

## Original Article

# SUBOXONE (Buprenorphine/Naloxone) Treatment alone is not enough to prevent relapse in Opioid dependence with co-morbid Psychiatric illness.

*Narayan Chaudhary, MD, Syed Jamal Mustafa, MD, Wisam Aljumaili, MD, Syed Kamal Mustafa, MD, Khalid Ahmad, MD, Sadaf Amir, MD, Omar Shah, MD*

## ABSTRACT:

Opiate Dependence is a condition of epidemic proportions with serious Bio-Psycho-Social and Socio-Economic ramifications. Traditionally most Chemically Dependency Treatments in past have been seen through a unidimensional lens, with blame being put firmly on the shoulders of the individual afflicted with the burden of Chemical Dependency issues. Fortunately this attitude continues to change and more treatment algorithms are recognizing and implementing a systemic multi-disciplinary approach to treating Chemical Dependency Patients. As this approach is gaining acceptance and momentum, treatment teams are more open to adopting this approach, and now a potential limitation might be in getting the patients and families on board with the approach of treating Opiate Dependence as well as the co-occurring psychiatric co-morbidities. It is often in a Psychiatric treatment setting, when patients are evaluated for Opiate Dependence and they are also found to have psychiatric comorbidity. Our study gave strength to the hypothesis that if we aggressively treat co-occurring psychiatric co-morbidities along with Opiate Dependence, patients responded positively by fewer relapses, and a prolongation in the time to relapse.

## INTRODUCTION:

Opioid misuse in the United States has been a problem, which recently appears to have become even a more significant problem. In 2010, an estimated 200,000 persons reported heroin use, 5.1 million individuals age 12 years and older reported non-medical use of prescription pain relievers in the past month (American Psychiatric Association, 2014). The number of individuals with Opioid dependence increased from 1.5 million in 2002 to 1.9 million in 2010 (American Psychiatric Association, DSM-5, 2014).

Opioid dependence is a cluster of physiological, behavioral, and cognitive symptoms, which together indicates repeated and continuing use of opioid drugs, despite significant problems related to such use.

Addiction is often characterized by periods of abstinence, followed by a relapse episode (O'Brien CP, 1998). The most important objective for clinicians is prolonging the time to relapse, and not necessarily preventing relapse (J., 2000).

Many previous studies has shown that relapse can increase due to a number of factors, including stress (TIP 40: Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction; SMA07-3939, 09/2004), environmental stimuli that signal the availability of the drug (Mattoo SK, 2009), and a high number of undesirable life events, physical changes in brain structure and modified neurotransmitter levels

due to drug use, also affect the probability of relapse (O'Brien CP, 1998).

Kaplan and Sadock, Concise Textbook of Psychiatry Third Edition 2008 indicates that the 12 month prevalence of Opioid use disorder in individuals 18 years and older in the United States is approximately 0.37% (Sadock BJ, 3rd edition. 2008. ) and that about 90% patient with opioid dependence have an additional psychiatric disorders e.g. Major Depressive Disorder, alcohol use disorder, antisocial personality disorder and anxiety disorder, etc (Sadock BJ, 3rd edition. 2008. ).

Traditionally, federally regulated programs such as methadone clinics have been at the forefront of treating opioid dependence patients. Fortunately since the past decade, The Drug Abuse Treatment Act of 2000 enabled US physicians with additional training to prescribe Buprenorphine/Naloxone (SUBOXONE) for Opioid Dependence Treatment in outpatient clinical setting (Wesson, (2010). Several factors favor use of SUBOXONE in outpatient clinics including convenient access, customizing dose to the needs of patients and integrated treatment of the psychiatry comorbidities (Feillin D, 2002).

