Medication Adherence, Healthcare Resource Utilization, and Costs Among Medicaid Beneficiaries With Schizophrenia Treated With Once-Monthly Paliperidone Palmitate or Once-Every-Three-Months Paliperidone Palmitate

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BACKGROUND

- Antipsychotics (APs) are the standard of care for schizophrenia[1,2]; however, poor adherence to oral APs is common, leading to increased risk of relapse among patients with schizophrenia[3,4]
- APs with reduced dosing frequency administered via injection improve adherence and persistence and may lead to better clinical outcomes for patients with schizophrenia
- Once-every-3-months paliperidone palmitate (PP3M) is the only AP currently available with a dosing frequency of every 3 months. It is indicated for patients with schizophrenia who have been adequately treated with once-monthly paliperidone palmitate (PP1M)
- Previous studies showed that switching from PP1M to PP3M was associated with improved adherence and persistence while reducing healthcare resource use and costs[5-7] among patients with schizophrenia insured through the Veterans Health Administration[5] or with commercial plans[7]
- Prevalence of schizophrenia is higher among Medicaid beneficiaries relative to beneficiaries of other insurance plans,[8] which may suggest a difference in unmet medical needs
- Overall, there are limited data on outcomes associated with transitioning to PP3M versus remaining on PP1M among adults with schizophrenia and enrolled in Medicaid

OBJECTIVES

- To compare adherence, persistence, healthcare resource use (HRU), and costs between Medicaid beneficiaries with schizophrenia who transition from PP1M to PP3M and those who remain on PP1M

METHODS

Data Source

- 4-state Medicaid data from Iowa (Q2 2014 to Q3 2016), Kansas (Q2 2014 to Q1 2019), Mississippi (Q2 2014 to Q1 2019), and Missouri (Q2 2014 to Q1 2019) were used
- Data included information on patient enrollment and demographics, as well as medical and pharmacy claims reimbursed by Medicaid

Study Design

- A retrospective observational matched cohort design was used
- 2 cohorts of patients with schizophrenia were identified
  - PP3M cohort: patients who received adequate treatment with PP1M (≥4 months of continuous PP1M coverage without gaps of >45 days) and then transitioned to PP3M
  - PP1M cohort: patients who received adequate treatment with PP1M and remained on PP1M
- The index date was defined as follows:
  - PP3M cohort: the index date was the first PP3M claim identified; only patients with adequate treatment with PP1M before the index date were retained
  - PP1M cohort: the index date was a random PP1M claim following the criterion of adequate treatment with PP1M
- PP1M and PP3M cohorts were not mutually exclusive (ie, patients in the PP1M cohort who had ≥12 months of continuous Medicaid enrollment before and on/after the index PP1M claim may have been eventually included in the PP3M cohort, provided that they met all inclusion criteria for both cohorts)
- Patient characteristics were described in the baseline period, defined as the 12-month period preceding the index date
- Outcomes were measured and compared during the 12-month follow-up period on/after the index date

Inclusion Criteria

- Patients were included in this study if they met the following inclusion criteria:
  - ≥2 claims (on different days) with a diagnosis of schizophrenia (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] code: 295.XX [excluding 295.7]; International Classification of Diseases, 10th Revision, Clinical Modification [ICD-10-CM] code: F20.XX, F21) at any time during the continuous Medicaid enrollment period, including ≥1 claim prior to the index date
  - ≥1 pharmacy or medical claim for PP1M on January 18, 2015, or afterward, to allow ≥4 months of continuous PP1M coverage before the date of PP3M approval
  - Aged ≥18 years old as of the first observed PP1M claim
  - Adequate treatment with PP1M just before the index date (defined as ≥4 months of continuous PP1M coverage without gaps of >45 days)
  - ≥12 months of continuous Medicaid enrollment pre-index date
  - ≥12 months of follow-up starting from the index date until the earliest of Medicaid disenrollment, end of data availability, death, or transition to PP3M (for the PP1M cohort only; the follow-up period was truncated at the transition to PP3M)
- Patients in the PP3M cohort additionally met the following criterion:
  - ≥1 pharmacy or medical claim for PP3M after adequate treatment with PP1M
- Patients in the PP1M cohort additionally met the following criterion:
  - ≥1 pharmacy or medical claim for PP1M after adequate treatment with PP1M, and no claims for PP3M before this PP1M claim

