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The Epidemiology and Treatment of Prescription Drug Disorders in the United States

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1. Introduction

The drug problem in the United States is a complex mosaic involving different types of drugs, consumption practices, and biological and psychological responses to their effects. Over the past two decades, the fields of psychiatry and neurology have witnessed dramatic scientific breakthroughs in understanding the actions of drugs that can be used to regulate the nervous system (Nestler, Hyman, & Malenka, 2009). This has led to a dramatic increase in use of these medications for treating a wide range of physical and mental disorders (Dasgupta et al., 2006). An unintended consequence of this increased level of availability is that a large proportion of these drugs are being consumed in excess of the dosage recommended by the manufacturer or prescriber, used to self-treat illnesses instead of seeking professional medical care, and/or combined with other drugs increase the desired effects. As a result, the numbers of unintentional poisonings and emergency room visits have nearly doubled. For instance, the latest figures from the Drug Abuse Warning Network (DAWN) indicate that in 2008, that nearly half of the 2 million emergency room visits to U.S. hospitals involved prescription medications. Approximately two-thirds of those visits that involved prescription medications were for prescription pharmaceuticals only and no co-occurring illicit drug or alcohol abuse (SAMHSA, 2006). In addition to the tremendous economic costs associated with overdoses involving prescription medications, the adverse social and mental/physical health effects, though difficult to directly quantify, are considerable.

The goal of this chapter is to present an overview of the current state of knowledge about the nonmedical use of prescription medications. Because of the sheer volume of the literature, this chapter cannot cover the entire breadth of this complex phenomenon. Therefore, the discussion is limited to those exhibiting features of dependence on prescription medications, as this is the most harmful pattern of use. Within the context of dependence, the goal is to present a concise review of the epidemiological data on the prevalence of dependence on prescription medications within various population sub-groups (e.g. youth, those with co-occurring illicit substance use disorders, and previous history of psychiatric illness). In addition, a brief summary is provided on the pharmacological properties that are likely to confer selective use of the particular drug

class for nonmedical use. Information on the prevalence of seeking treatment for a substance use disorder involving prescription drugs, unmet need for treatment, and types of evidence-based treatment available for each drug class is also presented. Surveillance data also indicate that nonmedical use occurs in a wide range of medication classes (e.g., anabolic steroids, over-the-counter cough medicines, antihistamines) (Compton & Volkow, 2006; Kuehn, 2007; Lankenau, Sanders, Bloom, & Hathazi, 2008). However, this chapter focuses on the three classes of medications where the epidemiological and physiological literatures indicate that the likelihood of transitioning beyond experimentation to dependence is greatest—pain relievers, stimulants, and sedatives/tranquilizers (Blanco et al., 2007). Unless otherwise noted, the source of the surveillance data is the 2005-2009 National Survey on Drug Use and Health (NSDUH). It is a cross-sectional survey of non-institutionalized youth (age 12-17) and adults (age 18+) in the United States that is conducted on an annual basis and arguably contains the richest source of data covering topics related to the nonmedical use of prescription medications (Colliver, Kroutil, Dai, & Gfroerer, 2006).

2. Taxonomy of nonmedical prescription drug use

The term *nonmedical use of prescription drugs* has been criticized in the literature because studies typically define it use as a single item. However, NMPD is a multidimensional construct that encompasses a wide range of motivations to use prescription medications (Boyd & McCabe, 2008). Unlike heroin or other illicit drugs, prescription medications can be used to treat legitimate medical conditions. With the exception of cocaine, most illicit drugs are defined by the Drug Enforcement Agency in the United States as having no medical therapeutic value and therefore are considered illegal to possess or dispense (Table 1).

An important side note deserves mentioning. Marijuana and cocaine have some level of medically accepted therapeutic value and are available in certain States only under extremely unique circumstances. For instance, marijuana is currently treated by the US federal government as having no medically accepted therapeutic value and is therefore considered illegal (See Table 2). A small number of States (e.g., California, Colorado) consider marijuana an acceptable treatment, such as for patients with glaucoma. In those states, it is available from a licensed prescriber and may be obtained from a specialized pharmacy licensed to dispense limited quantities to patients. Cocaine is used as a topical anesthetic for conditions of the eye and nose, including nasal cauterization. However, prescriptions for cocaine and marijuana are highly regulated.

