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ORIGINAL ARTICLE

Health care resource utilization and costs of California Medicaid patients with schizophrenia treated with paliperidone palmitate once monthly or atypical oral antipsychotic treatment

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ABSTRACT

Objective: To compare all-cause health care utilization and costs between patients with schizophrenia treated with once monthly paliperidone palmitate (PP1M; Invega Sustenna¹) and atypical oral antipsychotic therapy (OAT).

Methods: This was a retrospective claims-based analysis among adult California Medicaid (Medi-Cal) patients with schizophrenia having ≥ 2 claims for PP1M or OAT from 1 July 2009 to 31 December 2013 and continuous health plan enrollment for ≥ 1 year pre- and post-index date (PP1M or OAT initiation date). Baseline characteristics were reported descriptively. Propensity score matching with a 1:1 greedy match method was used to create two matched cohorts. Treatment patterns, all-cause health care utilization, and costs for the 12 month follow-up period were compared between the two matched cohorts.

Results: Two well matched cohorts of 722 patients were produced with similar baseline characteristics. During the 12 month follow-up period, PP1M patients were significantly less likely to discontinue treatment (30.6% vs. 39.5%, $p < .001$) or switch to a new therapy (21.6% vs. 27.7%, $p = .007$). PP1M patients had fewer inpatient visits (5.0 vs. 7.9, $p < .001$), lower mean hospitalization days (15.0 vs. 27.7 days, $p < .001$) and inpatient costs (\$5060 vs. \$10,880, $p < .001$). While pharmacy costs were significantly higher in the PP1M cohort (\$16,347 vs. \$9115, $p < .001$), total costs were not significantly different between the matched cohorts (\$25,546 vs. \$25,307, $p = 0.853$).

Conclusions: Patients with schizophrenia treated with PP1M had significantly fewer inpatient hospitalizations and associated costs with no significant difference in the total costs between the two cohorts. This study is subject to limitations associated with claims data such as miscoding, inability to examine clinical severity, etc.

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Introduction

Schizophrenia is a chronic, disabling mental disorder that affected at least 21 million patients worldwide in 2011¹. The peak ages of onset are 20–28 years for men and 26–32 years for women^{2,3}. According to the Global Burden of Disease study, schizophrenia accounts for 1.1% of the total disability-adjusted life years (DALYs)⁴. In 2002, the overall cost of schizophrenia was estimated to be \$62.7 billion, with \$30.3 billion accounting for total direct costs and \$32.4 billion indirect costs⁵. One-third to two-thirds of total direct health care costs are associated with inpatient hospital care due to relapses and re-hospitalizations, indicating that this disease imposes a significant clinical and economic burden on patients, payers, and society⁶.

Antipsychotic drugs form the cornerstone of treatment among patients with schizophrenia in reducing the severity and frequency of acute relapse episodes^{6–8}. Several drugs, including the atypical antipsychotics (risperidone [Risperdal

Consta²], olanzapine [Zyprexa Relprevv³], aripiprazole [Abilify⁴], paliperidone palmitate [Invega Sustenna]) and typical antipsychotics (haloperidol [Haldol⁵], fluphenazine [Prolixin⁵]), are available as oral antipsychotics (OATs) and/or long-acting injectables (LAIs)⁹. Atypical antipsychotics are associated with fewer extra-pyramidal side effects compared to the typical antipsychotics and are therefore the first-line therapeutic agents of choice^{6,10}. In practice, non-adherence to OATs is a frequent challenge and common cause of relapse, re-hospitalizations, increased symptom severity, longer inpatient stays, and higher hospital costs in patients with schizophrenia⁶. A study examining medication continuity in Medicaid beneficiaries diagnosed with schizophrenia suggested that only 61% of Medicaid-covered patients regularly refilled their antipsychotic drug prescriptions, which suggests that there is an opportunity to improve medication adherence in this population¹¹. According to a previous study conducted by Weiden *et al.*, California Medicaid (Medi-Cal)

patients who did not adhere to the prescribed antipsychotic therapy were at an increased hospitalization risk, leading to higher health care costs¹². It has also been observed that less than 12% of Medi-Cal patients with schizophrenia receive uninterrupted antipsychotic therapy, leading to a high rate of relapse and higher health care burden¹³. The Medi-Cal population is composed mainly of low-income and disabled patients. With a disproportionately high prevalence of schizophrenia among the Medi-Cal population¹⁴, the pervasive challenge of antipsychotic non-adherence may lead to increased hospitalizations and health care costs.

According to recent guidelines, LAIs may help patients with schizophrenia to overcome non-adherence compared to oral antipsychotics; LAIs have also been associated with reduced relapse episodes and lower rates of re-hospitalizations^{6,15,16}. Several studies comparing healthcare resource utilization and associated costs between LAIs and OATs and costs of LAIs with OATs have shown the beneficial effects of LAIs, such as reduced hospitalizations, as well as better economic and clinical outcomes^{17–21}.

