

INTRODUCTION

Prior research has established the critical role of maintenance antipsychotic drugs (APD) in the management of patients with serious mental illness in preventing relapse¹⁻³, and 25% to as many as 50% of mentally ill patients are not adherent to their prescription regimen.⁴⁻⁶

Unfortunately, such nonadherence is associated with several negative clinical outcomes in patients with schizophrenia (e.g. symptom recurrence, increased number of inpatient admissions, longer hospital stay)⁷⁻⁹ and bipolar disorder (e.g. increased mood symptoms, worse functioning).¹⁰

In addition, patients with serious mental illness have an increased risk for various substance use disorders, and concurrent substance use may contribute to treatment nonadherence.^{3,5-11}

OBJECTIVES

To assess the incidence of potential non-adherence among patients prescribed antipsychotic agents and to identify the use of illicit substances and/or non-prescribed medications in these patients through urine drug monitoring (UDM)

METHODS

- Between 2013 and 2016, 62,342 urine samples were obtained from patients prescribed APD.
- Samples were classified as APD positive (a positive LC/MS/MS result for APD parent and/or metabolite) or APD negative (negative LC/MS/MS).
- Samples were also classified as positive or negative for the following: non-prescribed opiate, synthetic opioids or benzodiazepines, cocaine and THC.
- Logistic regression analyses were used to calculate adjusted odds ratios (aOR) and 95% CIs.

Table 1. Antipsychotic Medications and Metabolites Tested

Drug	Metabolite(s)
Aripiprazole	Dehydroaripiprazole, OPC3373
Clozapine	n-desmethylclozapine
Haloperidol	
Lurasidone	Hydroxylurasidone
Olanzapine	n-desmethylolanzapine
Paliperidone	
Quetiapine	7-hydroxyquetiapine
Risperidone	9-hydroxyrisperidone
Ziprasidone	

RESULTS

- A total of 62,342 urine samples obtained from patients prescribed APD were retrospectively analyzed.
- The study population was 49.2% male (mean age, 41.6 ± 14.2 years)

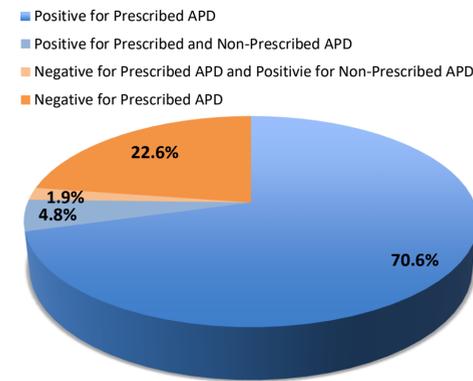
Table 2. Demographic Information*

Characteristics	N=62,342
Sex, n (%)	
Female	31,677 (50.8%)
Male	30,660 (49.2%)
Age	
Mean	41.6 ± 14.2 yrs
Median	43 yrs
Range	4 - 98 yrs
Age Group, n (%)	
<20 years	4,334 (7.0%)
20-29 years	9,205 (14.8%)
30-39 years	13,649 (21.9%)
40-49 years	14,278 (22.9%)
50-59 years	15,225 (24.4%)
60-69 years	4,855 (7.8%)
70 or more years	757 (1.2%)
Prescribed Antipsychotic Medication**	
Quetiapine	15,635 (25.1%)
Aripiprazole	11,663 (18.7%)
Risperidone	11,352 (18.2%)
Olanzapine	6,126 (9.8%)
Paliperidone	4,176 (6.7%)
Ziprasidone	2,903 (4.7%)
Haloperidol	2,496 (4.0%)
Clozapine	1,191 (1.9%)
Multiple	6,671 (10.9%)
Primary Payor Type, n (%)	
Commercial Insurance	5,115 (8.3%)
Medicaid	25,121 (40.3%)
Medicare	18,928 (30.4%)
Self-pay	12,878 (20.7%)
Region, n (%)	
Northwest	2,112 (3.4%)
Midwest	4,917 (7.9%)
South	53,628 (86.0%)
West	1,685 (2.7%)
Year Data Reported, n (%)	
2013	2,831 (4.5%)
2014	16,860 (27.1%)
2015	26,581 (42.7%)
2016	16,031 (25.7%)

* Note that there were a small number of samples for which some demographic data were missing.
 ** All doses and formulations were included. PRN prescriptions were not included. Patients prescribed >1 antipsychotic medication were categorized in the Multiple group.