Substances: Categories and Names	Examples of *Commercial* and Street Names	DEA Schedule* / How Administered**	Intoxication Effects / Potential Health Consequences
Depressants			
barbiturates	*Amytal, Nembutal, Seconal, Phenobarbital;* barbs, reds, red birds, phennies, tooies, yellows, yellow jackets	II, III, V/injected, swallowed	Reduced pain and anxiety; feeling of well-being; lowered inhibitions; slowed pulse and breathing; lowered blood pressure; poor

Substances: Categories and Names	Examples of *Commercial* and Street Names	DEA Schedule* / How Administered**	Intoxication Effects / Potential Health Consequences
benzodiazepines (other than flunitrazepam)	*Ativan, Halcion, Librium, Valium, Xanax*; candy, downers, sleeping pills, tranks	IV / swallowed	concentration/confusion, fatigue; impaired coordination, memory, judgment; respiratory depression and arrest, addiction
flunitrazepam****+	*Rohypnol*; forget-me pill, Mexican Valium, R2, Roche, roofies, roofinol, rope, rophies	IV / swallowed, snorted	*For barbiturates* – sedation, drowsiness/depression, unusual excitement, fever, irritability, poor judgment, slurred speech, dizziness *For benzodiazepines* – sedation, drowsiness/dizziness *For flunitrazepam* – visual and gastrointestinal disturbances, urinary retention, memory loss for the time under the drug's effects
Opioids and Morphine Derivatives			
codeine	*Empirin with Codeine, Fiorinal with Codeine, Robitussin A-C, Tylenol with Codeine*; Captain Cody, Cody, schoolboy; (with glutethimide doors & hours, loads, pancakes and syrup	II, III, IV / injected, swallowed	Pain relief, euphoria, drowsiness/respiratory depression and arrest, nausea, confusion, constipation, sedation, unconsciousness, coma, tolerance, addiction *For codeine* – less analgesia, sedation, and respiratory depression than morphine
fentanyl	*Actiq, Duragesic, Sublimaze*; Apache, China girl, China white, dance fever, friend, goodfella, jackpot, murder 8, TNT, Tango and Cash	II / injected, smoked, snorted	
morphine	*Roxanol, Duramorph*; M, Miss Emma, monkey, white stuff	II / injected, swallowed, smoked	
opium	laudanum, paregoric; big O, black stuff, block, gum, hop	II, III, V / swallowed, smoked	

Substances: Categories and Names	Examples of *Commercial* and Street Names	DEA Schedule* / How Administered**	Intoxication Effects / Potential Health Consequences
other opioid pain relievers (oxycodone, meperidine, hydromorphone, hydrocodone, propoxypene)	*Tylox, OxyContin, Percodan, Percocet*; oxy 90s, oxycotton, oxycet, hillbilly heroin, percs *Demerol, meperidine hydrochloride*; demmies, pain killer *Dilaudid*; juice, dillies *Vicodin, Lortab, Lorcet, Darvon, Darvocet*	II, III, IV/swallowed, injected, suppositories, chewed, crushed, snorted	
Stimulants			
amphetamines	*Biphetamine, Dexedrine*; bennies, black beauties, crosses, hearts, LA turnaround, speed, truck drivers, uppers	II/injected, swallowed, smoked, snorted	Increased heart rate, blood pressure, metabolism; feelings of exhilaration, energy, increased mental alertness/rapid or irregular heart beat; reduced appetite, weight loss, heart failure *For amphetamines* – rapid breathing; hallucinations/tremor, loss of coordination; irritability, anxiousness, restlessness, delirium, panic, paranoia, impulsive behavior, aggressiveness, tolerance, addiction *For cocaine* – aggression, violence, psychotic behavior/memory loss, cardiac and neurological damage; impaired memory and learning, tolerance, addiction *For methylphenidate* – increase or decrease in blood pressure, psychotic episodes/ digestive problems, loss of appetite, weight loss
cocaine	*Cocaine hydrochloride*; blow, bump, c, candy, Charlie, coke, crack, flake, rock, snow, toot	II/injected, smoked, snorted	
methamphetamine	*Desoxyn*; chalk, crank, crystal, fire, glass, go fast, ice, meth, speed	II/injected, swallowed, smoked, snorted	
methylphenidate	*Ritalin*; JIF, MPH, R-ball, Skippy, the smart drug, vitamin R	II/injected, swallowed, snorted	