The LAI paliperidone palmitate (PP1M) is a once-per-month injectable agent approved by the FDA in 2009 for the treatment of schizophrenia and in 2014 for schizoaffective disorders in adults²². Since PP1M is administered by a health care provider and can be administered less frequently than OATs, patients may be more likely to adhere to the medication, resulting in improved symptom control, relapse prevention and overall improvement in disease burden. According to studies conducted in Greece, Norway, and Sweden, PP1M has been shown to be a cost effective option compared to other LAIs and OATs^{23–25}. A recent study in the US among Veterans Affairs patients with schizophrenia treated with PP1M or OATs suggested that inpatient admission rates and associated costs were lower among those treated with PP1M²⁶. The generalizability of these studies' results may be limited due to different study designs, settings, or populations.

There are a limited number of real-world studies that have compared LAIs to OATs among Medicaid beneficiaries with schizophrenia. This study used a propensity-score matched PSM cohort design to compare all-cause health care utilization and costs of PP1M with atypical OATs. Results from this study should provide real-world comparative economic evidence which may in turn prove helpful to health care professionals in supporting the value of LAIs such as PP1M compared to atypical OATs.

Methods

Data source

This was a retrospective cohort study using health insurance claims from the Medi-Cal database, which provides information regarding outpatient care, inpatient care, and prescription drugs for low-income and disabled California residents. The Medi-Cal paid claims files include institutional claims, professional service claims, and pharmacy claims. Service claims include the date, type, place, and units (days) of service; paid and billed amount; primary and secondary

diagnosis codes; and provider identification. The pharmacy claims include the national drug code, fill date, days of supply, paid and billed amount, and quantity. Eligibility files consist of enrollment status for each month and enrollees' demographic information. The study period, 1 July 2008 to 31 December 2014, was based on the US Food and Drug Administration's approval of PP1M in 2009 and the study requirement of at least a 12 month baseline period. Data was collected from Medi-Cal paid claims and eligibility files for Medi-Cal enrollees.

Study population

To be eligible for this study, patients were required to have ≥ 2 diagnostic claims for schizophrenia (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] code: 295.xx) during the study period, and have evidence of ≥ 2 claims for PP1M or the same atypical OAT (aripiprazole, asenapine, iloperidone, lurasidone, olanzapine [including combination olanzapine/fluoxetine], paliperidone, quetiapine, risperidone or ziprasidone) within 60 days of each other during the identification period (1 July 2009 to 31 December 2013). The initiation date of the first PP1M or OAT prescription was designated as the index date. OAT patients were required to have no evidence of a PP1M injection during the 12 months pre-index date (baseline period) and no claims for their index OAT prescription for 6 months pre-index date.

Eligible patients were required to be ≥ 18 years of age, have continuous health plan enrollment for the 12 month baseline period and 12 months after the index date (follow-up period), no more than one prescription for any LAI antipsychotic between the first two index medications, and no prescription for clozapine during the study period, since Clozapine it is indicated for treatment of severely ill patients with schizophrenia who fail to respond adequately to standard antipsychotic treatment. Antipsychotic-naïve patients (no prescription for any atypical or typical OAT or LAI) during the 12 month baseline period were excluded from the analysis. Therefore, PP1M cohort patients may have had claims for OAT or LAI antipsychotics at any point during the study period. In order to ensure the thoroughness of the medication claims histories, patients with dual eligibility were also excluded. Patients were assigned to one of two mutually exclusive cohorts, the PP1M cohort or the OAT cohort, depending on their index antipsychotic medication.

Study variables

During the 12 month baseline period, demographics (age and gender), clinical characteristics (schizophrenia subtype, prior psychiatric medications use, polypharmacy [≥ 2 OAT prescriptions or administrations with an overlap of 60 days], comorbidities such as mental and general health conditions, antipsychotic medication proportion of days covered [PDC]), and economic variables (all-cause health care utilization and costs) were recorded. PDC was calculated for any and all antipsychotics in the pre-index period and determined as the

number of days covered by medication divided by the total days during the baseline period. The number of patients with a PDC of 0.00–0.50, 0.51–0.80 and 0.81–1.00 were also reported. Patients with a PDC gap of >30 days were also flagged.

During the follow-up period, antipsychotic treatment patterns and all-cause health care utilization and costs were captured for both the PP1M and OAT cohort. Treatment patterns included discontinuation (≥ 30 day gap in index treatment therapy), persistence (≤ 30 day gap between prescriptions), PDC (number of days covered by index medication/total days in the follow-up period), and switching (a pharmacy claim for a new medication within 90 days post-index therapy discontinuation). Time to discontinuation (in days) was also recorded. All-cause follow-up ambulatory (office and outpatient), emergency room (ER), inpatient, and pharmacy visits, as well as associated annual costs, were recorded. Hospitalization, length of stay (LOS), and total costs (inpatient + outpatient + pharmacy) during the 12 month follow-up period were also recorded.

