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Drug and alcohol trajectories among adults with schizophrenia: Data from the CATIE Study

Richard A. Van Dorn[a,*], **Sarah L. Desmarais**[b], **Stephen J. Tueller**[a], **Jennifer M. Jolley**[c], **Kiersten L. Johnson**[b], and **Marvin S. Swartz**[d]

Richard A. Van Dorn: rvandorn@rti.org; Sarah L. Desmarais: sdesmarais@ncsu.edu; Stephen J. Tueller: stueller@rti.org; Jennifer M. Jolley: jmjolley@email.unc.edu; Kiersten L. Johnson: kljeske@ncsu.edu; Marvin S. Swartz: marvin.swartz@duke.edu

[a]RTI International, 3040 E. Cornwallis Road, P.O. Box 12194, Research Triangle Park, NC 27709

[b]Department of Psychology, North Carolina State University, Campus Box 7650, Raleigh, NC 27695

[c]Cecil G. Sheps Center for Health Services Research, University of North Carolina at Chapel Hill, 725 Martin Luther King, Jr. Blvd, Campus Box 7590, Chapel Hill, NC 27599

[d]Department of Psychiatry & Behavioral Sciences, Duke University Medical Center, 238 Civitan Building, Box 3173, Durham, NC 27710

Abstract

Objective—The primary aim is to describe drug and alcohol trajectories in adults with schizophrenia.

Method—Growth mixture models were used to examine disordered and non-disordered use and abstinence in the Clinical Antipsychotic Trials of Intervention Effectiveness trial.

Results—Five classes—*always abstinent; fluctuating use, abuse, and occasional abstinence; occasional (ab)use; stopped (ab)use; abusing*—fit best. Overlap exists between *always abstinent* drug and alcohol classes; less overlap exists across other classes.

Conclusion—There is heterogeneity in drug and alcohol use among adults with schizophrenia. The lack of overlap between classes, save *always abstinent*, suggests modeling drug and alcohol use separately.

*Corresponding author: Richard Van Dorn, RTI International, 3040 E. Cornwallis Road, P.O. Box 12194, Research Triangle Park, NC 27709, Phone: (919) 541-6724, Fax: (919) 485-5555, rvandorn@rti.org.

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Conflict of interest
The authors report no conflicts of interest in connection with any aspect of the research reported in this article.

Contributors
Proposed the study: RAVD, SLD. Managed the literature searches: KLJ. Analyzed the data: ST. Interpretation of findings: RAVD, SLD, ST, JMJ, KLJ, MSS. Wrote the paper: RAVD, SLD, ST. Revised the paper: RAVD, SLD, ST, JMJ, KLJ, MSS. All authors contributed to and have approved the final manuscript.

Keywords

drug use; alcohol use; schizophrenia; longitudinal; growth mixture model

1. Introduction

Substance use is overrepresented in adults with schizophrenia compared to the general population (Regier et al., 1990) and increases risk for poor clinical, health, social, and legal outcomes (Swartz et al., 2006). Despite its high prevalence and deleterious consequences, substance use remains one of the most vexing clinical complications in this population. This, in part, may be due to the limited application of advanced statistical approaches, such as growth mixture modeling (GMM), that describe patterns of substance use over time.

There have been few applications of GMM to explore substance use trajectories in adults with mental illness (Xie et al., 2006; Xie et al., 2009). A few studies have applied GMM to examine psychiatric trajectories among adults with mental illness (Chi and Weisner, 2008) and medication response in adults with schizophrenia (Marques et al., 2011; Muthén and Brown, 2009). Additionally, studies that have utilized GMMs to investigate substance use have focused on disordered use or remission as opposed to including non-disordered use. Prior studies also have focused on patients with diagnosed, co-occurring mental and substance use disorders, instead of including subjects with subtly reducing or escalating patterns. Moreover, drug and alcohol trajectories have not been examined separately, though important differences may exist. Finally, measurement periods have been large, ranging from six weeks to four years. This study adds to the extant literature by examining drug and alcohol trajectories using GMMs and horizontal line plots (Tueller, 2013) in a large sample of adults with schizophrenia.

2. Method

2.1 Sample

Data are from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, a randomized clinical trial investigating the cost-effectiveness of atypical and conventional antipsychotic medications (N=1460). The CATIE study was conducted at over 50 U.S. sites. Only 7% of screened patients were excluded, and the sample resembled a usual-care, noninterventional sample (Swanson et al., 2006). Study design and entry criteria are presented elsewhere (Stroup et al., 2003). The CATIE protocol was approved by local IRBs, and participants gave written informed consent. The RTI International IRB approved the current study's protocol.