Outcome Measures

- Adherence to all APs and index medications was defined based on a proportion of days covered (PDC) ≥80% over the 6- and 12-month periods
  - Because the days of supply information was missing for PP3M and PP1M claims identified using medical claims, 90 and 30 days of supply were imputed, respectively, to align with each medication's label
- Persistence on index medications was defined as an absence of a gap >90 days (PP3M cohort) or >30 days (PP1M cohort) in the index medication supply over the 6-, 9-, and 12-month periods
- All-cause HRU and costs were reported over the 12-month follow-up period per-patient-per-year (PPPY); costs were adjusted for inflation using the medical care component of the US Consumer Price Index and were reported in 2019 US dollars
- Pharmacy costs were reported pre-discount, after the mandatory 23.1% discount on branded psychiatric drugs[9] and after the estimated cumulative discount of 70% on branded psychiatric drugs, which includes the Medicaid price inflation discount (70% on PP1M as of 2020)[10]

Statistical Analysis

- Patients in the PP1M cohort were matched 1:1 to patients in the PP3M cohort based on propensity scores modeled using a logistic regression adjusted for baseline characteristics: age, sex, race, state of residence, year of the index date, insurance type, Quan-Charlson comorbidity index (Quan-CCI), comorbidities, medical and pharmacy costs, PDC at 6 months, most recent period of continuous PP1M coverage in the pre-index period, proportion of new PP1M users, outpatient visits, 1-day mental health institute visits, and long-term care stays
- The balance of baseline characteristics between matched cohorts was assessed with standardized differences (<10% considered well-balanced)
- Adherence, persistence, and HRU were compared between matched cohorts using a generalized estimating equation model with a binominal distribution and a logit link to calculate odds ratios (ORs), 95% confidence intervals (CIs), and *P* values
- Ordinary least squares regressions were used to generate mean cost differences between the cohorts, and nonparametric bootstrap procedures with 499 replications were used to generate 95% CIs and *P* values

RESULTS

Baseline Characteristics

- A total of 374 patients met the criteria for inclusion in the PP3M cohort, and 2,000 patients met the criteria for inclusion in the PP1M cohort before matching
- Before matching, compared with PP1M patients, a smaller proportion of PP3M patients were female and black; PP3M patients had a lower prevalence of comorbidities, had lower HRU, and were adequately treated with PP1M for a longer period of time (**Table 1**)
- After matching, each cohort consisted of 374 patients, and characteristics between matched cohorts were well balanced (**Table 1**)

Table 1. Demographic and clinical characteristics evaluated during the 12-month baseline period

