

## Short Communication

### Predictors of Relapse in Patients with Opioid Addiction during Buprenorphine-Naloxone Maintenance Treatment

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#### Abstract

**Background:** Opioid abuse is an important public health issue. Buprenorphine-Naloxone Combination (BNC) is one of the most efficacious approaches for opioid withdrawal. Thus it is important to determine factors related with treatment outcomes in BNC maintenance treatment. Thus, we aimed to evaluate the predictors of three months compliance rate with BNC treatment among a sample of patients with opioid addiction.

**Methods:** In this retrospective study, we evaluated the records of patients who sought and had received any treatment with BNC for opioid addiction in an addiction treatment center during three months period. Relevant data such as socio-demographic variables, drug use history, and opioid use patterns were gathered from the records.

**Results:** At least three months after BNC maintenance treatment, relapse rate was 66.6%. Patients who were not married and those with an education of less than 8 years were more likely to relapse to opioid use. We also found a relationship between average daily heroin doses and relapse as reflected by illicit opioid use during treatment.

**Conclusions:** Future research is needed to reveal whether determining these factors and establishing adequate interventions may lead to improved treatment outcomes.

**Keywords:** Buprenorphine-Naloxone; Maintenance treatment; Relapse

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#### Introduction

It is well-known that the use of opioids such as heroin is one of the most serious social and health problems in the world and 0.4% of the global population is estimated to abuse opioid drugs [1,2]. Opioid abuse is an important public health issue for Turkey as well [3]. The treatments of opioid dependence and withdrawal symptoms are of clinical importance. Currently, it has been accepted that buprenorphine, Buprenorphine-Naloxone Combination (BNC), and methadone are equally effective in maintenance therapy of opioid-dependent patients and all of them have been shown to be more effective than placebo in relapse prevention [4-6]. In Turkey, however, only BNC is officially approved since April 2010 [7]. In addition, the prescription of BNC is limited by the Turkish Ministry of Health, allowing treatments only in specialized centers. Hence, the experience of maintenance treatment of opioid addiction is relatively low in Turkey. Up to now, no studies have examined factors associated with relapse and treatment retention in opioid dependent outpatients receiving BNC in Turkey.

The goal of this study was to evaluate the predictors of three months retention rate with buprenorphine-naloxone treatment among a sample of patients with opioid addiction.

#### Materials and Methods

A retrospective chart review of 60 patients with opioid addiction treated at the Akdeniz University, Alcohol and Substance Addiction Treatment and Research Center was conducted. Medical records of the patients were accessed via the center's database. We evaluated the records of all patients who sought and had received treatment with buprenorphine-naloxone for opioid addiction in the center from September 1, 2013 to November 31, 2013. Records were reviewed from the beginning of a patient's opioid treatment, through January 31, 2014, to ensure an opportunity for at least three months of data collection, even if the patient dropped out of treatment. Relevant data such as sociodemographic variables, drug use history, and opioid use patterns were gathered from the records.

Statistical analysis was done by SPSS statistical software (SPSS for windows 16.0, Inc., Chicago, IL, USA). The distribution of the data was tested using the Kolmogorov-Smirnov test. If distributed normally, data were shown as means and standard deviations and compared with Student's t-test. Non-normally distributed data were described as median (25<sup>th</sup> percentile; 75<sup>th</sup> percentile). The non-parametric Mann-Whitney U test was used to detect differences in non-normally distributed continuous variables between patients who relapsed and those in retention. Age was the only normally distributed variable and all other continuous variables were found to be non-normally distributed. Categorical variables were compared using chi-square test.

#### Results

The mean ( $\pm$ standard deviation) age of the study population was  $25.7 \pm 6.7$  years. There were only four (6.5%) females in the cohort. Most of the patients were single (78.3%) and unemployed (65%). At least three months after BNC maintenance treatment, relapse rate was

66.6%. The comparison of patients who had relapsed and those who had not relapsed is presented in Table 1.