2.2. Method

2.2.1. Substance use—The CATIE study used a multi-modal approach to assess alcohol and drug use: (a) SCIDs (First et al., 1996) completed at baseline by MA-level clinicians to diagnose past month substance use disorders; (b) Alcohol Use Scale and Drug Use Scale ratings (Drake et al., 1996) completed by an MD or other clinician regarding patients' substance use during the prior three months; (c) participants' self-reported alcohol and drug use during the prior three months; (d) family members/caregivers' ratings of participants' problems with excessive drug or alcohol use in the prior month; and (e) biological tests (hair radioimmunoassay and urinalysis for drug use). Results were used to determine alcohol and drug abuse/dependence, non-disordered use, and abstinence at each assessment as described in Van Dorn et al. (2012a) and Desmarais et al. (2012).

2.2.2. Procedures—The CATIE study included baseline, 1, 3, 6, 9, 12, 15, and 18 month and end-of-phase assessments.

2.2.3. Analysis—We utilized linear multilevel (clustered by study site) GMMs to examine intra-individual drug and alcohol trajectories using Mplus 7. GMMs were used to extend the estimation of inter-individual variation around one average latent growth curve that describes the intra-individual rate of change in substance use across time. A maximum-likelihood approach was used to classify participants into different latent trajectory classes, each representing a different unobserved subpopulation with its own average latent growth curve. Latent class membership for each participant was estimated by maximizing the posterior probability of group membership (Muthén, 2001, 2004; Muthén and Shedden, 1999). The Bayesian Information Criterion was used to compare GMMs with different numbers of classes (Nylund et al., 2007).[1] The first class (i.e., *always abstinent*) was fixed *a priori* using the training data option. Within class parameters were constrained to reflect this lack of variation. All other participants were allowed to be assigned to the first or any other class.

Missing data were addressed using maximum likelihood estimation assuming missingness at random (MAR), meaning that missingness assumptions hold after controlling for the variables that were related to missingness in the model (Enders, 2010). Exploratory analyses suggested that baseline drug and alcohol values were more strongly predictive of study attrition than other variables. Because baseline values were part of the model, we assumed MAR. All cases with at least one observation were included. In each GMM, class membership was regressed on age, education, sex, minority racial status, and any hospitalization three months prior to enrollment.

3. Results

Most participants were male (73.9%; n=1,079), white (60%; n=874), not married nor cohabitating (81.0%, n=1,181), and had completed high school (74.3%, n=1,085). At baseline, average age was 40.56 years (SD=11.10, range 18–65) and 39.7% (n=579) were not using, while 60.3% (n=881) reported some substance use.

Five-class models fit best for both drugs and alcohol. Participants were assigned to the class for which they had the greatest posterior probability of belonging (Lubke and Tueller, 2010). Figure 1 contains horizontal line plots of participants' drug and alcohol trajectories stratified by latent class. White, orange, and red lines designate abstinence, non-disordered use, and abuse/dependence, respectively. Latent classes and sample sizes within each class were *always abstinent* (class 1, drug: n=701, alcohol: n=627); *fluctuating use, abuse, and occasional abstinence* (class 2, drug: n=285, alcohol: n=356); *occasional (ab)use* (class 3, drug: n=307, alcohol: n=198); *stopped (ab)use* (class 4, drug: n=62, alcohol: n=220); and *abusing* (class 5, drug: n=102, alcohol: n=56). Note that drug users who stopped are in class 3 instead of 4, while alcohol (ab)users who stopped are in the class 4. Variances of the random intercepts and slopes were smaller in the alcohol models than drug models indicating greater individual differences in drug than alcohol trajectories.

There was considerable agreement between membership in the *always abstinent* drug and alcohol classes: 65.2% of those who always abstained from drugs also always abstained from alcohol. The next highest level of agreement was between the second classes: 51.6% of those in the *fluctuating use, abuse, and occasional abstinence* drug class were in the same

[1]The bootstrap likelihood ratio tests for testing k vs. k−1 classes are not available when using the training data option in Mplus.

alcohol class. The greatest discrepancy was found between *stopped (ab)use* classes: Only 11.8% of those who stopped alcohol (ab)use also stopped drug (ab)use.

Table 1 displays odds ratios (*OR*s) from regressing class on baseline factors within the GMMs; using baseline factors to predict class membership in the GMM helps to profile the unobserved subpopulation represented by each class. Rows contain the target class; columns contain the reference class. Using drug classes and hospitalization as an example, cases in class 2 were 2.59 times more likely to have been hospitalized in the 3 months prior to the baseline assessment than cases in class 1. Overall, the large number of statistically significant *OR*s highlights the differences in the likelihood of membership among the five classes by age, education, sex, minority racial status, and pre-study hospitalization.

