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Impact of tobacco, alcohol and cannabis use on treatment outcomes among patients experiencing first episode psychosis: Data from the national RAISE-ETP study

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Abstract

Aim: The primary aim of this study was to examine the effect of recent tobacco, alcohol and cannabis use on treatment outcomes among participants experiencing first episode psychosis (FEP).

Methods: Secondary data analyses were conducted on 404 participants enrolled in the Recovery After an Initial Schizophrenia Episode—Early Treatment Program (RAISE-ETP) study. RAISE-ETP investigated the effectiveness of a coordinated specialty care (CSC) intervention for FEP in community mental health agencies in the United States. Generalized estimating equations were used to examine whether recent tobacco smoking, alcohol, and cannabis use at baseline were associated with illness severity, number of antipsychotic pills missed, psychiatric symptoms and quality of life during the 24-month treatment period, after controlling for duration of untreated psychosis and treatment group.

Results: At baseline, roughly 50% (n = 209) of participants reported recent tobacco, 28% (n = 113) alcohol and 24% (n = 95) cannabis use. Tobacco smokers had higher levels of illness severity (β = .24; P < .005), a higher number of missed pills (β = 2.89; P < .05), higher psychiatric symptoms and lower quality of life during treatment relative to non-smokers. Alcohol users had a higher number of missed pills (β = 3.16; P < .05) during treatment and cannabis users had higher levels of illness severity (β = .18; P < .05) and positive symptoms (β = 1.56; P < .05) relative to non-users.

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Conclusions: Tobacco, alcohol and cannabis use are common in youth seeking treatment for FEP. Tobacco smoking was associated with more negative clinical outcomes. These findings have implications for including interventions targeting these areas of substance use within current CSC models.

Keywords

alcohol use; cannabis use; first episode psychosis; raise-ETP; tobacco use

1 | INTRODUCTION

Individuals with schizophrenia are approximately 5 times more likely to have a substance use disorder, relative to the general population (Regier et al., 1990). Up to 50% of those diagnosed with schizophrenia report recent alcohol use, while 30% report recent cannabis use (Fowler, Carr, Carter, & Lewin, 1998; Talamo et al., 2006) and up to 65% report tobacco use (Depp et al., 2015; McCreadie & Scottish Comorbidity Study Group, 2002).

Similar to those with schizophrenia, 50% of individuals with first-episode psychosis (FEP) meet criteria for a co-occurring alcohol use or cannabis use disorder and approximately 75% of those with FEP report tobacco use (Barnett et al., 2007; Barrowclough, Gregg, Lobban, Bucci, & Emsley, 2015; Kane, Robinson, et al., 2015). Those with FEP are roughly 3 times more likely to engage in tobacco smoking compared to those without psychosis and rates have been estimated to be twice as high as cannabis use within this population (Depp et al., 2015; Myles et al., 2012). Continued tobacco smoking, alcohol and cannabis use among young adults with FEP increases risk of psychiatric relapse (Wade et al., 2006), hospitalization (Atakan, 2008; Sorbara, Liraud, Assens, Abalan, & Verdoux, 2003), medication non-adherence (Faridi, Joober, & Malla, 2012; Lambert et al., 2010) and physical health problems (Atakan, 2008).

In early intervention programs, cannabis dependence is associated with increased psychotic symptoms and pre-treatment alcohol and cannabis use is associated with higher depressive symptoms (Stone et al., 2014; Turkington et al., 2009). Studies addressing the relationship between alcohol, cannabis or cigarette smoking and psychiatric outcomes among those receiving FEP intervention have been limited by focusing on only 1 substance at a time, not distinguishing between the separate effects of alcohol and cannabis use on treatment outcomes.

The objective of the present study was to determine whether pretreatment alcohol, cannabis and tobacco use predicts psychiatric symptoms and quality of life outcomes among participants with FEP, using data from the Recovery After an Initial Schizophrenia Episode-Early Treatment Program (RAISE-ETP) study (Kane, Schooler, et al., 2015; Kane, Robinson, et al., 2015). Illness severity and missed antipsychotic pills during the 24-month treatment period were assessed as secondary outcomes.

2 | METHODS

2.1 | Participants

A total of 404 participants between the ages of 15 and 40 years were recruited from 34 community mental health agencies sites as a part of the intent-to-treat sample. Seventeen sites were randomized into Coordinated Specialty Care (called NAVIGATE; $n = 223$) and 17 sites into community care (control condition; $n = 181$) to form the 2 treatment groups. Eligibility criteria and participant characteristics are described further in the main RAISE-ETP outcome publication (Kane, Robinson, et al., 2015).