A commonly accepted theory of the "reward pathway" in brain is said to be in the mesolimbic dopamine system. The circuit is activated by natural rewards, such as food, sex, social interactions. These same pathways can also be activated by substances such as Opiates. This pathway is therefore an important determinant of incentives and may motivate an individual to repeat

**Original Article**

destructive patterns of behaviors (American Psychiatric Association, DSM-5, 2014). Buprenorphine preferentially binds with strong affinity to the mu opioid receptor in the brain, preventing other opiates from binding to the receptor and consequently inhibiting the euphoric pleasurable effects of opioids (Feillin D, 2002). The clinic based availability of buprenorphine/naloxone (SUBOXONE) as a treatment option has significantly enhanced the accessibility to treatment for many patients, with consequent improvement in the quality of life as well (Fudala PJ, 2003).

Despite the fact that SUBOXONE treatment allows more convenient, flexible and individually tailored treatment for patients with Opiate Dependence, the numbers for incidence of relapse have not significantly changed in the past 10 years. It was hypothesized by the authors that unless co-morbid psychiatric issues are also addressed in SUBOXONE treatment protocols, the time to relapse and relapse rates will not be significantly changed with SUBOXONE alone.

**METHOD:**

Charts were reviewed in an outpatient psychiatric clinic setting where patients who met criteria for Opiate Dependence were treated using the PSPC SUBOXONE Treatment Protocol (PSTP). For the purposes of this study, relapse was defined as the use of non-prescribed opiates (as confirmed by 10 panel Drug Test) during the course of treatment, (with or without drop-out from the treatment protocol).

This study, retrospectively examined Relapse Rates (RR) and the Time To Relapse (TTR) for the patients once they started Out-Patient SUBOXONE Treatment using the PSTP.

PSPC SUBOXONE Treatment Protocol, (Syed Jamal Mustafa, 2014), is a structured treatment protocol followed at the Puget Sound Psychiatric Center. It starts with screening patients for Opiate Dependence to be treated in an outpatient setting, in the induction phase patients are gradually titrated up to a target dose of SUBOXONE of 8mg/2mg to 12mg/3mg, depending on their clinical needs. During this induction phase while the dose of SUBOXONE is being titrated up, the patients are provided with symptoms relief with a "rescue medication cocktail" which includes SERQUEL, NEURONTIN, CLONIDINE and BACLOFEN. After induction is complete the patients go into the maintenance phase of monthly SUBOXONE monitoring and medication checks, as well as preferably weekly, but at least twice a

month psychotherapy; and regular support groups (AA/NA). It is during this time that the patient is in active treatment of any co-morbid psychiatric disorders as well.

It has been the claim of the Puget Sound Psychiatric Center, that treatment of Opiate Dependence is better when conducted as per PSTP, (addressing both Opiate Dependence and Co-Morbid Psychiatric Disorders) this claim was tested by the chart review process and comparing to currently available national epidemiological figures.

Data was collected from 60 charts selected for a retrospective review. Data collected included patient demographics, diagnosis, substance use history, date of intake and relapse, relapse substances, reason of dropout or discharge. Treatment team included Buprenorphine certified psychiatrists, neurologist, Psychiatry Residents, Chemical dependency Certified Therapist. At intake, detailed history had been obtained, (including psychiatric, substance abuse, medical, and psychosocial histories). Urine Drug Screen (UDS) and clinically relevant routine labs had been ordered.

Patients who met criteria for Opiate Dependence were enrolled in the PSPC Suboxone Treatment Protocol (PSTP).

During the intake process it was noted that 88% of these patients also met criteria for one or more Psychiatric Co-Morbidities.

