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FACTORS PREDICTING THE LIKELIHOOD OF LURASIDONE INITIATION IN A US EMPLOYER DATABASE

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ABSTRACT

Objective: Understanding the characteristics' of patients that initiate a new antipsychotic in the market is important to determine the clinical-decision making patterns in real-world settings. To predict the demographic, diagnostic, comorbid, and prior drug utilization factors that may impact the likelihood of subjects initiating lurasidone, an analysis of a US employer data was conducted.

Methods: Analyses of administrative claims data from the Human Capital Management Services Research Reference Database comprised of multiple large geographically dispersed US employers from 2/1/2011(lurasidone launch) through 9/30/2012. All continuously enrolled subjects with a schizophrenia or bipolar disorder diagnosis with a prescription claim of lurasidone were classified as lurasidone subjects, those without a prescription claim for lurasidone were assigned to the control group. Demographics, Charlson comorbidity index score, specific bipolar disorder or schizophrenia diagnoses, and use of atypical antipsychotics were described using means for continuous variables and proportions for categorical variables. Factors predicting the likelihood of initiating lurasidone or other atypical antipsychotics were evaluated using stepwise logistic regression.

Results: From a total of 127 lurasidone subjects and 7754 controls, 43 lurasidone subjects (1.1%) and 3822 control subjects were eligible for analysis with 40.4% employees, 31.2% spouses, and 28.4% dependents. The employees/spouses were 67% female, mean age 44.1 (standard deviation=10.8) years and mean Charlson comorbidity index score of 0.72 (standard deviation=1.42). Dependents were 49% female, with mean age 20.7 (standard deviation=7.4) years and mean Charlson comorbidity index score of 0.27 (standard deviation=0.72). The most commonly used atypical antipsychotics were: aripiprazole=18.6%, quetiapine=18.3%, risperidone=11.6%, olanzapine=6.2%, and ziprasidone=5.7%. Logistic regression found subjects with schizoaffective disorder (ICD-9=295.7x) (odds ratio=3.6, P=0.0023); use of paliperidone (odds ratio=7.8, P<0.0001), ziprasidone (odds ratio=5.3, P<0.0001), or aripiprazole (odds ratio=2.1, P=0.0233); and younger ages (odds ratio=0.97, P=0.0244) were more likely to initiate lurasidone.

Conclusion: In this US employer database, subjects with a schizoaffective disorder and those using paliperidone, ziprasidone, or aripiprazole were over two times as likely to be initiated on lurasidone compared to the control group. Additionally, younger subjects were more likely to take lurasidone than older subjects.

BACKGROUND

- Characteristics of patients that are switched from one treatment option to another in real world settings can potentially help identify the patient profile or patient phenotype with greater likelihood for treatment response and potential long term success in serious mental illnesses like Schizophrenia and Bipolar Disorder.
- Bipolar disorder and schizophrenia are ranked 6th and 9th, respectively, among the top ten causes of disability in the World Health Organization's Global Burden of Disease study.(WHO, 2013; NAMI Global Burden)
  - In the United States, it is estimated that 4% of the population has bipolar disorder and about 1% has schizophrenia.(WHO, 2013; Porter & Kaplan, 2013)
- Lurasidone HCL is an atypical antipsychotic approved for the treatment of adult patients with schizophrenia in October 2010
- Comparative assessments of patient characteristics between those who initiate lurasidone vs those that do not initiate lurasidone may provide early insights about clinical decision-making and treatment patterns.

OBJECTIVE

- To understand the characteristics of patients that initiate a new antipsychotic in the market as an important aid in determining real-world clinical decision making patterns.
- To predict demographic, diagnostic, comorbid, and prior drug utilization factors that may impact the likelihood of initiating lurasidone.

METHODS

- The study focused on the time period from 2/1/2011(lurasidone launch) through 6/30/2012.

Data Source

- Data were extracted from adjudicated health insurance claims within the Human Capital Management Services Research Reference Database, which
  - Pools anonymous data from more than 30 geographically dispersed United States employers (including manufacturing, insurance, retail, transportation, telecommunications, health care, and pharmaceuticals).
  - Contains claims information from more than 1.8 million employees, plus more than 1 million spouses and eligible dependents,
  - Has a geographic representation throughout the United States,
  - Covers a variety of health plans,
  - Contains claims information from more than 1.8 million employees, plus more than 1 million spouses and eligible dependents, and
  - Has been used in prior Bipolar Disorder (Gardner 2006; Brook 2007) and Mental Health Comorbidity (Rajagopalan 2006) research.