		Relapse within 3 months (n= 40)	Retention within 3 months (n= 20)	P value
Age*		25.3 (5.9)	26.7 (8.2)	0.464
Gender**	Female	3 (7.5)	1 (5)	0.714
	Male	37 (92.5)	19 (95)	
Marital status**	Single	35 (87.5)	12 (60)	0.020
	Married	5 (12.5)	6 (30)	
	Divorced/widowed	0	2 (10)	
Education**	5 years	8 (20)	0	0.017
	8 years	19 (47.5)	16 (80)	
	11 years	12 (30)	2 (10)	
	>11 years	1 (2.5)	2 (10)	
Employment status**	Employed	14 (35)	7 (35)	0.616
	Unemployed	26 (65)	13 (65)	
Duration of opioid use prior to treatment**	< 1 year	3 (7.5)	5 (25)	0.173
	1-3 years	7 (17.5)	4 (20)	
	4-5 years	14 (35)	3 (15)	
	>5 years	16 (40)	8 (40)	
Comorbid cannabis use	Yes	7 (17.5)	5 (25)	0.494
	No	33 (82.5)	15 (75)	
History of suicide attempt	Yes	10 (25)	2 (10)	0.171
	No	30 (75)	18 (90)	
Age of first heroin use***		21 (16;23)	21.5 (16.5;24.8)	0.349
Average daily heroin dose prior to treatment (g/day)***		0.9 (0.4;1)	1 (0.8;3)	0.029

**Table 1:** Comparison of patients with relapse and retention.

\*Mean (standard deviation), Student's t-test; \*\*Number (percentile), chi-square test \*\*\*Median (25th percentile; 75th percentile), Mann-Whitney U test.

## Discussion

This study investigated the predictors of retention to BNC treatment in patients with opioid dependence. We found that marital and education statuses were predictors of relapse. Moreover, higher average daily heroin dose prior to maintenance treatment was associated with patient relapse.

Relapse rates during BNC treatment have been reported to vary significantly ranging from 13% to 40.8% in 3 months [8-10]; 39.6% to 51.6% in 6 months [11-14]; and 21.7% to 25% in 12 months period [15,16]. When compared with previous findings, we observed a relatively high relapse rate within 3 months in our study. This finding may be interpreted by the relatively short time of experience with BNC treatment in Turkey. High relapse rates in BNC treatment warrants further evaluation of predicting factors associated with relapse.

Only a few studies have investigated the factors predicting relapse in BNC maintenance treatment. Tkacz et al., [9] have found that none of the socio-demographic features noted at baseline were predictive

of relapse in 3 months follow up in BNC treatment. Ferri et al., [12], evaluating the chart review of 62 patients with opioid addiction, have shown that patients with comorbid anxiety disorders, active benzodiazepine use, or active alcohol abuse, were significantly more likely to relapse. In another study [10], however, higher rate of baseline depression was found to be associated with treatment compliance. Buprenorphine has been shown to be effective in treatment-resistant depression [17,18]. Thus, patients with depressive symptoms may benefit from BNC treatment and this may enhance treatment motivation. Moreover, the records of 69 US veterans who were receiving BNC treatment for opioid use disorder were evaluated and patients with a comorbid psychiatric disorder were found more frequently to be noncompliant to treatment [16]. Additional factors predicting relapse were comorbid benzodiazepine or cannabis use [19]. In our study, however, comorbid cannabis use was not associated with relapse.

Several limitations have to be considered when interpreting the findings of the present study. First, the retrospective design of the study may hinder establishing causality. Second, the study sample was relatively small to draw definite conclusions. Third, the follow up period was relatively short (3 months) and our findings do not shed light on long term results. Also, we did not conduct power analyses to calculate sample size.

Our results suggest that patients who were not married and those with an education of less than 8 years were more likely to relapse to opioid use. We also found a relationship between average daily heroin dose and relapse during treatment. The reason for this finding may indicate inadequate BNC dose among heroin dependent patients who use higher doses. Future research is needed to reveal whether determining these factors and establishing adequate interventions may lead to improved treatment outcomes.

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