrenia-related inpatient admissions (secondary diagnoses) during the 6-month period prior to the index admission date
- One or more claims with a primary diagnosis of bipolar or schizoaffective disorder, or two or more claims with a primary diagnosis of unipolar disorder during postdischarge period
- Aged 18 years or younger at the index admission date or aged 65 years or older at the follow-up end date
- Patients with dual eligibility (i.e., Medicaid and Medicare) and patients without mental health and substance abuse (MHSA) coverage.

Study Measures

Antipsychotic Adherence

- Adherence to antipsychotic medications (first and second generation) was assessed using the adherence measure proportion of days covered (PDC).
  - PDC = Total days of drug availability (days supply) in the period of evaluation ÷ (Number of days in the period of evaluation – Number of days hospitalized during the period of evaluation).
- The PDC method assesses drug availability for each day of the study period, rather than cumulative exposure as assessed in the commonly used medication possession ratio, and thus was deemed to be a more appropriate adherence metric for this study.
- Among patients with medical claims (i.e., physician office) for antipsychotic depot preparations (i.e., risperidone, fluphenazine, haloperidol), but without details on the days' supply, we used the following approved dosage duration as a proxy for the days' supply for the antipsychotic depot preparations:
  - Risperidone long-acting injection: 2 weeks
  - Haloperidol long-acting injection: 4 weeks
  - Fluphenazine long-acting injection: 4 weeks
- Patients with a PDC value of less than 0.8 (i.e., < 80% adherence) were classified as nonadherent, and patients with a PDC value of 0.8 or greater were classified as adherent.[4]
  - PDC was assessed for the preindex periods (i.e., 182-121, 120-61, and 60-0 days and overall 6 months) and postindex periods (i.e., 0-60, 61-120, and 121-182 days and overall 6 months).

Antipsychotic Depot Use

- We assessed depot antipsychotic use during each preindex and postindex period, and patients were classified "depot users" or "depot nonusers" based on presence or absence of a claim for depot antipsychotic (i.e., risperidone, fluphenazine, haloperidol) during each preindex and postindex period.

Health Care Utilization and Costs

- We ascertained all-cause and schizophrenia-related health care utilization and associated costs during the preindex and postindex periods.
- Medical claims with a primary diagnosis for schizophrenia or pharmacy claims for antipsychotics (first and second generation) were considered schizophrenia related.
- Health care costs were assessed for various care settings, including inpatient, outpatient, physician office, emergency department, pharmacy, and ancillary care.
  - Costs were adjusted to 2010 US dollars using the medical care component of the Consumer Price Index.

Other Study Measures

- We assessed patient characteristics, including age, sex, race, health plan type, basis of Medicaid eligibility, MHSA coverage, and index hospitalization discharge status.
- 6-month preindex period comorbidity burden was assessed using the Deyo-adapted Charlson Comorbidity Index score.

Statistical Analyses

- Unadjusted, descriptive statistics were generated for all analysis variables, which included frequency distributions for categorical variables and mean values, and standard deviations (SDs) for continuous variables.
- The study measures were stratified by indicators for preindex (182-121, 120-61, 60-0 days, overall 6 months) and postindex (0-60, 61-120, 121-182 days, overall 6 months) study periods.
- Differences in health care costs during the 6-month preindex period and 6-month postindex period were assessed using paired t-tests.
- No adjustment was made for multiplicity.

RESULTS

Patient Characteristics

- 2,541 hospital-discharged schizophrenia patients met all study inclusion/exclusion criteria, of which over 88% were "discharged to home self-care."
- Over 56% of the selected patients were male, and approximately 60% were black.
- Mean (SD) age of patients was 41.17 (12.18) years.
- A majority of patients (61%) had fee-for-service as their health coverage type and "blind/disabled individual" was the predominant reason for basis of Medicaid eligibility (94%).

