## Impact of Paliperidone Palmitate Versus Oral Atypical Antipsychotics on Health Care Resource Use and Costs in Veterans With Schizophrenia and Comorbid Substance Abuse



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#### **ABSTRACT**

Purpose: Almost half of all patients diagnosed with schizophrenia have a history of substance abuse (SA). However, data on treatment of schizophrenia with paliperidone palmitate (PP) among patients with comorbid SA are limited. The objective of this study was to compare all-cause and SA-related health care resource utilization and costs in veterans with schizophrenia and co-occurring SA who were treated with PP versus oral atypical antipsychotics (OAAs).

Methods: Veterans Health Administration electronic health record data were used to conduct a retrospective longitudinal study in veterans with schizophrenia who initiated PP or OAA between January 1, 2010 and June 30, 2016, had  $\geq$  12 months of enrollment before treatment initiation (baseline), were diagnosed with SA, and had  $\geq 1$  Global Assessment of Functioning score during baseline. Differences in baseline characteristics were adjusted for using inverse probability of treatment weighting. Adjusted cost differences and incidence rate ratios (IRR) for the association between PP versus OAA and all-cause and SA-related health care costs and health care resource utilization in the 12 months after treatment initiation were estimated with corresponding 95% CIs using weighted linear and Poisson regression models, respectively.

Findings: Of 6872 veterans in the study, 1684 (25%) and 5188 (75%) were treated with PP and OAA, respectively. After adjustment, PP was associated with fewer all-cause inpatient (IRR = 0.88; 95% CI, 0.85 to 0.90), mental health-related inpatient (IRR = 0.88; 95% CI, 0.85 to 0.91), and long-term care stays (IRR = 0.53; 95% CI, 0.44 to 0.64), but

more frequent mental health intensive case management visits (IRR = 1.51; 95% CI, 1.49 to 1.53) compared with OAA (all P < 0.001). Similarly, PP was associated with significantly lower rates of SA-related inpatient stays (IRR = 0.80; 95% CI, 0.77 to 0.83), mental health stays (IRR = 0.85; 95% CI, 0.82 to 0.88), long-term care stays (IRR = 0.22; 95% CI, 0.15 to 0.32), and outpatient visits (IRR = 0.78; 95% CI, 0.77 to 0.79) than OAA (all P < 0.001). Relative to OAA, patients treated with PP also had lower mean annual all-cause (cost difference = -\$10,473; 95% CI, -\$17,827 to -\$3491) and SA-related (cost difference = -\$8457; 95% CI, -\$12,710 to -\$3638) medical costs (all P < 0.001).

Implications: PP was associated with significant total medical cost savings resulting from fewer hospitalizations and lower rates of SA-related health care resource utilization compared with OAA in patients with schizophrenia and comorbid SA. Thus, PP appears to be a valuable treatment option for patients in this subpopulation. (Clin Ther. 2017;39:1380–1395) © 2017 The Authors. Published by Elsevier HS Journals, Inc.

Key words: atypical antipsychotics, long-acting injectable antipsychotics, paliperidone palmitate, schizophrenia, substance abuse.

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#### **INTRODUCTION**

Schizophrenia is a chronic mental illness that affects patients' perceptions of the world and hinders their abilities to develop interpersonal relationships. In 2008, the incidence of schizophrenia in the United States was estimated to be 15.2 per 100,000 persons, with a point prevalence of 4.6 per 1000. Almost half of all patients with schizophrenia also have a history of substance abuse (SA). This rate is much higher than that among individuals who are not diagnosed with schizophrenia, suggesting that there may be multiple factors and pathways contributing to the increased risk of SA among patients with schizophrenia.<sup>2,3</sup> For instance, the higher prevalence of SA in this patient group may be a result of the role that brain dopaminergic pathways play in drug use, and may explain why patients with schizophrenia may be inclined to use drugs in an attempt to counteract the negative effects they experience from schizophrenia.<sup>2,4,5</sup> This is particularly important, as SA can affect the clinical profile of patients and exacerbate symptoms. Other consequences of comorbid SA in patients with schizophrenia include more positive symptoms; relapse of psychosis; and increased risk of violence, suicide, incarceration, and side effects of antipsychotics (APs).<sup>6</sup>

Schizophrenia and other mental illnesses are common among veterans in the United States, and the incidence of schizophrenia in this population has increased over time.<sup>7-9</sup> In addition, the abuse of substances, particularly alcohol, painkillers, and other prescription medication, is more common among veterans than in the general population. 10 The US Department of Veterans Affairs health care system (Veterans Health Administration [VHA]) offers therapy and treatment programs for veterans seeking treatment for substance use disorders and schizophrenia, in addition to long-term home care, primary, specialty, and inpatient care, rehabilitation services, and other services to US military veterans. 11 As an integrated care system, the VHA provides a wide array of services to veterans with schizophrenia with comorbid SA.<sup>12</sup> This involves psychological interventions and pharmacotherapy with APs, with the goal of preventing relapse and reducing the severity of acute episodes. Treatment may involve the use of long-acting injectable therapies (LATs), which are administered monthly, or oral atypical antipsychotics (OAAs), which must be taken daily to ensure effectiveness. Nonadherence undermines the effectiveness of OAAs, and is a key predictor of relapse and hospitalization in schizophrenia. A study among patients with schizophrenia found that patients who were compliant with their prescribed therapies were less likely to have a substance use disorder.<sup>13</sup>

The efficacy of atypical APs and LATs in patients with dual diagnoses of schizophrenia and SA has been studied previously. 14,15 Atypical APs may help reduce cravings for substances and relapses of SA, in addition to reducing negative symptoms of schizophrenia. LATs may lead to improved adherence compared with the use of OAAs, as a result of their monthly administration. Additionally, the use of LATs necessitates greater contact between patients and health care providers, which may increase the chances that comorbidities, such as SA, will be detected and treated. However, the impact of LAT, and specifically paliperidone palmitate (PP), an atypical LAT dosed monthly and approved by the Food and Drug Administration in 2009 for acute and maintenance treatment of schizophrenia on health care resource utilization (HRU) and costs, is not well understood.

While PP treatment was found to be associated with significantly fewer inpatient admissions and total cost savings compared with OAAs, <sup>16</sup> few studies have examined the effect of treatment on HRU and costs in patients with schizophrenia and SA. This study compared all-cause and SA-related HRU and economic outcomes in US veterans with schizophrenia and comorbid SA treated with PP versus OAAs.

#### **METHODS**

#### Study Design and Patient Selection

Electronic medical records and cost data from the VHA were used to conduct a retrospective longitudinal cohort study among veterans with schizophrenia and comorbid SA. The VHA's Corporate Data Warehouse, an integrated and unified medical records system, contains information from all outpatient visits, hospital stays, treatments, prescriptions, laboratory results, billing, and benefits information. It also contains demographic and socioeconomic information, in addition to estimated costs of individual VHA hospital stays and health care encounters. Veterans' eligibility for VHA benefits is determined using priority groups based on factors such as disability, military exposures, and income. The study was approved by the Institutional Review Board at

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