High Dimensional Propensity Score Analysis of SSRI Treatment Effect in Patients with Alcohol Use Disorder and Post-Traumatic Stress Disorder

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Background

- Post Traumatic Stress Disorder (PTSD) and Alcohol Use Disorder (AUD) commonly co-occur with estimated rates of AUD as high as 85% in treatment-seeking patient populations with PTSD.[1]
- Patients with comorbid PTSD and AUD experience higher rates of psychosocial, and medical problems, and higher rates of inpatient hospitalization than those with AUD but not PTSD.[2]
- Literature investigating the effects of Selective Serotonin Reuptake Inhibitors (SSRIs) and other PTSD treatments on AUD symptoms are generally limited by small sample size and focus on alcohol consumption as opposed to outcomes related to functional status.[1]
- Comorbidity of PTSD and AUD is common within the Veteran's Affairs system, which provides a rich source of administrative treatment data for analysis.
- High dimensional propensity score adjustment (HDPSA) has emerged as an empirically useful strategy for assessing medication treatment effects using data available in most administrative healthcare databases.

Objectives

This study has two objectives:

1. To serve as a pilot investigation and proof-of-concept study to determine the applicability of high dimensional propensity score adjustment (HDPSA) techniques to dual diagnosis research, specifically PTSD with comorbid AUD.
2. To estimate SSRI treatment effects on healthcare utilization outcomes related to severity of AUD symptoms.

Design

- This study is a quasi-experimental, population-based, pharmacoepidemiologic cohort study of 4508 veterans seen at the North Texas Veterans Healthcare System between the years 2000 and 2015.
- Candidate patient records were identified from data contained within the Veteran's Affairs Central Data Warehouse using a validated selection algorithm.[3]
- Variable specification and selection were conducted using a multiple-step algorithm for HDPSA designed for use with healthcare claims data.[4]
- Six prespecified outcome measures were assessed including all-cause medical hospitalization, emergency room visits, and psychiatric admissions, and alcohol-related medical hospitalization, emergency room visits, and psychiatric admissions.
- The design and methodology of the study were approved by the North Texas Veterans Healthcare System Institutional Review Board.

Methodology

- Following selection (see selection algorithm for detail) patients with no prior SSRI use were assessed for initiation of and SSRI within 30 days of first PTSD diagnosis.
- Within the total patient population, the prevalence of inpatient and outpatient ICD-9 diagnosis codes, inpatient and outpatient Current Procedural Terminology (CPT) codes, and inpatient and outpatient medications (by drug name) occurring within 180 days prior to first PTSD diagnosis were determined from the VA Central Data Warehouse records.
- The top 10% of each data dimension (ICD-9 codes, CPT codes and medication names) were considered as potential covariates for propensity score generation. Covariates occurring in less than 100 patients were removed from consideration.
- Multiplicative bias (Bias M) was calculated based on relative risk of covariates given each outcome.
- Covariates were ranked by descending values of Log(BiasM). The top 10% of variables were selected for each distinct outcome measure.
- Demographics, service connection, and priority group status as well as the top 10% of variables determined for each outcome were used to generate propensity scores reflecting odds of SSRI initiation.
- A binary logistic regression model was constructed for each outcome including percent of study period taking medication, an interaction medication possession and percent of study period taking medication, as well as SSRI treatment status and propensity score.
- IBM SPSS Statistics version 24 with FUZZY extension was used for propensity score generation and statistical analysis.

Selection Algorithm

All Patients Seen at the North Texas Veterans Healthcare System between 01/01/2000 and 12/31/2015

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Alcohol Use Disorder inclusion criteria:
≥ 2 inpatient or outpatient visits within 2 years, or ≥ 1 discharge assigned ICD-9 diagnosis codes associated with alcohol use disorder: 291.0-291.9, 303.00-303.93, and 305.00 to 305.03.

