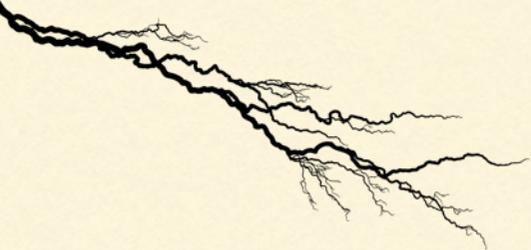

Prescription Pain Reliever Misuse: An Explanatory Study of the Social Factors Contributing to Prescription Pain Reliever Misuse

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ABSTRACT

Introduction: The opioid epidemic as a social problem has increasingly received more attention from the mass media as well as the scientific community. Despite all this attention substance use disorders involving prescription pain relievers affect roughly 1.9 million Americans annually. Aims: The purpose of this study was to understand the impact of mental health and risky behaviors such as alcohol use on propensity for non-medical prescription pain reliever use. Design & Methods: The data for this study came from the 2014 National Survey on Drug Use and Health A multivariate logistic regression analysis was run on a number of variables pulled from the survey. Results: The study showed that certain mental conditions and risky behaviors increase one's propensity for non-medical prescription pain reliever use. Discussion: The findings of the study suggest (1) future research is necessary to understand further the correlations among mental health, risky behavior, and non-medical prescription pain reliever use; (2) that greater attention by all stakeholders to one's mental health history is a significant factor in affecting the aforementioned epidemic; and (3) that greater attention to individual willingness to participate risky behavior (e.g., frequent alcohol consumption) could significantly impact the epidemic. Conclusion: The findings in this study can potentially assist healthcare providers in safer prescribing practices as well as other practical applications. With a broader knowledge of conditions correlated to the use of prescription pain relievers for non-medical reasons, the medical community could engage in safer prescribing of this potent medication.

Introduction

The U.S. has seen a steady increase in prescription drug abuse since the mid-1990's [1]. The aggressive treatment of pain as a chronic incurable condition has led to a large influx in availability of prescription drugs [2]. The U.S. alone accounts for 80% of the world's opioid supply and 99% of the world's hydrocodone supply [3]. This epidemic cost insurers 72.5 billion dollars in 2007 [4]. Though the problem of prescription drug abuse is not new to this country, the severity of the problem has reached new proportions [5].

Along with this influx, a gap has developed in understanding what conditions correlate with the use of prescription pain relievers for the purpose of getting high. The abuse of this supply of pain reliever medication demands the attention of the scientific community; a need exists to further understand some of the behaviors and mental conditions that contribute to prescription pain reliever misuse. The purpose of this study is to examine the impact of depression, mental distress, and social anxiety as well as alcohol consumption on the likelihood of using opioids non-medically in hopes of providing a greater understanding of this epidemic.

Literature Review

Periods of Depression & Opioid Use

With substance use disorder being at the heart of the opioid epidemic [4] it is important to understand certain traits an individual may possess that make him or her more susceptible to non-medical prescription pain reliever use. Mood disorders such as depression often go hand in hand with non-medical prescription opioid use [6]. Studies have shown that individuals who take higher dosages of pain medication also report periods of depression more frequently than those who are taking a lower dose [7,8].

Those who report depression are at a much higher risk of long term pain reliever misuse [7,9]. In many cases individuals that have never experienced any form of substance use in the past report pain reliever abuse to alleviate depressive symptoms [10]. Those that may have initially received their prescription for the purpose of treating acute pain are in turn far more inclined to take these opioids to treat the mental pain of their depressive symptoms [10].

The consumption of these opioids in order to relieve mental pain provides a paradox of sorts for the user, being that the depressive symptoms often worsen as the frequency of self-medication increases [8,9]. The user becomes dependent upon the opioids physically as well as mentally, which in turn can intensify the initial depressive symptoms [11]. Being that drug misuse is already signifi-

cantly higher in individuals who report depression [12], I propose the following hypothesis:

H1: Individuals who experience periods of depression are more likely to use prescription pain relievers non-medically than those who do not experience periods of depression.

Mental Distress & Opioid Use

Mental distress can manifest itself through a variety of psychiatric conditions such as suicidal ideations and manic depressive episodes [13]. These conditions in turn can also be linked to a highly-elevated risk of drug misuse [6,7,10,12,14]. Those who report a high level of mental distress in their life often characterized by feelings of hopelessness, restless nights and low self-worth, are much more susceptible to develop substance use disorders [15].