Statistical analysis

For the total study population, all measures including the patient's demographic and clinical characteristics, treatment patterns, all-cause health care utilization, and associated costs during the 12 month follow-up period were reported descriptively by the two treatment cohorts. Chi-square tests were used to evaluate the statistical significance of differences for categorical variables, and Student's *t*-tests were used to assess differences in the mean of continuous variables. The level of significance was set to $\alpha = 0.05$.

In order to determine the association of baseline variables with treatment cohorts, an unconditional stepwise logistic regression model was built that incorporated potential predictors of therapy as independent variables in the regression and group status (e.g. PP1M cohort vs. OAT cohort) as the outcome. A propensity score was then calculated for each study-qualified patient to represent the likelihood of receiving PP1M based on the patient's baseline data and to minimize the potential of confounding factors. Each patient in the PP1M cohort was matched 1:1 to a patient in the OAT cohort using greedy match method²⁷ within 0.001 units of the propensity score while controlling for the covariates age, gender, comorbidities (bipolar disorder, any depression disorder, attention deficit hyperactivity disorder, panic disorder, anxiety, suicide attempt and intentional injuries, substance abuse and alcohol abuse, diabetes, obesity), schizophrenia subtype, prior antipsychotic treatment PDC, and pre-index all-cause health care utilization. The quality of the match was assessed using descriptive statistics and visual inspection of the propensity score histograms (Figure 1). The highest-quality match showed no significant differences in baseline characteristics and fully congruent propensity histograms for the matched cohorts. All-cause health care utilization and cost outcomes were then compared between the matched cohorts using chi-square and *t*-tests for categorical and

continuous variables, respectively. There were no adjustments made for multiplicity.

Results

There were a total of 23,511 patients with ≥ 2 diagnostic claims for schizophrenia (PP1M cohort: 2666; OAT cohort: 20,845). After applying inclusion and exclusion criteria, there were 1939 patients in the PP1M cohort and 3786 patients in the OAT cohort (total $n = 5725$).

Baseline patient characteristics

The average age of OAT patients was higher than that of PP1M patients (42.9 vs. 40.7 years, $p < .001$). A lower proportion of OAT patients were male compared to PP1M patients (49.7% vs. 57.0%, $p < .001$). PP1M and OAT patients were similar with respect to schizophrenia sub-types (catatonic and paranoid type: 32.1% vs. 30.1%, $p = .108$; schizoaffective disorder: 36.0% vs. 35.5%, $p = .709$; other types: 31.9% vs. 34.4%, $p = .051$).

The Charlson Comorbidity Index (CCI) score was slightly higher among OAT patients than PP1M patients (0.5 vs. 0.4, $p < .001$), indicating a population with a higher degree of medical comorbidity. Compared to OAT patients, a significantly higher proportion of PP1M patients had other mental health disorders (57.6% vs. 51.0%, $p < .001$), including bipolar disorder (13.9% vs. 11.8%, $p = .022$) and substance or alcohol abuse (10.7% vs. 5.3%, $p < .001$), and a significantly lower proportion of patients had panic disorder (0.4% vs. 1.0%, $p = .022$) (Table 1). There was also a significant difference in baseline all-cause health care utilization and costs (Table 1). The number of unique antipsychotic medications in the baseline period was significantly higher among patients in the PP1M cohort (2.3 vs. 1.4, $p < .001$) and a significantly higher proportion of patients in the PP1M cohort showed evidence of polypharmacy (20.7% vs. 4.4%, $p < .001$; data not shown).

Matching

The propensity score matching resulted in well matched PP1M and OAT cohorts, each consisting of 722 patients. Patients in these cohorts appeared well matched with respect to mean age (40.4 years vs. 41.2 years, $p = .206$), gender (54.2% vs. 55.0% males, $p = .751$), clinical characteristics, baseline psychiatric medications, PDC, select comorbidities, and baseline all-cause health care utilization and costs (all $p > .05$; Table 1). The only significant difference observed among the post-matched cohorts was the number of patients with PDC 0–0.50 (45.8% vs. 40.3%, $p = .034$, Table 1).

Outcomes

During the 12 month follow-up period, PP1M patients were significantly less likely to discontinue treatment (30.6% vs. 39.5%, $p < .001$) or switch therapies (21.6% vs. 27.7%, $p = .007$), had better persistence (69.4% vs. 60.5%, $p < .001$),

Figure 1. Propensity score distribution for study qualified and propensity score matched cohorts. (a) Before matching. (b) After matching. OAT: Oral atypical antipsychotics; PP (please change to PP1M): Paliperidone Palmitate Once-Monthly.

and had a higher mean PDC (0.7 vs. 0.6, $p < .001$) compared to OAT patients (Table 2).