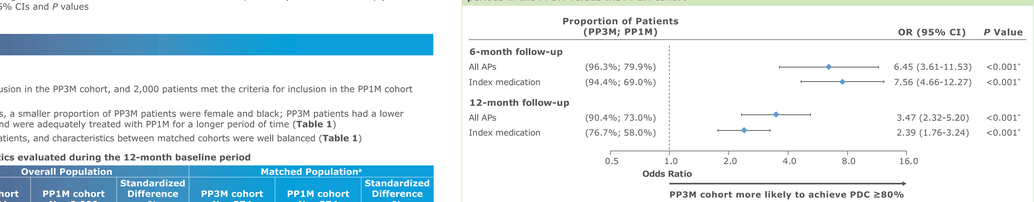
	Overall Population			Matched Population[a]		
Reported as mean ± SD [median] or n (%)	PP3M cohort N = 374	PP1M cohort N = 2,000	Standardized Difference %	PP3M cohort N = 374	PP1M cohort N = 374	Standardized Difference %
Age at index date, years	41.9 ± 12.1 [40.3]	42.3 ± 13.3 [40.9]	3.2	41.9 ± 12.1 [40.3]	42.1 ± 12.7 [40.1]	1.6
Female	114 (30.5)	674 (33.7)	6.9	114 (30.5)	114 (30.5)	0.0
Race						
White	209 (55.9)	1,009 (50.5)	10.9	209 (55.9)	202 (54.0)	3.8
Black	148 (39.6)	856 (42.8)	6.6	148 (39.6)	152 (40.6)	2.2
Hispanic	0 (0.0)	9 (0.5)	-	0 (0.0)	0 (0.0)	-
Other	10 (2.7)	60 (3.0)	2.0	10 (2.7)	10 (2.7)	0.0
Unknown	7 (1.9)	66 (3.3)	9.0	7 (1.9)	10 (2.7)	5.4
State						
Missouri	294 (78.6)	1,335 (66.8)	26.9	294 (78.6)	293 (78.3)	0.7
Kansas	45 (12.0)	250 (12.5)	1.4	45 (12.0)	46 (12.3)	0.8
Mississippi	32 (8.6)	330 (16.5)	24.2	32 (8.6)	35 (9.4)	2.8
Iowa	3 (0.8)	85 (4.3)	22.1	3 (0.8)	0 (0.0)	-
Insurance eligibility[b]						
Capitated	40 (10.7)	207 (10.4)	1.1	40 (10.7)	38 (10.2)	1.7
Fee for services	145 (38.8)	574 (28.7)	21.4	145 (38.8)	150 (40.1)	2.7
Capitated and fee for services	189 (50.5)	1,219 (61.0)	21.1	189 (50.5)	186 (49.7)	1.6
Dual Medicaid/Medicare coverage	82 (21.9)	592 (29.6)	17.6	82 (21.9)	77 (20.6)	3.3
Year of index date						
2015	76 (20.3)	441 (22.1)	4.2	76 (20.3)	75 (20.1)	0.7
2016	143 (38.2)	599 (30.0)	17.5	143 (38.2)	141 (37.7)	1.1
2017	119 (31.8)	690 (34.5)	5.7	119 (31.8)	120 (32.1)	0.6
2018	36 (9.6)	270 (13.5)	12.1	36 (9.6)	38 (10.2)	1.8
Quan-CCI	0.70 ± 1.15 [0.00]	0.98 ± 1.58 [0.00]	20.2	0.70 ± 1.15 [0.00]	0.65 ± 1.11 [0.00]	5.0
Mental health–related comorbidities						
Substance use disorder[c]	95 (25.4)	571 (28.6)	7.1	95 (25.4)	96 (25.7)	0.6
Anxiety	90 (24.1)	516 (25.8)	4.0	90 (24.1)	85 (22.7)	3.2
Tobacco use disorder	87 (23.3)	499 (25.0)	3.9	87 (23.3)	91 (24.3)	2.5
Any depression disorder	78 (20.9)	543 (27.2)	14.8	78 (20.9)	72 (19.3)	4.0
Bipolar disorder	78 (20.9)	523 (26.2)	12.5	78 (20.9)	75 (20.1)	2.0
Post-traumatic stress disorder	20 (5.3)	134 (6.7)	5.7	20 (5.3)	15 (4.0)	6.3
Non–mental health–related comorbidities						
Cardiovascular disease[d]	171 (45.7)	978 (48.9)	6.4	171 (45.7)	185 (49.5)	7.5
Diabetes	71 (19.0)	464 (23.2)	10.3	71 (19.0)	67 (17.9)	2.8
Obesity	49 (13.1)	287 (14.4)	3.6	49 (13.1)	44 (11.8)	4.1
COPD	52 (13.9)	262 (13.1)	2.4	52 (13.9)	48 (12.8)	3.1
Hypothyroidism	25 (6.7)	207 (10.4)	13.2	25 (6.7)	28 (7.5)	3.1
PDC by any AP						
6 months	0.95 ± 0.09 [1.0]	0.91 ± 0.13 [1.0]	29.2	0.95 ± 0.09 [1.0]	0.94 ± 0.10 [1.0]	3.0
12 months	0.85 ± 0.16 [0.9]	0.80 ± 0.20 [0.9]	25.8	0.85 ± 0.16 [0.9]	0.85 ± 0.17 [0.9]	0.8
Most recent period of adequate treatment with PP1M, days	467.94 ± 311.36 [406.0]	377.84 ± 263.42 [293.0]	31.2	467.94 ± 311.36 [406.0]	451.71 ± 293.42 [366.0]	5.4
New PP1M users[e]	120 (32.1)	680 (34.0)	4.1	120 (32.1)	135 (36.1)	8.5
Annual all-cause resource use						
≥1 inpatient stay	126 (33.7)	862 (43.1)	19.4	126 (33.7)	128 (34.2)	1.1
≥1 emergency room visit	145 (38.8)	946 (47.3)	17.3	145 (38.8)	157 (42.0)	6.5
≥1 outpatient visit	327 (87.4)	1,811 (90.6)	10.0	327 (87.4)	338 (90.4)	9.4
≥1 long-term care stay	22 (5.9)	283 (14.2)	27.8	22 (5.9)	32 (8.6)	10.3
Annual all-cause healthcare costs						
Medical costs	24,209 ± 30,832 [12,902]	30,710 ± 37,811 [19,563]	16.4	24,209 ± 30,832 [12,902]	23,690 ± 29,215 [12,604]	1.7
Pharmacy costs	33,958 ± 34,915 [29,557]	27,124 ± 47,476 [6,629]	18.8	33,958 ± 34,915 [29,557]	33,404 ± 38,079 [25,587]	1.5