4. Discussion

We report new findings from the CATIE study, comparing drug and alcohol trajectories for adults with schizophrenia identified using GMMs. This represents the first examination of substance use trajectories in this population. Five latent classes describe patterns of drug and alcohol use best in these patients: *always abstinent; fluctuating use, abuse, and occasional abstinence; occasional (ab)use; stopped (ab)use;* and *abusing*. There is substantial overlap between drug and alcohol *always abstinent* classes; however, overlap between other drug and alcohol classes was lower. Finally, baseline factors differ between classes as evidenced by the statistically significant odds ratios in Table 1 describing the differences in the likelihood of latent class membership by age, education, sex, minority racial status, and pre-study hospitalization.

Consistent with prior applications of GMM used to examine substance use in other samples (e.g., adolescents, non-clinical adults) (Chassin et al., 2004), the multiple classes indicate heterogeneity in substance use over time among adults with schizophrenia. This finding has important implications for research and practice. First, prior research on substance use among adults with schizophrenia has assumed homogeneity. Our findings suggest this assumption is inappropriate and support the need for approaches, such as GMM that model heterogeneity. Second, there was some within-class heterogeneity (see Figure 1), as seen by changes in the patterns of abstinence, use, and disordered use over time, indicating the need for ongoing, repeated assessments. Third, the lack of overlap between drug and alcohol classes, with the exception of *always abstinent*, as well as differential outcomes associated with drug and alcohol use (Van Dorn et al., 2012b), supports modeling drugs and alcohol separately.

With regard to clinical implications, our findings contribute to a literature supporting multiple, distinct substance use trajectories, suggesting the need to tailor treatment to individual patients. As noted above, some patients' substance use fluctuated (i.e., *fluctuating use, abuse, and occasional abstinence; occasional (ab)use*; and *stopped (ab)use*) whereas others demonstrated more stability (i.e., *always abstinent* and *abusing*). Treatments targeting individual patterns of use should be most effective, but require ongoing (re)assessment of use. Findings also support a harm reduction approach that allows for fluctuations in substance use, as well as consideration of readiness for change, towards the ultimate goal of abstinence (Kerfoot et al., 2011). For example, for those who transitioned to sustained abstinence, there were some fluctuations in use prior to sustained abstinence. Finally, research suggests that integrated treatment for psychiatric and substance use problems will improve outcomes for patients who demonstrate ongoing use (i.e., *fluctuating use, abuse, and occasional abstinence; occasional (ab)use;* and *abusing*) (Drake et al., 1998).

Overall, our findings suggest multiple trajectories of drug and alcohol use among adults with schizophrenia, as well as some overlap but also discrepancies between substance use classes.

Generalizability should be tested against other samples of adults with schizophrenia, as well as other mental illnesses. Future research also should explore heterogeneity in treatment response and other distal outcomes based on drug and alcohol trajectories among adults with schizophrenia (Xie et al., 2010). Growth mixture models represent one way to approach these important tasks.

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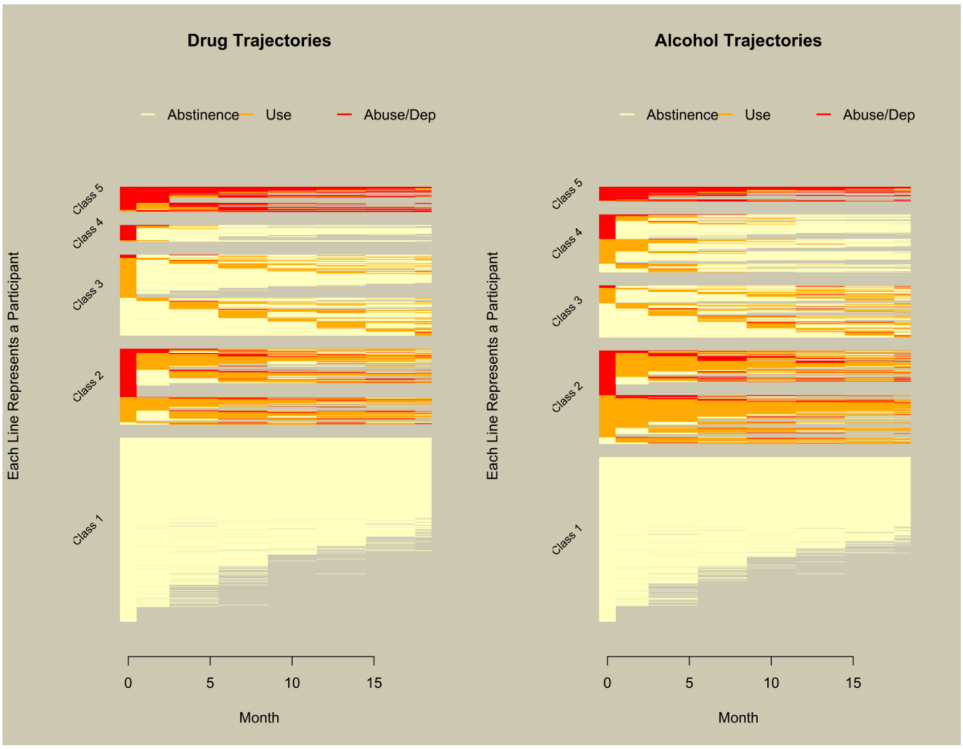

Figure 1.
Drug and alcohol trajectories plotted by latent class.