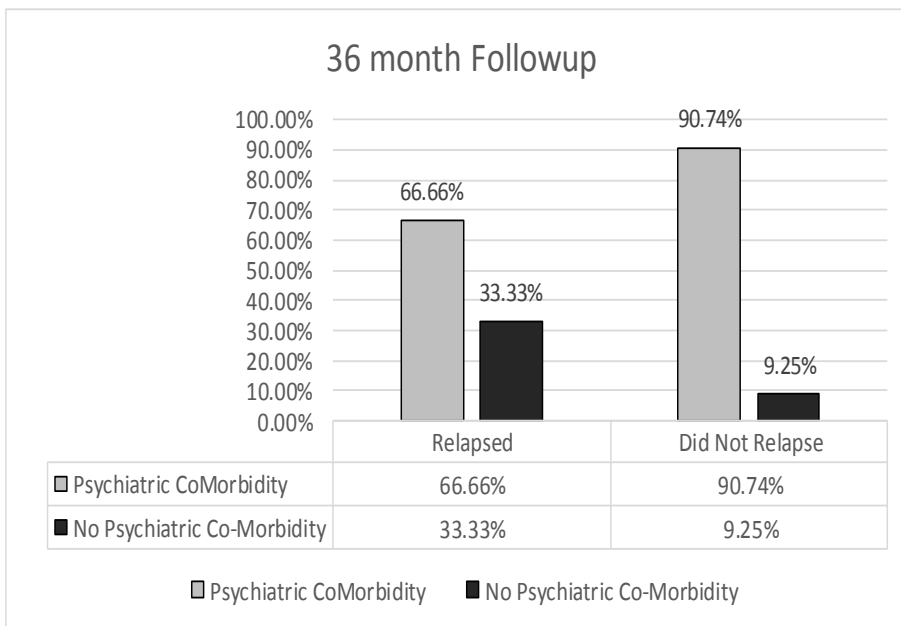
During the PSTP, Stabilization and Maintenance phases, psychiatric comorbidities were also addressed along with Opiate Dependence, and treatment was tailored within the PSTP format to suit the clinical needs of the patient.

At visits to the clinic Drug Screens are routinely obtained as part of the PSTP. Relapse was determined by positive drug test or patient self-report during the period of treatment. The primary outcome, time to relapse was calculated from the start date of buprenorphine till the date of positive opiate result at the clinic visit. Secondary outcomes measures such as Relapse Rate and associations between relapse and comorbid psychiatric disorder were separately calculated.

**RESULT:**

A total of 60 patients chart were reviewed. The age range of subjects reviewed was between 18-65 years. There were 32 males and 28 females

## Original Article



## DISCUSSION:

Opiate Dependence is a complex topic, the full magnitude of which is not completely understood at this time. It is commonly accepted that SUBOXONE is used to treat Opiate Dependence, however the definition of treatment for Opiate Dependence is the point of contention for many. Some purist may say that Opiate Dependence Treatment must mean being clean and free from the offending agent (Opiates in this case) and also there should be no relapse. Many professional

use the analogy of Diabetes Mellitus, and compare Opiate Dependence to such Chronic Illnesses. Irrespective of who is right or wrong, the bottom line is that Opiate Dependence has vast implications in Human Society, on the one hand Opiates help ease painful conditions, on the other hand its Addictive Qualities make Opiates debilitating for those individuals who succumb to the "Addiction", then of course comes the stigma of being an "addict". Many individuals who are dependent on Opiates have Psychiatric Co-Morbidities, and if the patients have Psychiatric Co-Morbidities, it is important to identify them early and treat them accordingly. If a co-morbidity is treated appropriately then Opiate Dependence Treatment with SUBOXONE can be very promising and can almost reach the goals of total abstinence.

Our findings show that when psychiatric co-morbidities are appropriately treated, the TTR (time to relapse) and RR (relapse rate) both change favorable. Furthermore with continued and ongoing treatment of the co-morbid psychiatric conditions, relapse can be something to completely overcome.

## CONCLUSION:

The high prevalence of psychiatric comorbidities highlights the need to adhere to a structured broad based treatment program such as the "Puget Sound Psychiatric Center SUBOXONE Treatment Protocol" (PSTP) which in our study has shown to be extremely successful in pre-

(non-pregnant, non-lactating). All patient had Opiate Dependence, 88.33% of these patients also had co-morbid psychiatric diagnosis, and 10% of these patients relapsed. It was noted that during the review period of almost 36 months, the mean Time To Relapse (TTR) was 22 months from the start of Buprenorphine treatment (the range of TTR was from the 15<sup>th</sup> month mark to the 34<sup>th</sup> month mark), the Median TTR was noted to be 20<sup>th</sup> month; whereas the Mode TTR was the 15<sup>th</sup> Month.