Figure 1. Antipsychotic Adherence Patterns 6 Months Prehospital Admission and 6 Months Posthospital Discharge
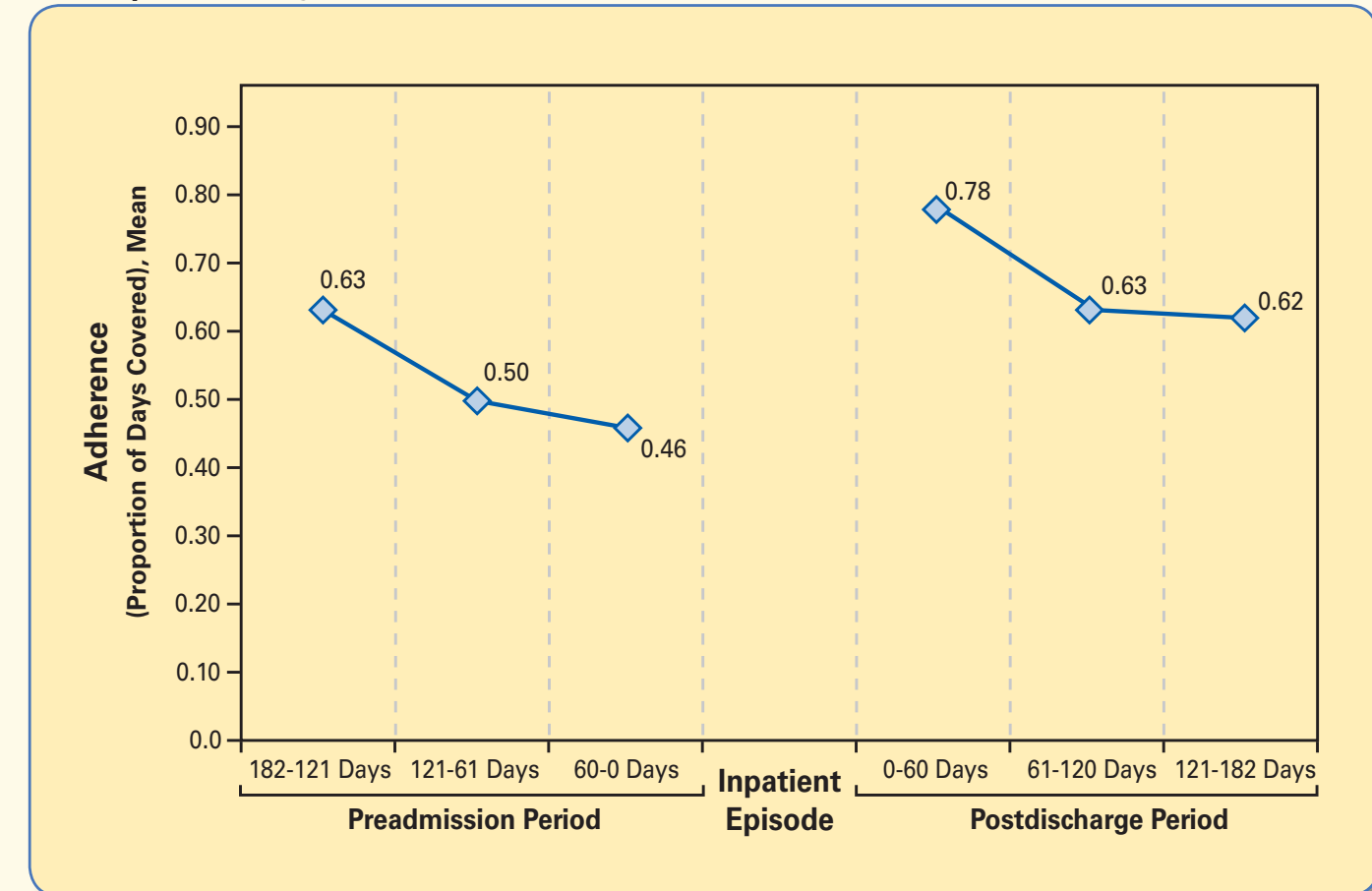

Table 1. Adherence[a] to Antipsychotic[b] Therapy and Depot Antipsychotic Use Among Hospital-Discharged Schizophrenia Patients