Schedule I and II drugs have high potential for abuse. They require greater storage security and have a quota on manufacturing, among other restrictions. Schedule I drugs are available for research only and have no approved medical use; Schedule II drugs are available only by prescription (unrefillable) and require a form for ordering. Schedule III and IV drugs are available by prescription, may have five refills in 6 months, and may be ordered orally. Most Schedule V drugs are available over the counter.

**Taking drugs by injections can increase the risk of infection through needle contamination with staphylococci, HIV, hepatitis, and other organisms.*

****Associated with sexual assaults.*

+Not available by prescription in the U.S.

Table 1. Selected Prescription Drugs with Potential for Abuse

Substance Category	Definition	Example Drugs
Schedule I	• Most restrictive level • Includes drugs or other substances with a high potential for abuse • No currently accepted medical use in the United States • Low level of safety • Not approved for use, distribution, manufacture, or importation	Heroin Marijuana Phencyclidine (PCP) Lysergic acid dithylamide (LSD)

Schedule II	• Drugs have high abuse potential
	• Have currently accepted medical use in treatment, with severe restrictions
		Cocaine
		Methamphetamine
		Amphetamines
		    Dextroamphetamine
		    Adderall®
		Morphine
		Oxycodone
		    OxyContin®
		Methylphenidate
		    Ritalin®

Schedule III	• Drugs have abuse potential less than that of Schedule I or II drugs
	• Have currently accepted medical uses in treatment
		Hydrocodone
		    Vicodin®
		Butalbital
		    Fiorinal®

Schedule IV	• Drugs have lower abuse potential than those of Schedule III drugs
	• Have currently accepted medical uses in treatment
		Alprazolam
		    Xanax®
		Diazepam
		    Valium®
		Propoxyphene
		    Darvon®

Schedule V	• Drugs have low abuse potential • Have recognized medical uses • Some pharmaceuticals contain drugs with higher abuse potential but in much lower concentrations relative to other ingredients	Cough medicines with codeine Robitussin AC®

Table 2. Drug Enforcement Agency's Controlled Substances Act Definitions of Substances Subject to Food and Drug Administration Regulation

Notwithstanding marijuana and cocaine, many illicit drugs were originally developed for medicinal purposes, but were deemed to have little or no efficacy, or having such a high abuse liability that they were prohibited as a legal medical treatment (e.g., heroin, LSD).

Therefore, prescription medications are unique in that their use is motivated by factors other than euphoria. For instance, prescription pain relievers are often used to treat legitimate medical injuries, but many patients self-treat without a doctor's prescription when a dosage of the drug is readily available to them (e.g., using a spouses prescription).

Attempts to develop survey items to capture the concept of nonmedical use has been challenging because there is no universally accepted definition as to what constitutes nonmedical use prescription drug use (NMPD). The National Survey on Drug Use and Health (NSDUH) frames the question as whether the respondent "used a particular drug that was not prescribed for you or was used only for the experience or feeling it caused." It is sometimes argued that the NSDUH definition of NMPD is overly inclusive, as it could include drugs that are used for self-treatment of a medical condition, but were not specifically prescribed by a physician (Huang et al., 2006). In contrast, another annual cross-sectional surveillance study focused on youth, the Monitoring the Future (MTF) study defines nonmedical prescription drug use as 'use of prescription medications without a doctor telling you to take them' (Johnston, O'Malley, Bachman, & Schulenberg, 2009). Then, the survey follows with queries about motivations about the most important reason for use, such as: experimentation, pain relief, euphoria. Understanding motivations for use are important because nonmedical users who use only for therapeutic value and those using for other reasons, such as for euphoria, are likely to have different profiles of risk and protective factors for use, abuse liabilities, and prevention and treatment needs (Zachny and Lichtor, 1998; Boyd and McCabe).