A lower proportion of PP1M patients had any inpatient visit (61.6% vs. 77.4%, $p < .001$), any outpatient ER visit (49.0% vs. 56.0%, $p = .008$), or any other outpatient hospital visit (78.8% vs. 89.6%, $p < .001$) compared with OAT patients. Additionally, compared with OAT-treated patients, PP1M patients had fewer mean hospitalization days (15.0 vs. 27.7 days, $p < .001$), mean inpatient visits (5.0 vs. 7.9, $p < .001$), mean outpatient ER visits (2.1 vs. 2.9, $p = .016$), and other outpatient hospital visits (13.1 vs. 16.2, $p = .004$) (Table 2, Figure 2).

While mean annual pharmacy costs were significantly higher among PP1M patients (\$16,347 vs. \$9115, $p < .001$),

the PP1M cohort incurred significantly lower inpatient visit costs (\$5060 vs. \$10,880, $p < .001$), outpatient ER visit costs (\$379 vs. \$547, $p = .021$), outpatient office visit costs (\$997 vs. \$1412, $p = .012$), and other outpatient hospital costs (\$2763 vs. \$3353, $p = .019$) compared to OAT patients. Total health care costs were not significantly different between the PP1M and OAT cohorts (\$25,546 vs. \$25,307, $p = .853$) (Table 2, Figure 3).

Discussion

This real-world comparative effectiveness study compared the all-cause health care utilization and associated costs between patients with schizophrenia treated with OATs and

Table 1. Baseline characteristics for study-qualified and PSM-matched cohorts.

	Study-qualified cohorts						Matched cohorts					
	PP1M Cohort (N = 1939)		OAT cohort (N = 3786)				PP1M cohort (N = 722)		OAT cohort (N = 722)			
	N/Mean	%/SD	N/Mean	%/SD	p-Value	STD	N/Mean	%/SD	N/Mean	%/SD	p-Value	STD
Age (mean)	40.7	12.0	42.9	12.5	<.001	17.6	40.4	12.4	41.2	12.5	.206	6.7
Gender (male)	1106	57.0%	1883	49.7%	<.001	14.7	391	54.2%	397	55.0%	.751	1.7
Clinical characteristics												
Schizophrenia sub-types												
Catatonic (295.2x) and paranoid type (295.3x)	623	32.1%	1138	30.1%	.108	4.5	219	30.3%	234	32.4%	.395	4.5
Schizoaffective disorder (295.7x)	698	36.0%	1344	35.5%	.709	1.0	253	35.0%	236	32.7%	.345	5.0
Other schizophrenia types	618	31.9%	1304	34.4%	.051	5.5	250	34.6%	252	34.9%	.912	0.6
Baseline psychiatric medications												
# Unique antipsychotic medications among patients who received antipsychotic prescriptions	2.3	1.2	1.4	0.7	<.001	90.5	1.8	1.0	1.8	1.0	.894	0.7
Baseline comorbidities												
Charlson Comorbidity Index score	0.4	0.9	0.5	1.1	<.001	15.0	0.4	0.9	0.4	0.8	.417	4.3
Any mental health disorder	1116	57.6%	1931	51.0%	<.001	13.2	400	55.4%	374	51.8%	.170	7.2
Bipolar disorder	270	13.9%	447	11.8%	.022	6.3	95	13.2%	92	12.7%	.814	1.2
Any depression disorder	423	21.8%	878	23.2%	.240	3.3	160	22.2%	158	21.9%	.899	0.7
Attention deficit hyperactivity disorder	17	0.9%	26	0.7%	.431	2.2	8	1.1%	4	0.6%	.246	6.1
Panic disorder	8	0.4%	37	1.0%	.022	6.8	7	1.0%	5	0.7%	.562	3.0
Anxiety	283	14.6%	558	14.7%	.885	0.4	108	15.0%	108	15.0%	1	0.00
Suicide attempt and intentional injuries	141	7.3%	271	7.2%	.875	0.4	51	7.1%	53	7.3%	.839	1.1
Substance abuse or alcohol abuse	208	10.7%	199	5.3%	<.001	20.3	56	7.8%	64	8.9%	.446	4.0
Diabetes	245	12.6%	546	14.4%	.064	5.2	87	12.1%	93	12.9%	.633	2.5
Obesity	148	7.6%	267	7.1%	.423	2.2	48	6.7%	55	7.6%	.474	3.8
Antipsychotic medications PDC												
% of patients with PDC 0–0.50	450	23.2%	2311	61.0%	<.001	82.9	331	45.8%	291	40.3%	.034	11.2
% of patients with PDC 0.51–0.80	558	28.8%	684	18.1%	<.001	25.5	181	25.1%	199	27.6%	.282	5.7
% of patients with PDC 0.81–1.00	931	48.0%	791	20.9%	<.001	59.5	210	29.1%	232	32.1%	.209	6.6
PDC gap >30 days	837	43.2%	2407	63.6%	<.001	41.8	434	60.1%	419	58.0%	.422	4.2
Baseline all-cause health care utilization												
Hospitalization days, n	20.1	45.4	22.5	60.3	.095	4.5	18.9	51.3	19.0	41.4	.978	0.1
Any inpatient visit	1469	75.8%	2351	62.1%	<.001	29.8	491	68.0%	487	67.5%	.822	1.2
Any ER visit	1133	58.4%	2230	58.9%	.733	1.0	426	59.0%	421	58.3%	.789	1.4
Inpatient visits, n	6.6	9.8	2.8	5.4	<.001	47.0	4.2	7.3	4.1	7.6	.883	0.8
ER visits, n	2.9	6.7	2.8	6.4	.376	2.5	2.9	6.7	2.9	6.3	.945	0.4
Outpatient office visits, n	10.5	24.1	13.8	31.1	<.001	11.9	11.5	29.5	10.8	21.1	.610	2.7
Other outpatient visits, n	16.9	21.4	6.2	13.1	<.001	60.4	10.1	12.7	9.8	23.6	.794	1.4
Pharmacy visits, n	28.5	20.3	22.3	20.6	<.001	30.7	23.9	18.7	23.9	19.4	.995	0.04
Baseline all-cause health care costs												
Inpatient visit costs	\$9240	\$20,629	\$12,620	\$42,388	<.001	10.1	\$8712	\$19,358	\$10,425	\$20,690	.105	8.5
Outpatient ER visit costs	\$524	\$1400	\$523	\$1320	.986	0.1	\$514	\$1335	\$597	\$1691	.301	5.4
Outpatient office visit costs	\$1309	\$6077	\$1488	\$3523	.231	3.6	\$1470	\$8452	\$1320	\$3156	.657	2.3
Other outpatient costs	\$3595	\$5078	\$1413	\$2995	<.001	52.3	\$2308	\$3895	\$2150	\$4652	.484	3.7
Pharmacy costs	\$10,647	\$8976	\$4556	\$8815	<.001	68.5	\$7162	\$7215	\$7175	\$11,600	.980	0.1
Total (outpatient + inpatient + pharmacy) costs	\$25,315	\$25,861	\$20,600	\$44,951	<.001	12.9	\$20,167	\$25,100	\$21,668	\$26,023	.265	5.9