A recent study on suicidality and non-medical prescription drug misuse found that those who displayed symptoms such as feelings of hopelessness and low self-worth showed some of the strongest correlations in non-medical prescription drug misuse [16]. The increased level of dopamine this opioid medication provides and the subsequent euphoric experience serves to kill some of the mental pain which accompanies this level of distress [17]. The medication can provide relief from intense feelings of hopelessness and provide one with an acceptance of their environment that was not previously attainable in their mental state [17]. Accordingly, I hypothesize the following:

H2: Those who experience frequent mental distress in their lives are more likely to use prescription pain relievers non-medically than those who do not experience frequent mental distress in their lives.

Social Anxiety and Prescription Pain Reliever Misuse:

Social anxiety disorder, i.e., an inability to perform daily tasks within one's social setting such as small talk with strangers, commonly correlates with substance use [18-20]. It often goes hand in hand with depressive episodes and can be linked to a variety of other forms of mental illness [21]. Pharmacotherapy is often utilized in the medical community as a treatment for social anxiety disorder, so it is easy to understand how an individual may experience relief via self-administered opioid medication [21]. Though the medications administered for this condition are not entirely similar in their effects they are each associated with higher concentrations of dopamine in the brain and are similar in this regard [21-23].

Prescription drug abuse being somewhat easy to conceal as opposed to other substances becomes a prime method of escape for individuals who experience emotional unrest in social settings [24]. These effects allow one's social environment to become much more acceptable and tolerable whereas prior to the pain reliever use the individual found their social duties almost impossible to carry out. Falling in line with what is stated above an inability to connect with one's social environment can lead to feelings of low self-worth and other forms of more serious mental distress which in turn makes one more susceptible to prescription pain reliever misuse [6,15]. It was based upon this research that I proposed the following hypothesis:

H3: Those who experience social anxiety are more likely to use prescription pain relievers non-medically than those who do not experience social anxiety.

Alcohol Use & Prescription Opioids

Periods of depression and other mental health conditions have demonstrated a positive correlation with a propensity for alcohol use [25]. Research also shows that individuals who use alcohol are more likely to abuse other substances one study showed a 57% prevalence of former alcohol use in young adults who report prescription pain reliever abuse [26,27]. Given these correlations it is important to consider the sequence in which one can often begin with alcohol use and graduate on to non-medical use of prescription pain relievers as it may better develop and widen the understanding of this complex epidemic [28].

Alcohol use is a rather socially accepted and well integrated aspect of our society [29]. One may find a social drink to be quite a relief yet refrain from using the substance addictively due to its effects which are rather hard to conceal, i.e. smell, slurred speech, loss of balance and things of this nature. A prescription drug however, when introduced to this individual, can be quite appealing in that it is easier to conceal, at least initially, and provides the same relief. Recent studies have in fact shown a link between alcohol consumption specifically and a propensity for non-medical use of prescription drugs [30-34]. Therefore, I propose the following hypothesis:

H4: As the frequency of daily alcohol consumption per week increases, the likelihood of using non-medical prescription pain relievers increases.

Research Design

Data & Ethics

The data for this study came from the National Survey on Drug Use and Health, conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA), an agency within the U.S. Department of Health and Human Services which primarily measures the prevalence and correlates of drug use in the United States [35]. The study was conducted using the CAI method (computer assisted personal interviewing), and it covered individuals aged 12 and older (N=67,838). However, for the purpose of this study, the sample was reduced to people who were at least 18 years old (N=54,959).

The researchers conducting the secondary data analysis maintained the highest ethical standards. The dataset analyzed is available to the general public and does not have present any identifying information about any participants. Moreover, the SAMHSA maintained the highest ethical standards in the initial collection of the data [35].

Measures

The dependent variable used throughout this study was non-medical prescription pain reliever use (See Table #1). The variable was based upon the following survey question: "Have you ever, even once, used any type of prescription pain reliever that was not prescribed to you or that you took for the experience or feeling it caused" (coded "Yes" = 1, "No"=0).