Study Cohorts

- All subjects included in this analysis were required to have one or more claims with a primary, secondary, or tertiary International Classification of Diseases, Ninth Revision (ICD-9) code for either:
  - schizophrenia (295.xx), or
  - bipolar disorder (296.0x, 296.1x, 296.4x, 296.5x, 296.6x, 296.7x, or 296.8x)
- Subjects with a prescription claim for lurasidone were classified as lurasidone subjects; those without a prescription claim for lurasidone were assigned to the control group.
- Subjects were required to have continuous eligibility from February 1, 2011 to September 30, 2012.
- The following descriptive characteristics were examined:
  - Demographics,
  - The Charlson comorbidity index score,
  - Diagnosis of bipolar disorder or schizophrenia by ICD-9 code,
  - Agency for Healthcare Research and Quality Specific Categories of comorbidities, and
  - Previous use of atypical antipsychotics.
- Analysis focused on means for continuous variables and proportions for categorical variables.

Statistical Analysis

- Stepwise logistic regression was used to identify the factors predicting the likelihood of initiating lurasidone among the pool of subjects with Bipolar Disorder and Schizophrenia diagnoses.

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RESULTS

- A total of 127 lurasidone subjects and 7754 controls were initially identified.
- After checking for continuous eligibility, 43 lurasidone subjects and 3882 control subjects were eligible for analysis (**Table 1**).
  - The overall population was comprised of employees (40.4%), spouses (31.2%), and dependents (28.4%).
  - The group of employees and spouses were 67% female, mean age 44.1 (standard deviation=10.8) years, and had a mean Charlson comorbidity index score of 0.72 (standard deviation=1.42).
  - Dependents were 49% female, mean age 20.8 (standard deviation=7.4) years, and had a mean Charlson comorbidity index score of 0.27 (standard deviation=0.72).

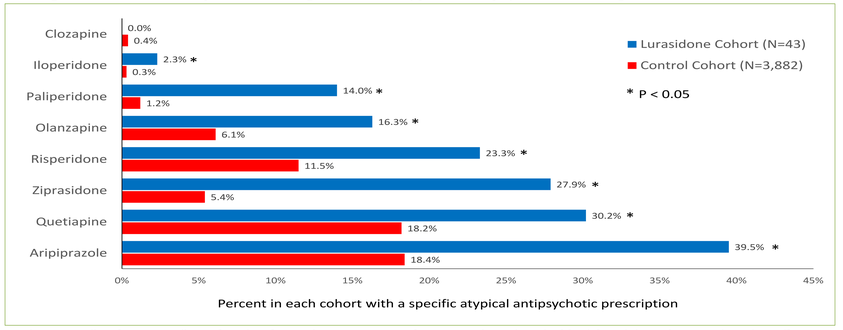
Table 1: Univariate Comparisons of Demographic and Other Characteristics

	Lurasidone Cohort (N=43)	Control Cohort (N=3,882)	P-value
Demographic Variables			
Employees	34.9%	40.5%	0.4553
Spouses	16.3%	31.3%	**0.0342**
Dependents	48.8%	28.2%	**0.0028**
Age, years, mean (SD)	31.1 (13.0)	37.5 (14.5)	**0.0040**
Female, %	55.8%	61.7%	0.4261
Annual Salary of Employee, mean (SD)	$93,162 ($60,807)	$69,523 ($56,388)	**0.0063**
Charlson Index, mean (SD)	0.72 (2.36)	0.59 (1.26)	0.7198
Study Condition (ICD-9 code)			
BP-I, Single Manic Episode (296.0x)	7.0%	10.8%	0.4258
Manic Disorder, Recurrent Episode (296.1x)	0.0%	1.1%	0.4947
BP-I, Most Recent Episode Manic (296.4x)	20.9%	11.5%	0.0562
BP-I Most Recent Episode Depressed (296.5x)	34.9%	22.0%	**0.0421**
BP-I Most Recent Episode Mixed (296.6x)	34.9%	17.0%	**0.0019**
BP-I Most Recent Episode Unspecified (296.7x)	23.3%	13.5%	0.0645
BP, Other and Unspedified (296.8x)	67.4%	57.2%	0.1789
Simple Type Schizophrenia (295.0x)	2.3%	0.4%	0.0717
Disorganized Type Schizophrenia (295.1x)	0.0%	0.1%	0.8124
Catatonic Type Schizophrenia (295.2x)	0.0%	0.3%	0.7129
Paranoid Type Schizophrenia (295.3x)	4.7%	2.9%	0.4824
Schizophreniform Disorder (295.4x)	0.0%	0.5%	0.6519
Latent Schizophrenia (295.5x)	0.0%	0.2%	0.7639
Schizophrenic D/O, Residual Type (295.6x)	0.0%	0.3%	0.7246
Schizoaffective Disorder (295.7x)	20.9%	4.6%	**<0.0001**
Other Specified Types of Schizophrenia (295.8x)	2.3%	0.5%	0.1099
Unspecified Schizophrenia (295.9x)	7.0%	2.4%	0.0543
Agency for Healthcare Research and Quality Category Description			
Thyroid disorders	18.6%	16.9%	0.7672
Diabetes mellitus without complications	14.0%	12.4%	0.7632
Diabetes mellitus with complication	7.0%	4.5%	0.4313
Other endocrine disorders	9.3%	6.8%	0.5182
Nutritional deficiencies	7.0%	10.5%	0.4480
Disorders of lipid metabolism	20.9%	25.9%	0.4611
Other nutritional; endocrine; metabolic disorders	25.6%	20.0%	0.3674
Headache; including migraine	32.6%	21.1%	0.0666
Other nervous system disorders	25.6%	21.5%	0.5182
Essential hypertension	20.9%	22.6%	0.7908
Nonspecific chest pain	7.0%	17.1%	0.0791
Cardiac dysrhythmias	23.3%	11.5%	**0.0170**
Other upper respiratory infections	44.2%	43.2%	0.8992
COPD and bronchiectasis	4.7%	6.6%	0.6051