2.2 | Study design

NAVIGATE included individualized medication management supported by a decision support software, family education, individual resiliency training, and supported education and employment. The control condition consisted of treatment as usual for the designated site/clinic. Treatment was conducted across a 24-month treatment period, preceded by the baseline month. Details regarding study design and the NAVIGATE intervention have been previously reported (Kane, Schooler, et al., 2015; Mueser et al., 2015).

2.3 | Measures

Self-reported current alcohol and cannabis use was collected at baseline, participants answered either “yes” or “no” in response to being asked, “Does the client currently use alcohol?” and “Does the client currently use marijuana?” Those who reported “yes” to alcohol use were classified as “alcohol users”, those who responded “yes” to cannabis use were classified as “cannabis users.” Self-reported cigarette smoking, participants answered “yes” or “no” to “Is the patient a current cigarette smoker?” Duration of untreated psychosis (DUP) was dichotomized into “DUP less than 90 days” and “DUP greater than 89 days” based on World Health Organization (WHO) recommendation that FEP treatment should occur within 3 months of onset of symptoms (Bertolote & McGorry, 2005). Outcome measures were the Positive and Negative Syndrome Scale (PANSS) 5 factor scores: negative, positive, uncontrolled hostility, disorganized thought, and anxiety and depression to measure psychiatric symptoms (Kay, Flszbein, & Opfer, 1987). The Clinical Global Impressions Scale (CGI) was used to assess the severity of illness (Guy, 1976), and the 21-item Heinrichs-Carpenter Quality of Life Scale (QLS) total and 4 domain scores: interpersonal relationships, instrumental role functioning, intrapsychic foundations and common objects and activities, were used to assess overall objective functional status and subjective quality of life (Heinrichs, Hanlon, & Carpenter, 1984). These outcome measures were administered at baseline and months 6, 12, 18, and 24. The number of antipsychotic pills missed during treatment was calculated by trained clinicians based on information collected from the Oral Antipsychotic Medication Adherence Review collected monthly.

2.4 | Statistical analysis

Descriptive analyses were conducted for the intent-to-treat sample ($N = 404$). Baseline comparisons using independent t tests for continuous variables between substance users and non-substance users were performed. To account for any missing data by using all available

pairs, generalized estimating equations (GEE) were utilized among the intent-to-treat sample to analyse the effect of tobacco smoking, and current alcohol and cannabis use at baseline on the PANSS subscales, CGI severity, QLS total and subscales, and the number of prescribed antipsychotic pills missed during the 24-month treatment period. Aside from current alcohol use (alcohol users vs non-alcohol users [reference group]), current cannabis use (cannabis users versus non-cannabis users [reference group]) and cigarette smoking (smokers vs non-smokers [reference group]) at baseline, DUP and treatment group were included as control variables. Unstandardized regression coefficients and 95% confidence intervals (CI) are presented for continuous outcomes with alpha set at $P < .05$. Analyses were performed using SPSS 24.0.

3 | RESULTS

3.1 | Baseline substance use and participant characteristics

In the entire sample, 51% ($n = 207$) reported current cigarette smoking, 28% ($n = 113$) reported current alcohol use, 24% ($n = 95$) reported current cannabis use and 11% ($n = 44$) reported both current alcohol and cannabis use. Clinical characteristics are presented in Table 1.

3.2 | Illness severity and missed pills

Table 2 displays the means and standard errors for primary and secondary outcomes from GEE. Tobacco smokers had significantly higher CGI scores ($\beta = .24$; 95% CI = 0.07–0.40, $P < .005$) and significantly higher number of missed pills than non-smokers ($\beta = 2.89$; 95% CI = 0.32–5.48, $P < .05$) during treatment (see Table 3). Cannabis users had significantly higher CGI scores than non-cannabis users ($\beta = .18$; 95% CI = 0.01–0.36, $P < .05$). Alcohol users had a significantly higher number of missed pills during treatment compared to non-alcohol users ($\beta = 3.16$; 95% CI = 0.31–6.01, $P < .05$). Table 3 displays results from all GEE models including control variables (DUP and treatment group).

3.3 | Psychiatric symptoms

Tobacco smokers had significantly higher scores on the PANSS total score ($\beta = 4.43$; 95% CI = 1.68–7.17, $P < .01$), negative symptoms subscale ($\beta = 1.30$; 95% CI = 0.12–2.48, $P < .05$), positive symptoms subscale ($\beta = 1.53$; 95% CI = 0.38–2.69, $P < .01$) and controlled hostility and excitement subscale ($\beta = .59$; 95% CI = 0.20–0.99, $P < .01$) during treatment relative to non-smokers. Cannabis users ($\beta = 1.56$; 95% CI = 0.31–2.81, $P < .05$) had significantly higher scores on the PANSS positive symptoms subscale during treatment relative to non-cannabis users. Alcohol use was not a significant predictor for PANSS subscales (see Tables 2 and 3).