Adherence	n	%	n	%	n	%	n	%
Preindex Period[c]	**182-121 Days**		**121-61 Days**		**60-0 Days**		**Overall 6-Month**	
PDC								
Mean (SD)	0.63	0.39	0.50	0.44	0.46	0.45	0.53	0.39
PDC categorical (80% threshold)								
Nonadherent total (PDC < 80%)	1,227	48.29	1,483	58.36	1,572	61.87	1,560	61.39
Adherent total (PDC ≥ 80%)	1,314	51.71	1,058	41.64	969	38.13	981	38.61
Total	2,541	100.00	2,541	100.00	2,541	100.00	2,541	100.00
Depot antipsychotic used								
No	2,447	96.30	2,452	96.50	2,445	96.22	2,415	95.04
Yes	94	3.70	89	3.50	96	3.78	126	4.96
Postindex Period[e]	**0-60 Days**		**61-120 Days**		**121-182 Days**		**Overall 6-Month**	
PDC								
Mean (SD)	0.78	0.27	0.63	0.40	0.62	0.42	0.69	0.32
PDC categorical (80% threshold)								
Nonadherent total (PDC < 80%)	940	36.99	1,204	47.38	1,183	46.56	1,240	48.80
Adherent total (PDC ≥ 80%)	1,601	63.01	1,337	52.62	1,358	53.44	1,301	51.20
Total	2,541	100.00	2,541	100.00	2,541	100.00	2,541	100.00
Depot antipsychotic used								
No	2,410	94.84	2,415	95.04	2,401	94.49	2,353	92.60
Yes	131	5.16	126	4.96	140	5.51	188	7.40

[a] Adherence measures during the 6-month preindex period and 6-month postindex period.
[b] Antipsychotic therapy included first- and second-generation antipsychotic medications.
[c] 6-month period prior to the index admission date defines the preindex period.
[d] Defined as at least one claim for depot antipsychotic preparation, including risperidone, fluphenazine, and haloperidol.
[e] 6-month period following the index hospital event discharge date defines the postindex period.

### Antipsychotic Adherence and Depot Use (Table 1, Figure 1)

- The overall 6-month preindex period mean (SD) PDC was lower compared with the 6-month postindex period mean PDC (0.53 [0.39] vs. 0.69 [0.32]). Similarly, greater proportions of patients were adherent (PDC ≥ 0.8) to antipsychotic therapy during the postindex period compared with the preindex period (51.2% vs. 38.6%).
- Leading up to index inpatient admission, a steady decline in the adherence rate was observed during the 6-month preindex period. The mean adherence rate was 63% during the 182-121–day period, which declined to 50% during the 121-61–day period and 46% during the 60-day–period just prior to the index inpatient admission (i.e., 60-0–day period).
- Compared with the 60-0–day period prior to index inpatient admission, greater mean adherence was observed during the 0-60–day period immediately following discharge (0.46 [0.45] vs. 0.78 [0.27]; mean difference: 0.33).
- Overall, 63% of patients were adherent to antipsychotics during the 0-60–day period following hospital discharge, which declined to 53% during the 61-120–day period and remained stable during 121-180 day–period (53%).
- Compared with the 6-month preindex period, the proportion of patients using depot preparation was greater during the 6-month postindex period (5.0% vs. 7.4%).

Health Care Utilization and Costs (Figures 2 and 3)

- We found the following when we compared the 6-month postindex period with the 6-month preindex period.
  - All-cause utilization was significantly greater for various care settings, including inpatient visits (P < 0.001), physician office visits (P < 0.001), emergency department visits (P = 0.003), outpatient visits (P = 0.002), pharmacy claims (P < 0.001), and ancillary care (P < 0.001).