BP-I: bipolar I disorder

- Within this study, the most commonly used atypical antipsychotics are shown in **Figure 1**.
- Several significant univariate differences existed between the Lurasidone cohort and the Control cohort (**Table 1** and **Figure 1**):
  - In the Lurasidone cohort there were fewer spouses and more dependents than in the Control cohort.
  - The average age was 6.4 years younger and average annual salaries were $23,640 higher in the Lurasidone cohort than in the Control cohort.
  - Lurasidone cohort patients were more likely to have Depressed or Mixed Bipolar 1 Disorder, Schizoaffective Disorder, or Cardiac Dysrhythmias than Control cohort patients.
  - Lurasidone cohort patients were more likely to have taken any of the atypical antipsychotics in **Figure 1** except clozapine.

Figure 1: Percent of Population Using Different Atypical Antipsychotics during 2/1/2011 to 9/30/2012



- When controlling for potentially confounding factors, logistic regression for initiating lurasidone (**Table 2**) found that subjects with a schizoaffective disorder diagnosis (ICD-9 code 295.7x), previous use of paliperidone, ziprasidone, or aripiprazole use, or younger age were significantly more likely (each P<0.03) to initiate lurasidone

Table 2. Multivariate Logistic Regression Results - Modeling the Probability of Taking Lurasidone in Patients With Bipolar Disorder or Schizophrenia During 2/1/2011 to 9/30/2012

	Logistic Regression			Odds Ratio			Probability of Taking Lurasidone	
Significant Variables	Coefficient	Standard Error	P-Value	Mean	95% Confidence Limits		Patients with the Characteristic	Patients without the Characteristic
Intercept	-4.2600	0.4502	<0.0001					
Age	-0.0265	0.0118	0.0244	0.974	0.952	0.997		
Schizoaffective Disorder (295.7x)	1.2763	0.4187	0.0023	3.583	1.577	8.141	2.38%	0.68%
Previous use of Ziprasidone	1.6666	0.3637	<0.0001	5.294	2.595	10.799	3.36%	0.65%
Previous use of Paliperidone	2.0510	0.5135	<0.0001	7.776	2.842	21.272	5.18%	0.70%
Previous use of Aripiprazole	0.7488	0.3302	0.0233	2.114	1.107	4.039	1.31%	0.62%

DISCUSSION

- The results from the study suggest that patients who initiate lurasidone are likely to be younger, have schizoaffective disorder and have previously used paliperidone, ziprasidone, or aripiprazole.
- These findings may suggest that lurasidone is likely to be prescribed to those who may have failed on multiple atypical antipsychotics such as paliperdone, ziprasidone and aripiprazole. It is plausible that physicians are in active search for medications with good metabolic profile and/or efficacy. The trials of paliperdone, ziprasidone and aripiprazole may have failed to satisfy the needs of individual patients.

LIMITATIONS

- This study has limitations associated with retrospective claims data, including the lack of clinical diagnostic information and the lack of disease severity information.
- Small sample size in the data set may also limit the generalizability of findings.

CONCLUSIONS

- This analysis of a United States employer database found that lurasidone is over two times more likely to be initiated in subjects with a schizoaffective disorder and those with previous use of paliperidone, ziprasidone or aripiprazole compared to the control group.
- Younger subjects were also significantly more likely to initiate lurasidone.
- Future research is needed to replicate the analysis in databases with larger sample sizes, and longer timeframes to correlate subjects' characteristics and prescription patterns.

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