The independent variables utilized fell under the categories of "Mental Health", "Adult Depression", and "Alcohol." First, depression was measured using the survey question, "In the last thirty days have you experienced periods of depression lasting several days or longer" (0="No" and 1="Yes"). Second, mental distress was operationalized by the survey question, "In the last 30 days how frequently have you experienced thoughts of hopelessness." The response options were; (1) "All of the time," (2) "Most of the time," (3) "Some of the time," (4) "A little of the time," and (5) "None of the time," but it was recoded as (0) "Never" ("None of the Time") (1) "Sometimes" ("Some of the time" and "A little of the time"), and (2) "Often" ("All of the time" and "Most of the time"). Third, social anxiety was operationalized by the survey question, "In the last thirty days how much difficulty have you had talking to strangers?" The questions response options were (1) "No difficulty," (2) "Mild difficulty," (3) "Moderate difficulty," (4) "Severe Difficulty," and (5) "Did Not Participate," but it was recoded as (0)

“No Difficulty”, (1) “Some Difficulty” (“Mild Difficulty” and “Moderate Difficulty”), (2) “Severe Difficulty,” and (3) “Did Not Participate.” Finally, alcohol consumption was measured using the survey question, “On average, how many days did you drink an alcoholic beverage each week during the past 12 months.” The response options ranged from 0 to 7. Initially the survey question only dealt with individuals who reported drinking, and essentially excluded those who did not drink assigning it a value (99). For the purpose of this study, however, the value of (99) was recoded to be (0), in order to account for individuals who reported not drinking at all.

The control variables in this study were age, education, income, and gender. The variables age and income were initially scale variables that were recoded into categorical variables. Initially age included those aged 12-17 years old however for this study these values were excluded and only those aged 18 or older were considered. The final coding for age was as follows; (0) 18-25, (1) 26-34, (2) 35 and older. The finally coding for income was as follows; (0) less than 20,000, (1) 20,000-49,999, (2) 50,000-74,999, (3) 75,000 or more. The variable of education was a categorical variable initially containing 11 response options which were as follows; (1) “5th grade or less,” (2) “6th grade,” (3) “7th grade,” (4) “8th grade,” (5) “9th grade,” (6) “10th grade,” (7) “11th grade,” (8) “12th grade,” (9) “Freshman/13th year,” (10) “Sophomore/14th year or Junior/15th year,”(11) “Senior/16th year or Grad/Prof School.” The response options 1-7 were recoded (0) “Less Than High school;” response option 8 was recoded as (1) “High School Graduate;” response options 9 and 10 were recoded as (2) “Some College;” and response option 11 was recoded as (3) “College Graduate.” Gender was coded as (0) “Male” and (1) “Female.”

Table #1: Descriptive Statistics

	No	Yes			Total		
	N (% valid)	N (% Valid)			N/100%		
Non-Med. P.R. Use	8,094 (14.7)	46,865 (85.3)			54,959		
	No	Yes			Total		
	N (% Valid)	N (% Valid)			N/100%		
Depressed	25,160 (67.5)	12,088 (32.5)			37,248		
	Male	Female			Total		
	N (% Valid)	N (% Valid)			N/100%		
Female	26,331 (47.7)	28,829(52.3)			55,160		
	Never	Not Often	Often			Total	
	N(% Valid)	N(% Valid)	N(% Valid)			N/100%	
Hopelessness	24,322(65.3)	11,139 (29.9)	1,778 (4.8)			37,239	
	18-25	26-34	35 & Older			Total	
	N (% Valid)	N (% Valid)	N (% Valid)			N/100%	
Age	18,142(48.5)	5,446(14.6)	13,836(37.0)			37,424	
	No Difficulty	Some Difficulty	Severe Difficulty	Did Not Participate			Total
	N (% Valid)	N (% Valid)	N (% Valid)	N (% Valid)			N/100%
Social Anxiety	17,932 (59.5)	9,862(32.7)	1,374(4.6)	964 (3.2)			30,123
	< H.S.	High School	Some College	College Graduate			Total
	N (% Valid)	N (% Valid)	N (% Valid)	N (% Valid)			N/100%
Education	5,705(15.2)	11,869(31.7)	11,380(30.4)	8,470(22.6)			37,424
	< 20k	20k – 49k	50k -74k	75k or more			Total
	N (% Valid)	N (% Valid)	N (% Valid)	N (% Valid)			N/100%
Income	13,048 (23.7)	17,841(32.3)	8,861(16.1)	15,410(27.9)			55,160
	Mean	SD	Min	Max			N
Alcohol, Weekly	1.07	1.71	0	7			27,506