Variables controlled for the PSM were age, gender, comorbidities (bipolar disorder, any depression disorder, attention deficit hyperactivity disorder, panic disorder, anxiety, suicide attempt and intentional injuries, substance abuse and alcohol abuse, diabetes, obesity), schizophrenia subtype, prior antipsychotic treatment PDC and pre-index health care resource utilization.

OAT: oral antipsychotic therapy; PP1M: paliperidone palmitate once monthly; SD: standard deviation; STD: standardized difference.

Table 2. Clinical outcomes, health care utilization and costs for matched PP1M and OAT cohorts (12 month follow-up period).

	PP1M Cohort (N = 722)		OAT Cohort (N = 722)			
	N/Mean	%/SD	N/Mean	%/SD	p-Value	STD
Clinical Outcomes						
Discontinuation	221	30.6%	285	39.5%	<.001	18.6
Time to discontinuation	139.1	87.0	133.9	87.1	.503	6.0
Persistence	501	69.4%	437	60.5%	<.001	18.6
PDC	0.7	0.3	0.6	0.3	<.001	26.8
Switching	156	21.6%	200	27.7%	.007	14.2
Follow-up All-cause Health Care Utilization						
Any inpatient visit	445	61.6%	559	77.4%	<.001	34.8
Any outpatient ER visit	354	49.0%	404	56.0%	.008	13.9
Any outpatient office visit	602	83.4%	618	85.6%	.245	6.1
Any other outpatient visit	569	78.8%	647	89.6%	<.001	29.9
Any pharmacy visit	722	100.0%	722	100.0%		0.0
Hospitalization days, <i>n</i>	15.0	45.8	27.7	60.2	<.001	23.8
Inpatient visits, <i>n</i>	5.0	8.8	7.9	10.8	<.001	30.2
Outpatient ER visits, <i>n</i>	2.1	5.6	2.9	7.1	.016	12.7
Outpatient office visits, <i>n</i>	9.6	25.3	11.2	23.6	.196	6.8
Other outpatient visits, <i>n</i>	13.1	15.0	16.2	24.3	.004	15.2
Pharmacy visits, <i>n</i>	30.6	19.2	30.7	21.6	.932	0.4
Follow-up All-cause Health Care Costs						
Inpatient visit costs	\$5060	\$14,036	\$10,880	\$25,061	<.001	28.7
Outpatient ER visit costs	\$379	\$1253	\$547	\$1500	.021	12.1
Outpatient office visit costs	\$997	\$2131	\$1412	\$3896	.012	13.2
Other outpatient costs	\$2763	\$4278	\$3353	\$5247	.019	12.3
Pharmacy costs	\$16,347	\$8578	\$9115	\$6760	<.001	93.6
Total (outpatient + inpatient + pharmacy) costs	\$25,546	\$18,589	\$25,307	\$29,154	.853	1.0

OAT: oral antipsychotic therapy; PP1M: paliperidone palmitate once monthly; SD: standard deviation; STD: standardized difference; PDC: Proportion of days covered; ER: Emergency Room.