AP, antipsychotic; CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; PDC, proportion of days covered; PP1M, once-monthly paliperidone palmitate; PP3M, once-every-3-months paliperidone palmitate; SD, standard deviation.
[a]Patients were matched 1:1 on 5-percentile propensity score buckets, modeled using logistic regression adjusted for baseline characteristics (see Statistical Analysis section).
[b]Evaluated at the claims level based on all claims in the baseline period.
[c]Excluding nicotine dependence.
[d]Including hypertension and hyperlipidemia.
[e]Evaluated among patients with ≥12 months of continuous enrollment prior to the first observed PP1M claim.

Adherence

- Patients in the PP3M cohort were more likely to be adherent to any AP and to the index medication than patients in the PP1M cohort (**Figure 1**)
  - During the 6-month follow-up period, patients in the PP3M cohort were 6.5 and 7.6 times more likely to be adherent to any AP and to the index medication, respectively (all *P* < 0.001)
  - During the 12-month follow-up period, patients in the PP3M cohort were 3.5 and 2.4 times more likely to be adherent to any AP and to the index medication, respectively (all *P* < 0.001)

Figure 1. Likelihood of adherence (PDC ≥80%) to all APs or index medication in the 6- or 12-month follow-up periods in the PP3M versus the PP1M cohort

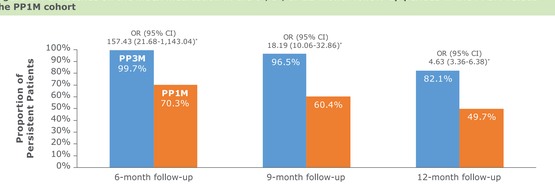


*Indicates statistical significance at the <0.05 level.
AP, antipsychotic; CI, confidence interval; OR, odds ratio; PDC, proportion of days covered; PP1M, once-monthly paliperidone palmitate; PP3M, once-every-3-months paliperidone palmitate.

Persistence

- During the 6-, 9-, and 12-month follow-up periods, patients in the PP3M cohort were 157.4, 18.2, and 4.6 times more likely to be persistent on the index medication than patients in the PP1M cohort, respectively (all *P* < 0.001; **Figure 2**)

Figure 2. Persistence on the index medication in the 6-, 9-, or 12-month follow-up periods in the PP3M versus the PP1M cohort

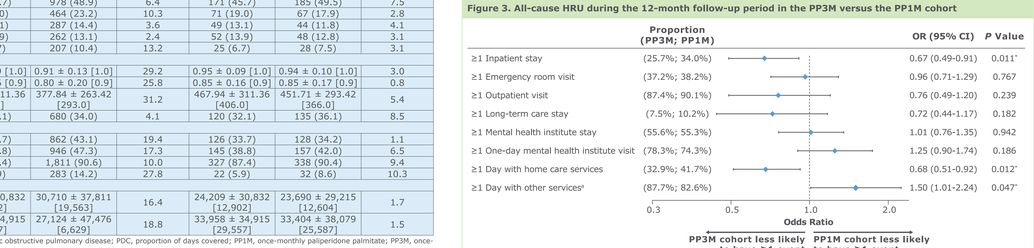


*Indicates statistical significance at the <0.05 level.
CI, confidence interval; OR, odds ratio; PP1M, once-monthly paliperidone palmitate; PP3M, once-every-3-months paliperidone palmitate.