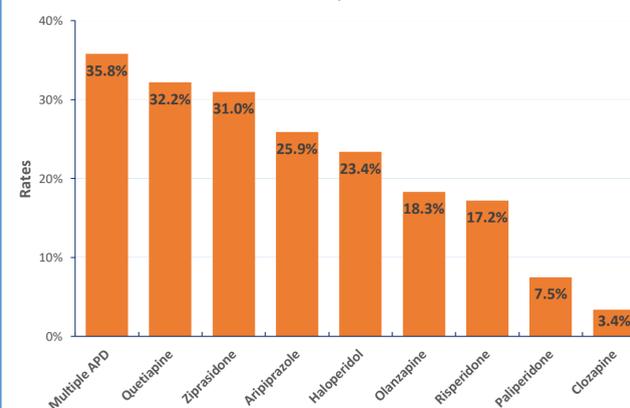
RESULTS

Figure 1. UDM Results of Prescribed Antipsychotic Drugs (APD) N=62,342



- Overall, UDM was positive for APD in 75.3% of samples and negative in 24.7%, and varied widely by prescribed drug.
- A non-prescribed APD (either parent or metabolite) was found in 6.7% of samples (4.8% had both the prescribed APD present and an additional non-prescribed APD, and 1.9% were missing the prescribed APD with a different APD found).

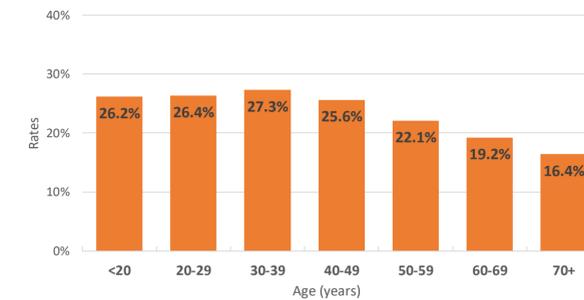
Figure 2. Negative UDM Results by APD Prescribed N=62,342



- Patients prescribed quetiapine, ziprasidone, or multiple APDs had the highest rate of negative samples (32.2%, 31.0% and 35.8%, respectively).
- Patients on aripiprazole, risperidone, olanzapine, and haloperidol being in the mid-range (25.9%, 17.2%, 18.3% and 23.4%, respectively).
- Samples from those on paliperidone and clozapine were least commonly negative (7.5% and 3.4%, respectively).

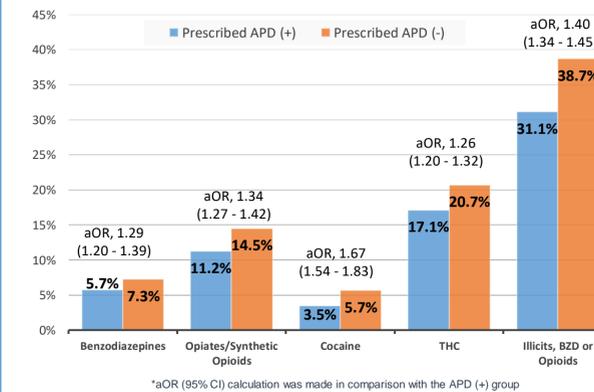
RESULTS

Figure 3. Negative UDM Results for APD by Age Group



- Patients ages <40 had the highest rate of negative test results (26-27%), which steadily declined with every decade of life thereafter (compared to ages 30-39, aOR 0.88 (95% CI: 0.84, 0.93); 0.75 (95%CI: 0.71, 0.79); 0.69 (95%CI: 0.63, 0.75); and 0.61 (95%CI: 0.49, 0.75), for each increasing age category, respectively).

Figure 4. Non-Disclosed Substances Detected by UDM



- APD negative individuals were more likely than APD positive to have a non-prescribed opiate/synthetic opioid found (14.5% vs. 11.2%; OR 1.34; 95% CI, 1.27-1.42, as well as a non-prescribed benzodiazepine (7.3% vs. 5.7%; OR 1.29; 95% CI 1.20-1.39).
- They also were more like to have THC found (20.7% vs. 17.1%; OR 1.26; 95% CI, 1.20-1.32), or cocaine found (5.7% vs. 3.5%; OR 1.67; 95% CI, 1.54- 1.83).

LIMITATION

This data set reflects unique samples and not unique patients; multiple results for negative results or potential substance misuse from the same patient may be contributing to an overstatement of the problem.

CONCLUSIONS

- Results of these analyses are consistent with the published literature showing that medication nonadherence and substance misuse are common problems in patients treated with antipsychotic medications.
- In this analysis, potential nonadherence to prescribed antipsychotic therapy was associated with increased use of marijuana, cocaine, and non-prescribed opioids and benzodiazepines.
- These data suggest that UDM in patients who are prescribed APD can be of value in both monitoring adherence to APD therapy, and in identifying the use of inappropriate prescription and non-prescription substances.
- Nonadherence to antipsychotic treatment may be the single most important modifiable factor contributing to psychotic relapse and hospitalization in patients with mental illness.
- Identification of medication nonadherence and/or substance misuse through UDM may allow for early clinical intervention, thereby improve therapeutic outcomes.

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DISCLOSURES & CONTACT

- Drs Ko and Smith are employees of Ameritox LLC, Baltimore, MD.
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