Findings

Out of 54,900 respondents about 85% (85.3%) stated they had never used prescription pain relievers non-medically while about 15% (14.7%) stated that they did use prescription pain relievers non-medically. According to the binary multivariate logistic regression analysis about 17% (Nagelkerke $r^2 = 0.17$) of the variance in non-medical prescription pain reliever use can be explained by periods of depression, mental distress, social anxiety, and alcohol consumption (Model $\chi^2 = 1285.56$; $p < 0.001$). First, consistent with H1, those who are depressed are about 60% more likely to use prescription pain relievers for non-medical reasons than those who do not report frequent periods of depression ($\text{Exp}[\beta] = 1.61$; $p < 0.001$). Second, consistent with H2, those who experience mental distress often are about 58% more likely to report the use of prescription pain relievers for non-medical reasons than those who do not ($\text{Exp}[\beta] = 1.58$; $p < 0.001$).

Consistent with H3 those who experience social anxiety are about 67% more likely to report non-medical prescription pain reliever misuse than those who do not experience social anxiety ($\text{Exp}[\beta] = 1.67$; $p < 0.001$). Consistent with H4, as number of days per week that one reports consuming alcohol increases, the likelihood of reporting non-medical prescription pain reliever use increases by about 40% ($\text{Exp}[\beta] = 1.40$; $p < 0.001$).

Regarding the control variables, although the findings regarding gender was consistent with previous research, the findings related to age, education, and income were surprising. Specifically, women were just over 27% less likely than men to use prescription pain relievers for non-medical purposes ($\text{Exp}[\beta] = 0.73$; $p < 0.001$). People between the ages of 26 and 34 are just over 19% more likely to use prescription pain relievers for non-medical purposes than people between the ages of 18 and 25 ($\text{Exp}[\beta] = 1.19$; $p < 0.05$); however, people who are 35 years old or older were over 50% less likely to use prescription pain relievers for non-medical purposes than those between the ages of 18 and 25 ($\text{Exp}[\beta] = 0.49$; $p < 0.001$). Moreover, people with a college degree had the only statistically significant difference in the use of prescription pain relievers for non-medical purposes than those with less than a high school degree. Interestingly, people with a college degree were just over 17% less likely to use prescription pain relievers for non-medical purposes than people with less than a high school degree ($\text{Exp}[\beta] = 0.83$; $p < 0.05$). Income, however, was surprisingly statistically insignificant.

Table #2: A Multivariate Logistic Regression Analysis of The Impact of The Independent Variables on The Likelihood of Non-Medical Prescription Pain Reliever Use.

	B(S.E.)	Exp(B)	95% C.I.
Periods of Depression	0.47***(.05)	1.61	1.44, 1.79
Sense of hopelessness (Never)			
Not Often	0.20*** (0.06)	1.22	1.10, 1.36
Often	0.46 ***(.10)	1.58	1.29,1.93
Social Anxiety (No Difficulty)			
Some Difficulty	0.37*** (0.06)	1.45	1.30, 1.61
Severe Difficulty	0.51 ***(.12)	1.57	1.33, 2.10
Did Not Participate	0.28 (0.15)	1.32	0.99, 1.75
Weekly Alcohol Consumption	0.33 ***(.01)	1.40	1.36, 1.43
Age (18-25)			
26-34	0.18* (0.07)	1.19	1.04, 1.36
35 and older	-0.71*** (0.06)	0.49	0.44, 0.56
Education (Less Than High School)			
HS Graduate	-0.03 (0.08)	0.97	0.83, 1.14
Some College	0.03 (0.08)	1.03	0.88, 1.21
College Graduate	-0.19* (0.09)	0.83	0.70, 0.98
Income (Less Than 20,000)			
20,000-49,999	-0.013(0.07)	0.99	0.87, 1.12
50,000-74,999	-0.03 (0.08)	0.97	0.83, 1.13
75,000 or more	-0.12 (0.07)	0.88	0.77, 1.02
Female	-0.32*** (0.05)	0.73	0.66, 0.80
Constant		-2.20*** (0.09)	
Model χ^2		1285.56***	
Nagelkerke r^2		.166	

* $p < .05$; ** $p < .01$; *** $p < .001$

Discussion

This study sought to examine non-medical prescription pain reliever use, alcohol consumption, mental health, and the correlations that exist between these variables. The findings indicate that indeed certain risky behaviors and mental health conditions correlate directly with a propensity for non-medical prescription pain reliever use. The findings in this study can potentially assist healthcare providers in safer prescribing practices as well as other practical applications. With a broader knowledge of conditions that correlate with the use of prescription pain relievers for non-medical reasons the medical community can engage in safer prescribing of this exceptionally potent medication.