In the United States, there is a tremendous gulf among legislative stakeholders in terms of a formal taxonomy for nonmedical prescription drug use and problematic levels of use. The Food and Drug Administration has urged manufactured to focus on "Physical Dependence" and "Tolerance" (Dasgupta, Henningfield, Ertischek, & Schnoll, 2011) in the assessment of abuse liability for prescription medications. The National Institutes of Health (NIH) is concerned both the physical and psychological aspects of addiction that are linked to extant diagnostic criteria, such as the American Psychiatric Association's Diagnostic and Statistical Manual (DSM) or the International Classification of Diseases (ICD) categories of abuse and dependence (Compton & Volkow, 2006). The United States Drug Enforcement Agency (DEA) takes a more scientific approach, focusing on the legal requirements (e.g., number and timing of refills, quantity dispensed under a single prescription, written versus ePrescribing) that is tied to a drug's particular abuse liability (Katz et al., 2007). The words "abuse" and "misuse" have often been used interchangeably, but may be used to define separate acts of nonmedical use. The term Abuse may refer to use that involves seeking a euphoric "high" and misuse typically refers to "intentional use that involves a legitimate prescription that is used in amounts not directed by the prescriber or to treat another medical condition." An additional piece of this complicated taxonomy is whether the drug was prescribed for the user or whether they obtained it illicitly (e.g., stole/obtained from friends/family, forged written prescription, feigned symptoms to a prescriber with liberal prescribing habits [pill mills] (Boyd & McCabe, 2008).

In 2003, the College on Problems on Drug Dependence, the largest professional society in the United States dedicated solely to the advancement of knowledge about drug abuse, published a position statement about prescription pain relievers (Zacny et al., 2003). The statement urged for a formal clarification of the term nonmedical use that is broad enough to include motivations for use for inclusion on national surveillance surveys, such as the NSDUH. However, the purpose of this chapter focuses on the epidemiology and treatment

of levels of use that are problematic and in need of specialty substance abuse treatment. Therefore, clarification of the term nonmedical use is less important than resolution of the diagnostic criteria that can be used to assess problem use, such as the DSM or ICD classifications of abuse or dependence. There is some debate about the degree to which opioids differ in their abuse liability and phenotypic expression of abuse and/or dependence symptoms (Wu, Woody, Yang, & Blazer, 2011; Wu, Woody, Yang, Mannelli, & Blazer, 2011). However, DSM and ICD criteria are generally accepted measures that can be easily translated onto epidemiological surveys to estimate the population in need of substance abuse treatment services for prescription drug-related problems. There are many clinical tools that are used to diagnose problem use for different therapeutic classes, as well as biological challenge tests of physical dependence (Kosten, Bianchi, & Kosten, 1989). At one end of the continuum, there is concern that the "one-size fits all" approach to defining the concepts of abuse and dependence may not operate similarly across all substances even within a therapeutic class (e.g., extended release having lower abuse liability than immediate release oxycodone) (Dasgupta, et al., 2011). At the other end of the continuum, there is an argument that abuse and dependence are a continuum, which is derived from an underlying biopsychosocial propensity (Krueger et al., 2002). Regardless of the placement on the spectrum, the term *Addiction* refers to a chronic and relapsing pattern of use and is defined by essentially three characteristics: compulsive use, loss of control in limiting intake, and altering behavioral activities in support of drug consumption. Medical professionals typically employ more specific terminology aligned within clinical (e.g., DSM or ICD criteria) criteria when referencing disordered patterns of substance use, such as abuse and/or dependence.