Amongst those patients who relapsed 33.33% had no psychiatric co-morbidities. Whereas of the patients who did not relapse 90.73% had Psychiatric Co-Morbidities, The psychiatric co-morbidities included ADHD, Anxiety Disorder, Depressive Disorders and Mood Disorders (including possible Bipolar Disorders).

These results indicate that those patient who were being treated with the PSTP, with or without Psychiatric co-morbid conditions had a better prognosis, and a lower relapse rate (RR) and longer Time To Relapse (TTR). Smyth BP, et al report that up to 90% of all people with Opiate Dependence relapse.

The study also revealed that for those patients without co-morbid psychiatric illness the RR (Relapse Rate) was almost three times higher than for patients without psychiatric co-morbidities.

## Original Article

venting relapse at a rate phenomenally under the national averages.

The focus of the PSTP, is not just the Opiate Dependence, but that Psychiatric Co-Morbidities should be treated aggressively and consequently Opiate Dependency can be brought under much success.

This approach is in line with the understanding of Ferri M. et al (M., January 2014) that comorbid psychiatric or substance abuse conditions, psychosocial stability, and a patient's adherence history with other medications may all influence compliance with buprenorphine and prevent relapse. O'Brien, C.P. et al (O'Brien CP, 1997) suggested that there is association between comorbid depression and higher treatment retention in heroin dependent patients (O'Brien CP, 1997), our findings partly are in agreement, showing that if the patients' co-morbidity is being adequately treated then they stay in treatment longer with fewer relapses.

Our study has a number of limitations, the most notable one being its small sample size and the duration of treatment for this co-hort. Another limitation is the retrospective chart review study design. These factors limit the ability to control quality of assessment and collection of more detail data. However it does fuel the fire to gain knowledge and prepare for a future follow-up and larger study.

This study confirms that, SUBOXONE is effective treatment in preventing relapses and prolonging relapse time when the psychiatry comorbidity is simultaneously and aggressively treated in specialized outpatient setting.

## References

- American Psychiatric Association. (2014). *Diagnostic and Statistical Manual-5*. American Psychiatric Association Press. ISBN 0890425558.
- O'Brien CP. (1997). A range of research-based pharmacotherapies for addiction. *Science*. . *Science*, 278: 66–70. .
- Feillin D, O. P. (2002). Office-based treatment of opioid-dependent patients. *New England Journal of Medicine*, 347:817–823.
- Fudala PJ, B. T. (2003). Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. *New England Journal of Medicine*, 349:949–958.
- Stewart J.(2000). Pathways to relapse: The neurobiology of drug- and stress-induced relapse to drug-taking. . *J Psychiatry Neuroscience*, 25:125–136. .
- Ferri M. (January 2014). Predictive Factors for Relapse in Patients on Buprenorphine Maintenance. *American Journal On Addictions*. , 23 (1):62-67.
- Mattoo SK, C. S. (2009). Psychosocial factors associated with relapse in men with alcohol or opioid dependence. *Indian Journal Medical Research*. , 130:702–708. .
- O'Brien CP, C. A. (1998). Conditioning factors in drug abuse: Can they explain compulsion? *J Psychopharmacology*, 12:15–22.
- Sadock BJ, S. V. (3rd edition. 2008. ). *Kaplan and Sadock's Concise Textbook of Clinical Psychiatry*. . Philadelphia: 3rd edition. Philadelphia: Lippincott, Williams and Wilkins.
- SM., S. (4th ed. 2013. ). *Essential Psychopharmacology: Neuroscientific Basis and Practical Applications*. . New York: : Cambridge University Press.
- Syed Jamal Mustafa, MD. (2014). Puget Sound Psychiatric Center Suboxone Treatment Protocol Out-patient Induction and Maintenance Treatment for Opioid Dependent Adults). *PUSH Journal of Psychiatry and Clinical Psychology*, 1:1:13.
- TIP 40: *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction; SMA07-3939*. (09/2004) US Department of Health & Human Services.
- Wesson, D. R. ((2010). Buprenorphine in the Treatment of Opiate Dependence. *Journal Of Psychoactive Drugs*, 42(2), 161-17 .