The findings of the analysis relating to non-medical prescription pain reliever misuse, periods of depression (H1), mental distress (H2), and social anxiety (H3) support previous research which shows comorbidity between common mental health diagnosis and prescription pain reliever use [9,36]. The analysis shows a very significant increase in propensity for non-medical prescription pain reliever misuse and periods of depression as well as frequency of mental distress and social anxiety. This increased propensity could be linked to a theory known as “chemical disassociation”, a chemically induced form of psychogenic disassociation [37]. The individual, as a result of his or her mental illness, finds reality impossible to endure and thus seeks relief via “chemical disassociation” or self-medication [38-40].

The relief this medication provides unfortunately becomes contraindicative after a certain period of time, in that the initial mental pain in which it originally served to numb comes back in greater degree [41]. The mental pain that the medication was intended to reduce is only eased for a period of time, after the medication wears off the individual is met with the previous pain as well as the pain of his or her actions such as; guilt, remorse, and shame. The cycle of this pain can in turn foster dependence as the individual requires more medication each time to reduce the level of pain he or she feels.

The significant correlation in these findings can be helpful to providers in the healthcare community (i.e. counselors, primary care physicians, specialists) as well as any party who has a potential influence on the individuals use of prescription pain relievers (friends and loved ones i.e. social circle). Particularly of interest to the individuals in one’s social circle are the findings related to H4 which found that as alcohol consumption increased individual’s propensity for the use of prescription pain-relievers for non-medical reasons increased significantly. Alcohol consumption being more widely accepted as a social adhesive in many situations can serve to demon-

strate the level of risk that one may have to abuse pain relievers which may have initially been prescribed for medical reasons.

Rather serendipitous findings, however, were the insignificance of income and the particular significance of age and education. First, the findings demonstrate that the prescription drug epidemic has its impact on the individual regardless of socio-economic status, and that, contrary to commonsense notions, drug abuse is not exclusive to certain income brackets. Second, those who are between the ages of 26 and 34 were of a significantly higher risk to abuse prescription pain relievers than those who were between the ages of 18 and 25. These findings invoke deeper thought in that this age bracket would typically be considered to be in their “prime.” One’s body is generally considered to be in excellent shape at this time and often recovers quickly from any accrued injuries. This claim is not substantiated however due to the findings that they seem to be suffering the most from a propensity to abuse prescription pain relievers. Finally, those who reported having a college degree did demonstrate a less significant propensity for non-medical prescription pain reliever use than those who reported simply a high school education.

Limitations

The dataset used in this study is statistically representative of the U.S. adult population however it had a few substantive and operational limitations. The variable of depression in H1 was dichotomous (1) “yes” (0) “no” which did not allow for a clear understanding of the severity of depression one experienced. Though the variables for H2 and H3 are linked directly to the operationalized definitions in the hypothesis they are not the sole characteristics of said conditions. This allows for some limitations on understanding the impact of independent variables in H2 and H3 on the dependent variable. In future research scholars, could potentially expand each hypothesis into more variables associated with each condition essentially providing a single, more in-depth, study per hypothesis. The control variables also invoke the need for greater research on social factors that influence this epidemic, this study only briefly discusses these factors as they were not the primary focus of the research.

Conclusions

Prescription drug abuse has reached epidemic proportions nationwide. The findings of this study further reinforce the notion that substance abuse correlates directly with mental health as well as risky behaviors. The connection that this study makes between mental health, risky behavior and propensity for non-medical prescrip-

tion pain reliever use will hopefully inspire scholars to further examine this devastating social problem and its correlating conditions. The research in this study only addressed a small piece of the complex issue of prescription pain reliever abuse in America. Given these findings however and the impact which this epidemic has already had on the American people it is my hope that this study will beckon scholars of the scientific community to expedite further research on this issue.