Figure 2. All-Cause Health Care Costs for Prehospital Admission and Posthospital Discharge Periods, by Care Settings
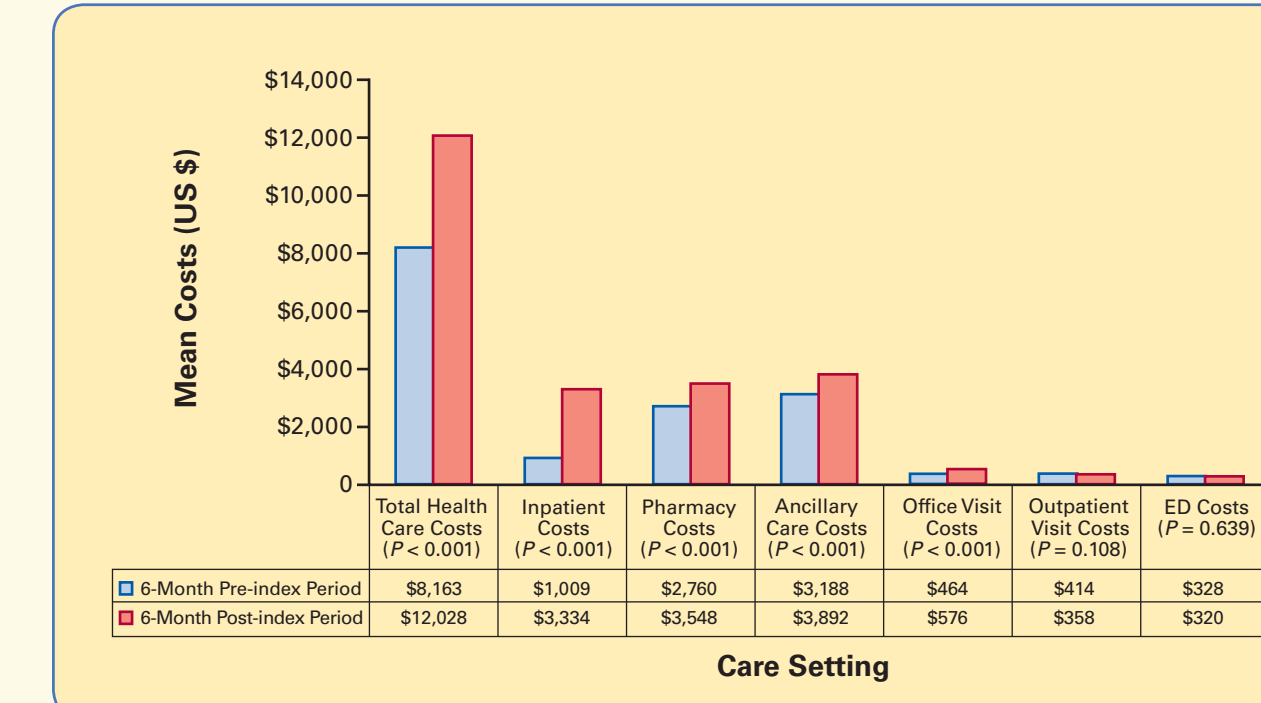
P values comparing differences in all-cause health care costs based on paired t-tests.

Figure 3. Schizophrenia-Related Health Care Costs for Prehospital Admission and Posthospital Discharge Periods, by Care Settings
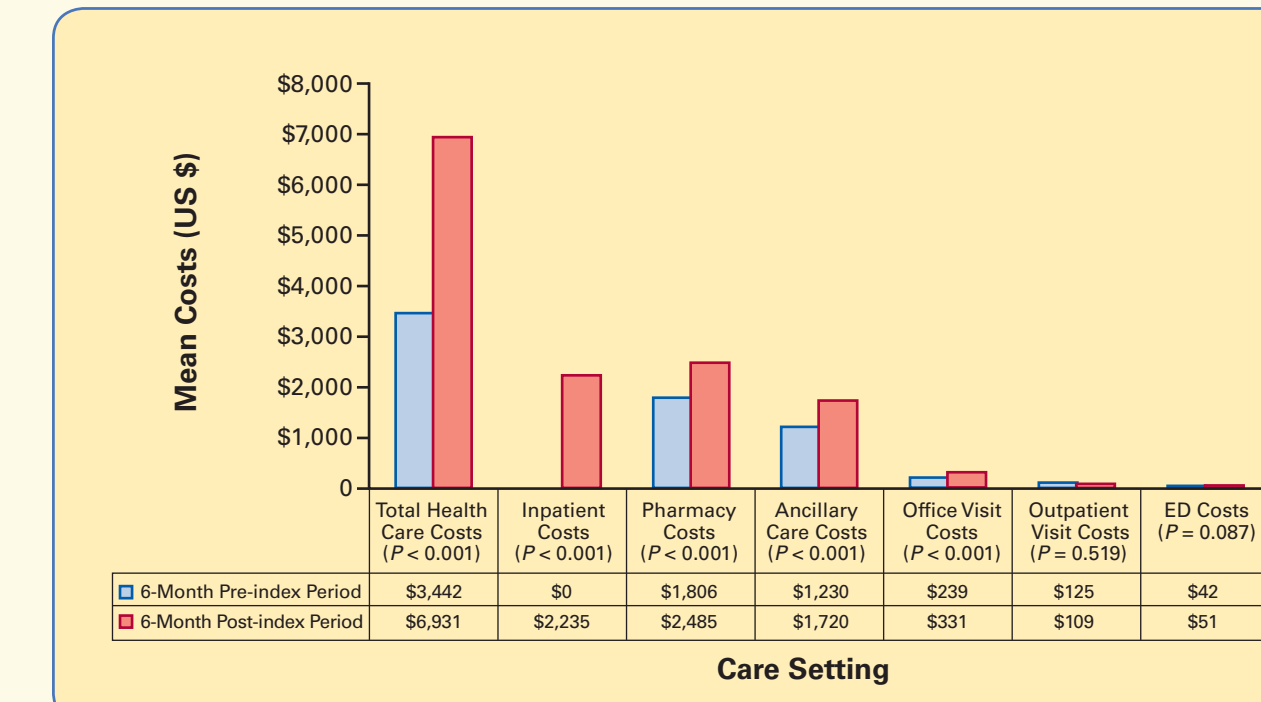
P values comparing differences in schizophrenia-related health care costs based on paired t-tests.