Figure 2. All-cause health care utilization of matched PP1M and OAT cohorts. PP1M: paliperidone palmitate once monthly; OAT: oral antipsychotic therapy; ER: emergency room.

Figure 3. All-cause health care costs of matched PP1M and OAT cohorts. PP1M: paliperidone palmitate once monthly; OAT: oral antipsychotic therapy; ER: emergency room.

those treated with PP1M. To the best of our knowledge, this is the first study which compares the treatment patterns (discontinuation, persistence, switching), all-cause health care utilization, and costs among patients prescribed PP1M or OATs in the Medi-Cal population.

Previous large, randomized controlled trials have reported high antipsychotic discontinuation rates among patients with schizophrenia^{7,28}. A non-randomized study conducted by Tiihonen *et al.* reported that 54% of 2588 patients with schizophrenia discontinued their antipsychotic treatment during the first 30 days after hospital discharge¹⁵. Despite high overall discontinuation rates among this population, the pairwise comparison between LAIs and their equivalent oral formulations showed that LAIs were associated with a significantly lower risk of discontinuation¹⁵. The results of our study are consistent with the above-mentioned study as well as other previous studies, suggesting that the patients prescribed PP1M had significantly lower discontinuation, switching rates, and non-adherence (calculated by PDC) compared to those prescribed OATs^{29,30}. High discontinuation rates among OAT cohort patients may be due to a lack of motivation and cooperation, or the frequent daily administration of the drug compared to PP1M patients who visit a health care professional once a month for the drug administration^{10,15,17,31}. Greater adherence to LAI therapy helps physicians make beneficial decisions and distinguishes compliance failure from efficacy failure, which can help to prevent the switching of medications^{15,30}.

Results from our descriptive analysis demonstrated that baseline characteristics differed among patients who were initiated on PP1M versus those on OATs. Some notable differences between the PP1M and OAT cohorts' baseline characteristics included the proportion of patients with evidence of polypharmacy, number of unique antipsychotic medications as well as all-cause health care utilization and costs. Thus, PSM is an effective methodology to control for baseline differences. After comparing the well matched cohorts, the current study found that patients in the PP1M cohort had significantly fewer all-cause inpatient, outpatient ER, and outpatient visits compared to those who initiated OATs. While these differences led to lower associated inpatient, outpatient ER, outpatient office, and outpatient costs, the PP1M cohort had higher mean pharmacy costs, resulting in similar total all-cause total costs between cohorts. Although PP1M was observed to be associated with higher pharmacy costs vs. OATs, it is important to keep in mind the current study applied pharmacy costs without considering rebates, thus it is likely that Medi-Cal would experience cost savings associated with PP1M use after pharmacy rebates are considered. Our results are consistent with two previous studies comparing health care costs and utilization among patients with schizophrenia who were on PP1M or OATs^{10,26}. A study conducted among Medicaid-covered patients with schizophrenia suggested that patients who initiated treatment with a LAI had overall reduced hospitalizations, LOS, and hospital charges, better medication adherence, and lower utilization of health services¹¹. Results from this study reported outcomes among all LAIs; however, our study reported exclusively on PP1M. Previous studies have reported that

the prescription of LAIs is associated with a 50–65% decrease in the length of inpatient stay and a lower risk of re-hospitalizations leading to better global outcomes^{6,15,24}.

Despite the advantages of LAI antipsychotics associated with lower costs and hospitalizations compared to OATs, there are several barriers to the utilization of LAIs in the United States, such as negative attitudes of health care professionals, treatment settings, and insurance coverage^{32,33}. Also, patient-related factors such as pain of injection, fear of loss of autonomy, and reluctance contribute to the lower utilization of these LAIs³⁴. The unavailability of experienced health care professionals may also contribute to the limited outpatient use of LAIs. The results from our study, along with consistent results from previous studies, should help highlight the advantages of LAIs over OATs; the adherence advantage is especially noteworthy, as long treatment duration is a major driver of better clinical and functional outcomes in the long-term treatment of patients with schizophrenia²⁹. Lower use of inpatient services is also a key advantage of LAIs over OATs since it provides economic benefit which is a key factor from the payers' perspective²⁶.

The results of our study should be interpreted within the context of several limitations. Given that this was an analysis of claims data, inherent limitations of claims database analyses need to be considered: these include unavailability of clinical measures, the possibility of information bias due to coding errors, and lack of generalizability beyond the population studied. Treatment selection bias, which is clearly depicted in the histogram (Figure 1), shows the likelihood of patients in each of the cohorts to be treated with PP1M. According to the histogram, patients in the OAT cohort were less likely to receive a PP1M treatment. Therefore, through application of the propensity score matching approach using a greedy matching method, patients in the PP1M cohort were successfully matched to those in the OAT cohort resulting in similar distribution of individual probabilities of receiving PP1M. The other limitation of this study is that we only compared one LAI, PP1M, with other OATs. Since the main focus of our study was to help health care professionals understand the value of PP1M rather than LAIs in general, interpretations should be made cautiously.