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References

- [1] Quinones S. Dream land: The true tale of Americas opiate epidemic. New York, NY. Bloomsbury Press, 2015.
- [2] Johnson S. Disciplinary action and pain relief: An analysis of the pain relief act. *J Law Med Ethics*. 1996; 24:319-327.
- [3] Manchikanti, L. National drug control policy and prescription drug abuse: Facts and fallacies. *Pain Physician*. 2007;10:399-424.
- [4] Volkow N, Friedan T, Hyde P, et al. Medication assisted therapies: Tackling the opioid overdose epidemic. *J Med*. 2014; 370:2063-2066.
- [5] Compton W, Volkow N. Major increase in opioid analgesics abuse in the United States: concerns and strategies. *Drug Alcohol Depend*. 2006;81:103-107.
- [6] Martins SS, Fenton MC, Keyes KM, et al. Mood and anxiety disorders and their association with non-medical prescription opioid use and prescription opioid-use disorder: longitudinal evidence from the National Epidemiologic Study on Alcohol and Related Conditions. *Psychological Med*. 2012;42(06):1261-72.
- [7] Hooten WM, Shi Y, Gazelka HM, Warner DO. The effects of depression and smoking on pain severity and opioid use in patients with chronic pain. *PAIN*. 2011;152(1):223-9.
- [8] Merrill JO, Von Korff M, Banta-Green CJ, et al. Prescribed opioid difficulties, depression and opioid dose among chronic opioid therapy patients. *Gen Hosp Psychiatry*. 2012;34(6):581-7.
- [9] Braden JB, Sullivan MD, Ray GT, et al. Trends in long-term opioid therapy for non-cancer pain among persons with a history of depression. *Gen Hosp Psychiatry*. 2009;31(6):564-70.
- [10] Grattan A, Sullivan MD, Saunders KW, et al. Depression and prescription opioid misuse among chronic opioid therapy recipients with no history of substance abuse. *Ann Fam Med*. 2012;10(4):304-11.
- [11] Brady KT, Sinha R. Co-occurring mental and substance use disorders: the neurobiological effects of chronic stress. *Am J Psychiatry*. 2005;162(8):1483-93.
- [12] Manchikanti L, Giordano J, Boswell MV, et al. Psychological factors as predictors of opioid abuse and illicit drug use in chronic pain patients. *J Opioid Manag*. 2007;3:89-100
- [13] Soloff PH, Lynch KG, Kelly TM, et al. Characteristics of suicide attempts of patients with major depressive episode and borderline personality disorder: a comparative study. *Am J Psychiatry*. 2000;157(4):601-8.
- [14] Martins SS, Keyes KM, Storr CL, et al. Pathways between non-medical opioid use/dependence and psychiatric disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Drug Alcohol Depend*. 2009;103(1):16-24.
- [15] McCauley JL, Danielson CK, Amstadter AB, et al. The role of traumatic event history in non-medical use of prescription drugs among a nationally representative sample of US adolescents. *J Child Psychol Psychiatry*. 2010;51(1):84-93.
- [16] Zullig KJ, Divin AL. The association between non-medical prescription drug use, depressive symptoms, and suicidality among college students. *Addict Behav*. 2012;37(8):890-9.
- [17] Khantzian EJ. The self-medication hypothesis of substance use disorders: a reconsideration and recent applications. *Har Rev Psychiatry*. 1997;4(5):231-44.
- [18] Buckner JD, Schmidt NB, Lang AR, et al. Specificity of social anxiety disorder as a risk factor for alcohol and cannabis dependence. *J Psychiatr Res*. 2008;42(3):230-9.
- [19] Kilpatrick DG, Ruggiero KJ, Acierno R, et al. Violence and risk of PTSD, major depression, substance abuse/dependence, and comorbidity: results from the National Survey of Adolescents. *J Consult Clin Psychol*. 2003;71(4):692.
- [20] Daughters SB, Lejuez CW, Bornoalova MA, et al. Distress tolerance as a predictor of early treatment dropout in a residential substance abuse treatment facility. *J Abnorm Psychol*. 2005;114(4):729.