3.4 | Quality of life

Tobacco smokers had significantly lower total QLS scores ($\beta = -.31$; 95% CI = −0.53 to −0.09, $P < .01$), instrumental role functioning ($\beta = -.56$; 95% CI = −0.93 to −0.19, $P < .01$), intrapsychic foundations ($\beta = -.34$; 95% CI = −0.55 to −0.13, $P < .01$) and common objects and activities QLS subscale scores ($\beta = -.25$; 95% CI = −0.48 to −0.01, $P < .05$) compared

to non-smokers during treatment. Cannabis and alcohol use was not a significant predictor for QLS subscales.

4 | DISCUSSION

Consistent with previous studies we found that up to 50% of adolescents and young adults with FEP reported either alcohol or cannabis in the month prior to treatment (Colizzi et al., 2016; Myles et al., 2012). We also found that approximately 50% reported tobacco use at the time of enrolment into RAISE-ETP. To our knowledge this is the first study to examine the effects of alcohol, cannabis and tobacco smoking on psychiatric outcomes of youth with FEP, across 2 years of treatment, while accounting for confounding factors known to influence outcomes. Cigarette smoking was consistently associated with higher ratings of psychiatric symptoms and functional impairment, more missed pills and lower ratings of quality of life. In contrast, alcohol use was only associated with decreased medication adherence, while cannabis use was associated with greater impairment in overall functioning (CGI score) and positive symptoms.

While, others have observed an association between tobacco smoking and greater symptomatic and functional impairment in youth experiencing FEP (Depp et al., 2015; Myles et al., 2012). Few FEP programs focus on tobacco smoking, or more generally, substance use. Therefore, given its high prevalence and impact on psychiatric outcomes, it is imperative that these programs actively prevent and treat tobacco smoking. It is possible that low-cost and feasible interventions for tobacco smoking may be effective for those with FEP, relative to those with chronic psychotic disorder, who have a longer history tobacco use. Improving treatment for alcohol and cannabis use is also important given the prevalence of these problems and the potential to prevent long-term addiction.

Limitations of this study include the assessment of alcohol, cannabis and tobacco use were based on self-report measures which may increase social desirability. Future studies among individuals with FEP should verify self-report measures using more objective evidence of substance abuse such as biomarkers (McDonell et al., 2017). Further, this secondary data analysis was based on a treatment seeking, rather than an epidemiological sample. Therefore, the estimates of substance use prevalence might not apply to community samples, and results might not apply to non-US populations. Finally, while associations between substance use and outcomes were observed, the effect sizes observed were not large and may also be related to multiple comorbities. However, the high prevalence of tobacco smoking and the consistent association between tobacco smoking and outcomes supports the importance of targeting tobacco smoking in this population.

5 | CONCLUSIONS

The results from this secondary data analysis offers support for integrating evidence-based treatment options for substance use, with a particular focus on smoking for individuals receiving treatment for FEP.

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TABLE 1

Participants' characteristics at baseline by treatment group

	Overall *N* = 404		NAVIGATE *n* = 223		Community care *n* = 181	
Item	**M (SD)**	**% (*n*)**	**M (SD)**	**% (*n*)**	**M (SD)**	**% (*n*)**
Psychiatric diagnosis						
Schizophrenia		53.0 (214)		50.7 (113)		55.8 (101)
Schizoaffective		20.0 (81)		19.3 (43)		21.0 (38)
Schizophreniform		16.6 (67)		19.3 (43)		13.3 (24)
Psychotic disorder		10.4 (42)		10.8 (24)		9.9 (18)
Alcohol use disorder (lifetime)		36.4 (147)		39.5 (88)		32.6 (59)
Recent alcohol use disorder (30 d)		4.5 (18)		4.5 (10)		4.4 (8)
Current alcohol users		28.2 (113)				
# of drinks (per week)	3.54 (4.07)		3.42 (3.41)		3.68 (4.79)	
# days drunk (past 30 d)	1.49 (4.10)		1.52 (3.89)		1.45 (4.38)	
Cannabis use disorder (lifetime)		34.7 (140)		37.2 (83)		31.5 (57)
Recent cannabis use disorder (30 d)		10.6 (43)		11.2 (25)		9.9 (18)
Current cannabis users		23.7 (95)		23.6 (52)		23.8 (43)
# of days cannabis was used (past 30 d)	10.89 (11.14)		10.62 (10.86)		11.23 (11.57)	
Heavy cannabis users		26.3 (25)		26.9 (14)		25.6 (11)
Current tobacco use—smoking		51.4 (207)		49.5 (110)		53.6 (97)
# of days tobacco was used (past 30 d)	26.06 (7.89)		26.05 (7.54)		26.07 (8.30)	