This study contributes valuable information^{10,35–37}. Future studies should be conducted to compare all LAIs and OATs while considering direct and indirect sources of health care utilization and costs. Raising awareness regarding the benefits of using LAIs is necessary in order to reduce relapses and improve health-related quality of life for patients with schizophrenia.

Conclusion

This large database analysis demonstrated that patients with schizophrenia treated with PP1M had fewer mean annual hospitalizations and shorter mean LOS compared to a matched cohort of patients treated. Patients who were treated with PP1M had a lower rate of discontinuations and index drug switches, better persistence, and higher PDC. Patients who were treated with PP1M also had significantly

fewer inpatient, ambulatory, and ER visits. Although pharmacy costs were significantly higher among PP1M patients, there was no difference in total annual health care costs between PP1M and PAT patients among the PP1M and OAT cohort patients.

Transparency

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Author contributions: All authors conceived of the study design. L.W. and O.B. analyzed and interpreted the data. All authors contributed to the writing of this manuscript. All authors read and approved the final manuscript.

Declaration of financial/other relationships

J.A.P. and D.D. have disclosed that they are paid employees of Janssen Scientific Affairs LLC. L.W. and O.B. have disclosed that they are employees of STATinMED Research, which is a paid consultant to Janssen Scientific Affairs LLC. H.Y. has disclosed that he is a paid consultant to STATinMED Research, which is a paid consultant to Janssen Scientific Affairs LLC.

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Notes

1. Invega Sustenna is a registered trade name of Janssen Pharmaceuticals, Inc Titusville, NJ
2. Risperdal Consta (Janssen Pharmaceuticals, Inc., Titusville, NJ)
3. Zyprexa Relprevv (Eli Lilly & Co, Indianapolis, IN)
4. Abilify (Otsuka America Pharmaceutical, Inc, Rockville, MD)
5. Haldol (various), and Prolixin (various)