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PTSD inclusion criteria:
≥ 2 inpatient or outpatient visits within 2 years, or ≥ 1 discharge assigned an ICD-9 diagnosis code associated with Post-Traumatic Stress Disorder: 309.81

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Final Inclusion Selection Criteria:
No SSRI use prior to first recorded PTSD Diagnosis

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Final patient population n = 4508
- SSRI prescribed within 30 days n = 2030
- No SSRI prescribed within 30 days n =2478

Population Demographics (n=4508)

Gender	Male	94.0 %	Marital Status	Married	39.9 %
	Female	6.0 %		Divorced	39.5 %
Race	Black or African American	30.4 %		Widow/widower	2.6 %
	Caucasian	53.1 %		Never Married	18.1 %
	Hispanic/Latino	8.4 %	Average Age (Years)	45.2 ± 13.7	
	Other	8.1 %			

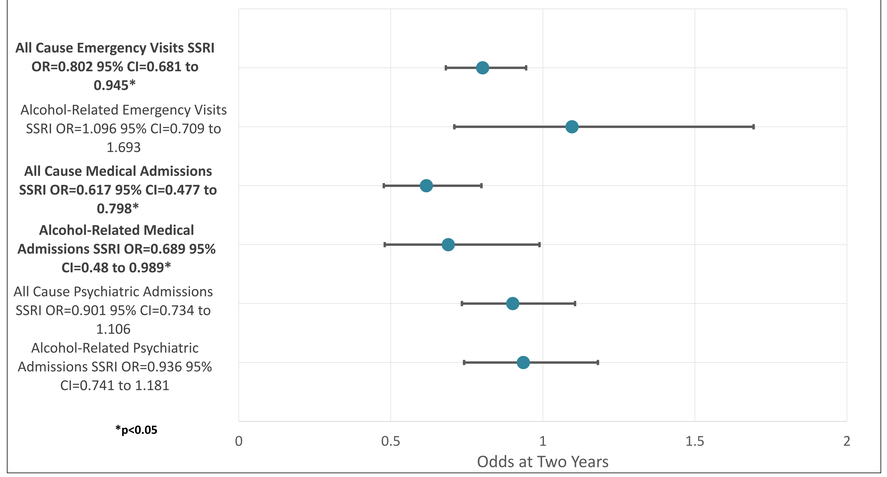
SSRI Treatment Status and Adherence

SSRI treatment status	SSRI prescribed within 30 days of PTSD diagnosis (n=2030)	No SSRI prescribed within 30 days of PTSD diagnosis (n=2478)
Average Medication Adherence (Medication possession ratio * percent of trial time taking medication)	0.408 ± 0.335	0.136 ± 0.244
Total days of any SSRI medication in trial period	385.3 ± 275.7 days	118.6 ± 206.4 days

Population SSRI Usage

SSRI used (% of total population)	Citalopram	71.4%
	Escitalopram	9.4%
	Fluoxetine	31.8%
	Paroxetine	19.6%
	Sertraline	79.4%

Results



- A significant negative relationship was observed between dichotomized SSRI usage and all-cause emergency room visits (p=0.008, OR=0.802 95% CI =0.681 to 0.945).
- A significant negative relationship was observed between dichotomized SSRI usage and all-cause medical admissions (p<0.001, OR=0.617, 95% CI= 0.477 to 0.798).
- A significant negative relationship was observed between dichotomized SSRI usage and alcohol-related medical admission (p=0.044, OR=0.689, 95% CI = 0.480 to 0.989).

Conclusions/Future Directions

Objective 1:

- The HDPSA procedure and analysis allowed for the identification and inclusion of a greater total number of patients with comorbid PTSD and AUD than any prior investigation.
- HDPSA-based analysis appears to be ideal for dual-diagnosis research within the VA system from which large amounts of administrative healthcare data can be leveraged for use in high dimensional models.

Objective 2:

- Initiation of treatment with SSRI medication within 30 days of initial PTSD diagnosis significantly reduced odds of all-cause medical admission, all-cause emergency room visits, and alcohol-related medical admission within two years in a single-hospital VA population diagnosed with PTSD and AUD.
- Based on the trend of lower but nonsignificant odds of several outcomes, the study appears to have been underpowered to detect significant differences in some outcome measures. Studies with larger, more diverse patient populations and more events will provide greater power for detection of SSRI treatment effects.

Future Directions:

- These results demonstrate appreciable clinical benefit, in terms of reduced hospital service utilization, of prescribing an SSRI immediately after PTSD diagnosis to patients with AUD.
- As this study was conducted in a single VA system, future studies with more diverse patient populations and greater number of events will provide more generalizable results.

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Disclosures

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