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Table 1

Odds ratios from the GMMs regressing class on demographic variables and baseline hospitalization.

	Alcohol						Drugs				
Hospitalized in 3 Months Prior to Enrollment											
	C1	**C2**	**C3**	**C4**	**C5**		**C1**	**C2**	**C3**	**C4**	**C5**
C1		**0.39**	1.11	0.75	**0.51**	C1		**0.60**	1.08	0.53	0.58
C2	**2.59**		**2.88**	**1.94**	1.32	C2	**1.66**		**1.79**	0.87	0.97
C3	0.90	**0.35**		0.68	**0.46**	C3	0.92	**0.56**		0.49	**0.54**
C4	1.33	**0.51**	1.48		0.68	C4	1.90	1.15	2.06		1.11
C5	**1.97**	0.76	**2.19**	1.48		C5	1.71	1.03	**1.85**	0.90	
Age											
	C1	**C2**	**C3**	**C4**	**C5**		**C1**	**C2**	**C3**	**C4**	**C5**
C1		1.01	**1.03**	**1.03**	1.02	C1		**1.04**	1.01	**1.04**	**1.04**
C2	1.00		**1.03**	1.02	1.01	C2	**0.96**		**0.98**	1.00	1.00
C3	**0.97**	**0.97**		1.00	0.99	C3	0.99	**1.02**		1.02	1.03
C4	**0.97**	0.98	1		0.99	C4	**0.96**	1.00	0.98		1.00
C5	0.98	0.99	1.02	1.01		C5	**0.96**	1.00	0.97	1.00	
Minority Racial Status											
	C1	**C2**	**C3**	**C4**	**C5**		**C1**	**C2**	**C3**	**C4**	**C5**
C1		0.79	1.67	0.85	0.77	C1		**0.36**	**0.60**	0.6	**0.38**
C2	1.27		2.12	1.09	0.98	C2	**2.76**		**1.65**	1.65	1.04
C3	0.60	0.47		**0.51**	0.46	C3	**1.67**	**0.61**		1.00	0.63
C4	1.17	0.92	**1.95**		0.91	C4	1.68	0.61	1.00		0.63
C5	1.29	1.02	2.15	1.10		C5	**2.66**	0.96	1.59	1.58	
Graduated High School											
	C1	**C2**	**C3**	**C4**	**C5**		**C1**	**C2**	**C3**	**C4**	**C5**
C1		1.41	1.61	1.40	0.85	C1		**1.64**	1.17	1.33	1.28

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	Alcohol						Drugs				
Hospitalized in 3 Months Prior to Enrollment											
	C1	**C2**	**C3**	**C4**	**C5**		**C1**	**C2**	**C3**	**C4**	**C5**
C2	0.71		1.14	1.00	0.60	C2	**0.61**		0.71	0.81	0.79
C3	0.62	0.87		0.87	0.53	C3	0.86	1.40		1.14	1.10
C4	0.71	1.00	1.15		0.61	C4	0.75	1.23	0.88		0.97
C5	1.17	1.66	1.89	1.65		C5	0.78	1.27	0.91	1.03	
Male Sex											
	C1	**C2**	**C3**	**C4**	**C5**		**C1**	**C2**	**C3**	**C4**	**C5**
C1		**0.56**	0.89	**0.33**	**0.33**	C1		**0.29**	0.92	0.32	**0.34**
C2	**1.78**		1.59	0.59	0.59	C2	**3.50**		**3.23**	1.13	1.18
C3	1.12	0.63		**0.37**	**0.37**	C3	1.08	**0.31**		0.35	**0.37**
C4	**3.03**	1.70	**2.70**		1.00	C4	3.09	0.88	2.85		1.04
C5	**3.03**	1.70	**2.70**	1.00		C5	**2.96**	0.84	**2.73**	0.96	

Note. Rows contain the target group and columns contain the reference group.

Bold entries are significantly different from 1 at the .05 level. Age is a continuous variable with mean=40.56, SD=11.11. C1 is the always abstinent class, C2 is the fluctuating use, abuse, and occasional abstinence class, C3 is the occasional (ab)use class, C4 is the stopped (ab)use class, and C5 is the abusing class.