HRU

- Patients in the PP3M cohort were 33% times less likely to have ≥1 inpatient admission (*P* = 0.011) and 32% times less likely to have ≥1 day with home care services use (*P* = 0.012; **Figure 3**)

Figure 3. All-cause HRU during the 12-month follow-up period in the PP3M versus the PP1M cohort

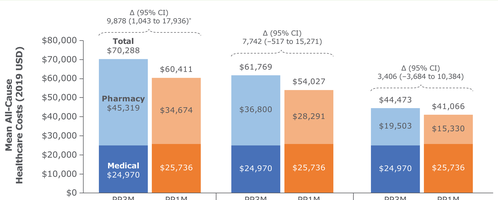


*Indicates statistical significance at the <0.05 level.
CI, confidence interval; HRU, healthcare resource use; OR, odds ratio; PP1M, once-monthly paliperidone palmitate; PP3M, once-every-3-months paliperidone palmitate.
[a]Other services include but are not limited to independent laboratory services and services received in Federally Qualified Health Centers.

Healthcare Costs

- Mean medical costs were similar for patients in the PP3M ($24,970) and PP1M ($25,736) cohorts over the 12-month follow-up period (mean cost difference = −$767, *P* = 0.854)
- Higher total healthcare costs in the PP3M versus the PP1M cohort (mean cost difference = $9,878, *P* = 0.028) were offset after applying discounts on pharmacy costs of branded psychiatric drugs
  - The mean difference in total healthcare costs decreased to $7,742 (*P* = 0.064) after accounting for the 23.1% discount on branded psychiatric drugs, and decreased further to $3,406 (*P* = 0.289) after accounting for the cumulative 70% discount on branded psychiatric drugs (**Figure 4**)

Figure 4. Medical and pharmacy[a] costs during the 12-month follow-up period in the PP3M versus the PP1M cohort



*Indicates statistical significance at the <0.05 level.
CI, confidence interval; PP1M, once-monthly paliperidone palmitate; PP3M, once-every-3-months paliperidone palmitate; USD, US dollars.
[a]Pharmacy costs were reported without discount, with the mandatory 23.1% discount on branded psychiatric drugs[9] and with the estimated cumulative discount of 70% on branded psychiatric drugs, which includes the Medicaid price inflation rebate (70% on PP1M as of 2020).[10]

Limitations

- Findings are not generalizable to patients without health insurance or with non-Medicaid insurance plans and may not be representative of the Medicaid population in states other than those included in the analysis
- Pharmacy claims do not account for whether the medication dispensed was taken as prescribed (PP3M and PP1M were primarily identified through pharmacy claims); additionally, samples were not captured in claims data; these factors potentially lead to misestimated adherence, and true initiation of treatment might not have been captured
- Because comorbid conditions are measured based on ≥1 claim with a diagnosis, certain conditions may be underreported if a patient did not have a visit to follow-up on the condition or overreported if a diagnosis was a rule-out
- There is a possibility of immortal time bias because patients were required to be adequately treated with PP1M for ≥4 months prior to the first PP3M claim or a random PP1M claim to qualify for inclusion in the study
- Results may be subject to residual confounding because of unmeasured factors (ie, information not available in claims data) and, for patients with dual Medicaid/Medicare coverage, utilization and costs may be conservatively reported since services reimbursed by Medicare were not captured in the data

CONCLUSIONS

- **In this study, patients who transitioned to PP3M had better adherence and persistence relative to those who remained on PP1M**
- **Moreover, patients who transitioned to PP3M experienced lower rates of inpatient admissions and days with home care services than those who remained on PP1M**
- **Medical costs as well as total healthcare costs, after applying the mandatory 23.1%[9] and the cumulative 70%[10] discounts on branded psychiatric drugs, were similar between the 2 cohorts**

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Disclosures

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