References

1. van Os J, Kapur S. Schizophrenia. *Lancet* 2009;374:635-45
2. Hassett A, Ames D, Chiu E, eds. *Psychosis in the Elderly*. Boca Raton, FL: CRC Press, 2005
3. Castle D, Wessely S, Der G, et al. The incidence of operationally defined schizophrenia in Camberwell, 1965–84. *Br J Psychiatry* 1991;159:790-4
4. Rössler W, Salize HJ, van Os J, et al. Size of burden of schizophrenia and psychotic disorders. *Eur Neuropsychopharmacol* 2005;15:399-409
5. Wu EQ, Birnbaum HG, Shi L, et al. The economic burden of schizophrenia in the United States in 2002. *J Clin Psychiatry* 2005; 66:1122-9
6. Lafeuille MH, Laliberté-Auger F, Lefebvre P, et al. Impact of atypical long-acting injectable versus oral antipsychotics on rehospitalization rates and emergency room visits among relapsed schizophrenia patients: a retrospective database analysis. *BMC Psychiatry* 2013;13:221
7. Lieberman JA, Stroup TS, McEvoy JP, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med* 2005;353:1209-23
8. Emsley R, Oosthuizen P, Koen L, et al. Oral versus injectable antipsychotic treatment in early psychosis: post hoc comparison of two studies. *Clin Ther* 2008;30:2378-86
9. NAMI. Arlington, Long-acting Injectable Antipsychotics Fact sheet. VA: National Alliance on Mental Illness, 2013 May. Available at: http://www2.nami.org/factsheets/lai_factsheet.pdf [Last accessed 30 August 2016]
10. Xiao Y, Muser E, Lafeuille MH, et al. Impact of paliperidone palmitate versus oral atypical antipsychotics on healthcare outcomes in schizophrenia patients. *J Comp Eff Res* 2015;4:579-92
11. Brown JD, Barrett A, Caffery E, et al. Medication continuity among Medicaid beneficiaries with schizophrenia and bipolar disorder. *Psychiatric Serv* 2013;64:878-85
12. Weiden PJ, Kozma C, Grogg A, et al. Partial compliance and risk of hospitalization among California Medicaid patients with schizophrenia. *Psychiatr Serv* 2004;55:886-91
13. McCombs JS, Nichol MB, Johnstone BM, et al. Antipsychotic drug use patterns and the cost of treating schizophrenia. *Psychiatr Serv* 2000;51:525-7
14. Wu EQ, Shi L, Birnbaum H, et al. Annual prevalence of diagnosed schizophrenia in the USA: a claims data analysis approach. *Psychol Med* 2006;36:1535-40
15. Tiihonen J, Haukka J, Taylor M, et al. A nationwide cohort study of oral and depot antipsychotics after first hospitalization for schizophrenia. *Am J Psychiatry* 2011;168:603-9
16. Kirk Morton N, Zubek D. Adherence challenges and long-acting injectable antipsychotic treatment in patients with schizophrenia. *J Psychosoc Nurs Ment Health Serv* 2013;51:13-18
17. Haddad PM, Taylor M, Niaz OS. First-generation antipsychotic long-acting injections v. oral antipsychotics in schizophrenia: systematic review of randomised controlled trials and observational studies. *Br J Psychiatry Suppl* 2009;52:S20-S8
18. Chue P, Llorca P, Duchesne I, et al. Hospitalization rates in patients during long-term treatment with long-acting risperidone injection. *J Appl Res* 2005;5:266-74
19. Olivares JM, Rodriguez-Morales A, Diels J, et al. Long-term outcomes in patients with schizophrenia treated with risperidone long-acting injection or oral antipsychotics in Spain: results from the electronic Schizophrenia Treatment Adherence registry (e-STAR). *Eur Psychiatry* 2009;24:287-96
20. Taylor M, Currie A, Lloyd K, et al. Impact of risperidone long acting injection on resource utilization in psychiatric secondary care. *J Psychopharmacol* 2008;22:128-31
21. Fuller M, Shermock K, Russo P, et al. Hospitalisation and resource utilisation in patients with schizophrenia following initiation of risperidone long-acting therapy in the Veterans Affairs Healthcare System. *J Med Econ* 2009;12:317-24
22. Invega Sustenna (paliperidone palmitate). Available at: <http://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=022264>
23. Einarson TR, Geitona M, Chaidemenos A, et al. Pharmacoeconomic analysis of paliperidone palmitate for treating schizophrenia in Greece. *Ann Gen Psychiatry* 2012;11:18
24. Einarson TR, Vicente C, Zilbershtein R, et al. Pharmacoeconomic analysis of paliperidone palmitate versus olanzapine pamoate for chronic schizophrenia in Norway. *Acta Neuropsychiatr* 2013; 25:85-94
25. Mehnert A, Nicholl D, Pudas H, et al. Cost effectiveness of paliperidone palmitate versus risperidone long-acting injectable and olanzapine pamoate for the treatment of patients with schizophrenia in Sweden. *J Med Econ* 2012;15:844-61
26. Baser O, Xie L, Pesa J, et al. Healthcare utilization and costs of Veterans Health Administration patients with schizophrenia treated with paliperidone palmitate long-acting injection or oral atypical antipsychotics. *J Med Econ* 2015;18:357-65

27. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res* 2011;46:399-424
28. Kahn RS, Fleischhacker WW, Boter H, et al. Effectiveness of antipsychotic drugs in first-episode schizophrenia and schizophreniform disorder: an open randomised clinical trial. *Lancet* 2008;371:1085-97
29. Zhu B, Ascher-Svanum H, Shi L, et al. Time to discontinuation of depot and oral first-generation antipsychotics in the usual care of schizophrenia. *Psychiatr Serv* 2008;59:315-17
30. Peng X, Ascher-Svanum H, Faries D, et al. Decline in hospitalization risk and health care cost after initiation of depot antipsychotics in the treatment of schizophrenia. *Clinicoecon Outcomes Res* 2011;3:9-14
31. Kozma CM, Slaton T, Dirani R, et al. Changes in schizophrenia-related hospitalization and ER use among patients receiving paliperidone palmitate: results from a clinical trial with a 52-week open-label extension (OLE). *Curr Med Res Opin* 2011;27:1603-11
32. Jaeger M, Rossler W. Attitudes towards long-acting depot antipsychotics: a survey of patients, relatives and psychiatrists. *Psychiatry Res* 2010;175:58-62
33. Heres S, Schmitz FS, Leucht S, et al. The attitude of patients towards antipsychotic depot treatment. *Int Clin Psychopharmacol* 2007;22:275-82
34. Patel MX, Taylor M, Davis AS. Antipsychotic long-acting injections: mind the gap. *Br J Psychiatry Suppl* 2009;52:S1-S4
35. Xiao Y, Muser E, Fu DJ, et al. Comparison of Medicaid spending in schizoaffective patients treated with once monthly paliperidone palmitate or oral atypical antipsychotics. *Curr Med Res Opin* 2016;32:759-69
36. Pesa JA, Muser E, Montejano LB, et al. Cost and resource utilization among Medicaid patients with schizophrenia treated with paliperidone palmitate or oral atypical antipsychotics. *Drugs – Real World Outcomes* 2015;2:377-85
37. Morrato EH, Parks J, Campagna EJ, et al. Comparative effectiveness of injectable paliperidone palmitate versus oral atypical antipsychotics: early postmarketing evidence. *J Comp Eff Res* 2015;4:89-99