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TABLE 2

Alcohol and cannabis users and smokers at baseline and clinical characteristics during treatment (means and standard errors)

	Alcohol use		Cannabis use		Tobacco use	
Clinical characteristics	**Alcohol users**	**Non-alcohol users (REF)**	**Cannabis users**	**Non-cannabis users (REF)**	**Smokers**	**Non-smokers (REF)**
PANSS total score	NS		NS		70.44 (1.11)**	66.01 (1.16)
PANSS negative	NS		NS		18.22 (0.44)*	16.91 (0.47)
PANSS positive	NS		21.97 (0.53)*	20.41 (0.39)	21.82 (0.43)**	20.28 (0.46)
PANSS disorganized thought	NS		NS		NS	
PANSS uncontrolled hostility	NS		NS		6.63 (0.19)**	6.04 (0.18)
PANSS anxiety depression	NS		NS		NS	
QLS total mean score	NS		NS		2.84 (0.08)**	3.15 (0.09)
QLS interpersonal relations	NS		NS		NS	
QLS instrumental	NS		NS		1.96 (0.13)**	2.52 (0.16)
QLS intrapsychic	NS		NS		3.13 (0.08)**	3.47 (0.08)
QLS common objects	NS		NS		3.54 (0.08)*	3.79 (0.10)
Missed medications	11.05 (2.13)*	7.89 (0.95)*	NS		10.92 (1.13)*	8.02 (0.96)
CGI severity	NS		3.63 (0.08)*	3.45 (0.05)	3.66 (0.06)**	3.42 (0.07)

DUP and treatment group were covariates.

*$P < .05$

**$P < .01$

***$< P < .001$.

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TABLE 3

Alcohol and cannabis users at baseline and clinical characteristics during 24-mo treatment (Beta's, confidence intervals and *P* values)

	Alcohol users			Cannabis users			Tobacco smokers		
Clinical characteristics	***β***	**95% CI**	***P* value**	***β***	**95% CI value**	**P value**	***β***	**95% CI**	***P* value**
PANSS total	NS			NS			4.43	1.68 to 7.17	<.01
PANSS negative	NS			NS			1.30	0.12 to 2.48	<.05
PANSS positive	NS			1.56	0.31–2.81	<.05	1.53	0.38 to 2.69	<.01
PANSS disorganized thought	NS			NS			NS		
PANSS hostility	NS			NS			0.59	0.20 to 0.99	<.01
PANSS depression	NS			NS			NS		
QoL total mean score	NS			NS			−0.31	−0.53 to −0.09	<.01
QOL interpersonal relations	NS			NS			NS		
QOL instrumental	NS			NS			−0.56	−0.93 to −0.19	<.01
QOL intrapsychic	NS			NS			−0.34	0.55 to −0.13	<.01
QOL common objects activities	NS			NS			−0.25	−0.48 to −0.01	<.05
Missed medications	3.16	0.31–6.01	*P* < .05	NS			2.89	0.32 to 5.48	<.05
CGI severity	NS			0.18	0.01–0.36	<.05	0.24	0.07 to 0.40	<.005

	Treatment group			DUP		
Clinical characteristics	***B***	**95% CI**	***P* value**	***β***	**95% CI**	***P* value**
PANSS total	NS			7.56	−4.85 to 10.28	<.001
PANSS negative	NS			1.31	0.18 to 2.44	<.05
PANSS positive	NS			2.87	1.73 to 4.02	<.001
Disorganized thought	NS			NS		
PANSS hostility	NS			0.76	0.34 to 1.18	<.001
PANSS Depression	NS			NS		
QoL total	NS			0.33	−0.54 to −0.13	<.01
Interpersonal relations	NS			NS		
Instrumental	NS			NS		
Intrapsychic	NS			−0.24	−0.44 to −0.03	<.05
Common objects activities	NS			NS		
Missed medications	6.35	3.71–8.99	<0.001	NS		

	Treatment group			DUP		
Clinical characteristics	***B***	**95% CI**	***P* value**	***β***	**95% CI**	***P* value**
CGI severity	NS			0.46	0.30 to 0.62	<.001