- All-cause heath care costs were significantly greater for various care settings, including inpatient visits (mean $3,334 vs. $1,009; P < 0.001), physician office visits (mean $576 vs. $464; P < 0.001), pharmacy (mean $3,548 vs. $2,760; P < 0.001), ancillary care (mean $3,892 vs. $3,188; P < 0.001), and total health care costs (mean $12,028 vs. $8,163; P < 0.001).
- Schizophrenia-related utilization increased significantly for various care settings, including office visits (P < 0.001), outpatient visits (P < 0.001), pharmacy claims (P < 0.001), and ancillary care (P < 0.001).
- Schizophrenia-related heath care costs were significantly greater for various care settings, including physician office visits (mean $331 vs. $239; P < 0.001), pharmacy (mean $2,485 vs. $1,806; P < 0.001), ancillary care (mean $1,720 vs. $1,230; P < 0.001), and total health care costs (mean $6,931 vs. $3,442; P < 0.001).
- The schizophrenia-related pharmacy costs and adherence rate to antipsychotics followed a similar pattern. Adherence rate to antipsychotics (0.53 vs. 0.69; percentage change: 30.2%) and schizophrenia-related pharmacy costs (mean $1,806 vs. $2,485; percentage change: 37.6%) were lower in the 6-month preindex period and both increased considerably during the 6-month postindex period.
- The primary drivers of higher schizophrenia-related postindex period costs were inpatient and pharmacy utilization.

LIMITATIONS

- Assessment of administrative claims-based adherence assumes that the prescription refilled is consumed as expected.
  - However, in certain instances, patients may discontinue, stockpile, or discard medication, thus leading to overestimation of PDC.[5]
- The data do not contain information on several patient clinical (e.g., severity, side effects, contraindications, drug interactions) and sociodemographic (e.g., educational level, income, occupational status) characteristics, which may have an effect on adherence and health care utilization. Moreover, details on medications used during an inpatient stay were not available.
- We used the Medicaid paid amount in assessing health care costs for the pre- and post-index periods.
  - However, this approach does not account for patients' out-of-pocket expenses (e.g., copayment, coinsurance, health savings account) and may underestimate the total direct economic burden.
- These findings may not be generalizable to individuals enrolled in other federal (e.g., Medicare, Veterans Administration), commercial health plans, or to individuals without health coverage. Additionally, we used several inclusion and exclusion criteria, such as continuous Medicaid enrollment, which may also limit generalizability.

DISCUSSION AND CONCLUSIONS

- To the best of our knowledge, this is the first study to assess patterns in antipsychotic adherence at various clinically relevant prehospital admission and posthospital discharge periods among patients with schizophrenia.
- Overall, the adherence rate steadily declined from 63% during the 182-121–day period to 46% during the 60-0–day period prior to the index inpatient admission.
  - The lower adherence (46%) observed during the 60-day prior to the index inpatient admission may have been one of the reasons for the inpatient admission.
- Typically, studies have focused on long-term adherence (e.g., 365 days) measures, primarily because patients require lifelong medication use for managing schizophrenia. However, our study findings indicate that assessing adherence over smaller intervals may serve as a helpful tool to identify high-risk patients.
- In comparison with the preadmission period, greater schizophrenia-related health care costs were observed among these patients following hospital discharge.
- Identifying these high-risk patients and designing adherence-related interventions may help reduce the likelihood of inpatient admissions and in turn lower the associated downstream costs.[6,7]

REFERENCES

Please see handout for a complete reference list.

DISCLOSURES

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