- [21] K Kilts CD, Kelsey JE, Knight B, et al. The neural correlates of social anxiety disorder and response to pharmacotherapy. *Neuropsychopharmacology*. 2006;31(10):2243-53.
- [22] Tan KR, Rudolph U, Lüscher C. Hooked on benzodiazepines: GABA A receptor subtypes and addiction. *Trends Neurosci*. 2011;34(4):188-97.
- [23] Hyman SE, Malenka RC, Nestler EJ. Neural mechanisms of addiction: the role of reward-related learning and memory. *Annu. Rev. Neurosci*. 2006;29:565-98.
- [24] Botvin GJ, Baker E, Renick NL, et al. A cognitive-behavioral approach to substance abuse prevention. *Addict Behav*. 1984;9(2):137-47.
- [25] Peirce RS, Frone MR, Russell M, et al. A longitudinal model of social contact, social support, depression, and alcohol use. *Health Psychol*. 2000;19(1):28.
- [26] Fiellin LE, Tetrault JM, Becker WC, et al. Previous use of alcohol, cigarettes, and marijuana and subsequent abuse of prescription opioids in young adults. *J Adolesc Health*. 2013;52(2):158-63.
- [27] Stinson FS, Grant BF, Dawson DA, et al. Comorbidity between DSM-IV alcohol and specific drug use disorders in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Drug Alcohol Depend*. 2005;80(1):105-16.
- [28] Saunders KW, Von Korff M, Campbell CI, et al. Concurrent use of alcohol and sedatives among persons prescribed chronic opioid therapy: prevalence and risk factors. *J Pain*. 2012;13(3):266-75.
- [29] World Health Organization. 2004. "Global Status Report on Alcohol 2004" Department of Mental Health and Substance Abuse. 1-88
- [30] McCabe, Sean Esteban, James A. Cranford and Carol J. Boyd. 2006. "The relationship between past-year drinking behaviors and nonmedical use of prescription drugs: Prevalence of co-occurrence in a national sample." *Drug and Alcohol Dependence*. 84(3): 281-288.
- [31] McCabe, Sean Esteban, James A. Cranford, Brady T. West. "Trends in prescription drug abuse and dependence, co-occurrence with other substance use disorders, and treatment utilization: Results from two national surveys" *Journal of Addictive Behaviors*. 33(10): 1297-1305. 2006
- [32] McCabe, Sean Esteban, Brady T. West and Henry Wechsler. 2007. "Trends and college-level characteristics associated with the nonmedical use of prescription drugs among US college students from 1993 to 2001." *Addiction*. 102(3): 455-465.
- [33] McCabe, Sean Esteban, Christian J. Teter, Carol J. Boyd, John R. Knight, and Henry Wechsler. 2005. "Nonmedical use of prescription opioids among U.S. college students: Prevalence and correlates from a national survey." *Addictive Behavior*. 30(4): 789-805.
- [34] McCabe, Sean E, Brady T. West, Michele Morales, James A. Cranford and Carol J. Boyd. 2007. "Does early onset of non-medical use of prescription drugs predict subsequent prescription drug abuse and dependence? Results from a national study." *Addiction*. 102(12): 1920-1930.
- [35] Center for Behavioral Health Statistics and Quality. (2014). 2013 National Survey on Drug Use and Health Public Use File Codebook, Substance Abuse and Mental Health Services Administration, Rockville, MD
- [36] Sullivan, Mark D., Mark J. Edlund, Lily Zhang, Jurgen Unutzer, Kenneth B. Wells. 2006. "Association Between Mental Health Disorders, Problem Drug Use, and Regular Prescription Opioid Use". *Journal of Internal Medicine*. 166(19): 2087-2093.
- [37] Somer, Eli., Libby Altus, Karni Ginzburg. 2010. "Dissociative psychopathology among opioid use disorder patients: exploring the "chemical dissociation" hypothesis" *Comprehensive Psychology*. 51(2010): 419-425
- [38] Carrigan, Maureen H., Carrie L. Randall. 2003. "Self-Medication in Social Phobia: A Review of The Alcohol Literature". *Journal of Addictive Behaviors*. 28 (2): 269-284.
- [39] Robinson, Jennifer, Jitender Sareen, Brian J. Cox, James Bolton. 2009. "Self-Medication of Anxiety Disorders with Alcohol and Drugs: Results from a Nationally Representative Sample". *Journal of Anxiety Disorders*. 23: 38-45.
- [40] Bolton, James, Brian Cox, Ian Clara, Jitender Sareen. 2006. "Use of Alcohol and Drugs to Self-Medicate Anxiety Disorders in a Nationally Representative Sample". *The Journal of Nervous Disorders and Mental Disease*. 194(11): 818-825.
- [41] Hauser, Winfried, Fritjof Bock, Peter Engeser, Thomas Tolle, Anne Wilweber-Strumpf, Frank Petzke. 2014. "Long Term Opioid Use in Non-Cancer Pain". *Deutsches Arztebl International*. 111: 732-740.