For the remainder of this chapter, we present data on problem levels of prescription drug use using the DSM-IV/ICD classification scheme of abuse and/or dependence. This scheme is the most widely employed diagnostic tool for problem use on national surveillance data systems, and are used to frame the nation's perspective and conversation related to research, prevention, treatment, and public policy toward the nonmedical use of prescription drugs. Within this diagnostic taxonomy, hierarchical criteria are used to ensure that substance use disorders are classified by whether symptoms are directly tied to substance use or a separate psychiatric disorder or illness. For example, mood and anxiety disorders (APA, 2006) have exclusionary criteria because a common symptom of withdrawal (e.g., "dope sick") may involve symptomotology that overlaps with mood and anxiety disorders, such as "feeling downhearted and blue" or "nervousness". This task is complicated by the high rate of comorbidity between mental (i.e., mood, anxiety, and personality) and substance use disorders (McLellan, Lewis, O'Brien, & Kleber, 2000; NIDA, 1999; O'Brien et al., 2004).

Evaluating a substance use disorder has been established using criteria that can be implemented by a clinician, or a trained interviewer using a semi-structured instrument, such as the Structured Clinical Interview for DSM Axis II disorders (First, 2002). There are also many diagnostic tools that are fully structured and can be implemented in the context of a research interview. These include the Composite International Diagnostic Interview [CIDI] (Green et al., 2011; Haro et al., 2006; Kessler et al., 2004)and the Associated Disabilities Interview Schedule [AUDADIS] (Grant et al., 2003; Grant, Harford, Dawson, Chou, & Pickering, 1995). Ascertaining the count of the population in need of services is a challenge because of the resources needed to execute a full diagnostic exam on a

sufficiently large enough sample that permits generalization to the population as a whole. However, such a task is critical for policymakers to help identify and prioritize placement of finite resources that are funded through public monies. As mentioned earlier, there are a small number of surveys that collect data annually on nonmedical use of prescription drugs, but only one implements a fully-structured diagnostic interview for substance use disorders annually for youth (age 12-17) and adults (ages 18 or older—the National Survey on Drug Use and Health (SAMHSA, 2008). Other annual surveys administer brief screening scales that can be used to assess probable case based on a small number of items. A drawback is that they lack the sensitivity and specificity to accurately assess the number in need of treatment (Aldworth et al., 2010; Novak, Colpe, Barker, & Gfroerer, 2010). Therefore, in-depth diagnostic scales provide the best approach to capturing the complex phenomena of substance abuse disorders, despite the length and expense in their implementation.

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) distinguishes problematic substance use along two categorical rubrics (shown in Table 3):

- ABUSE: Captures a maladaptive pattern of use that causes significant impairment in social, mental, and physical life-world domains. An example is missing work or failing to attend to household obligations because of use. Continued use despite consistent interpersonal or social problems associated with use is another hallmark system.

- DEPENDENCE: Is defined by a maladaptive pattern of use with adverse clinical consequences. Dependence involves two physical aspects: (1) *Tolerance*—refers to the decrease in the physical or psychological effects of a constant dosage of a drug over time; and (2) *Withdrawal*—refers to a physiological state of adverse mental and physical symptoms (e.g., nausea, insomnia, muscle aches/pains, These symptoms will vary depending upon how long the medication was taken and the type of medication.

In the next section, we summarize the epidemiology of nonmedical prescription drug use, with an emphasis on disordered patterns of use as defined by DSM-IV criteria (APA, 2002). Surveillance data are drawn from the National Survey on Drug Use and Health (SAMHSA, 2009). The NSDUH is an annual, nationally representative survey of youth (age 12-17) and adults (age 18 or older) in the United States. The procedures and characteristics of the sample have been published extensively elsewhere (SAMHSA, 2008). Briefly, the sample includes approximately 65,000 respondents each year. The target population is the civilian, noninstitutionalized population of the United States (including civilians living on military bases) and residents of noninstitutional group quarters (e.g., college dormitories, group homes, civilians dwelling on military installations) and persons with no permanent residence (homeless people in shelters and residents of single rooms in hotels). The NSDUH collects information on a large range of illicit substances, including consumption patterns, treatment utilization, and diagnoses aligned with the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for abuse and/or dependence (APA, 2000) for alcohol and selected drugs. For this paper, Substance use treatment was coded if the respondent reported any therapy or treatment, including detoxification and treatment for any medical problems associated with their drug use. Unmet treatment need was defined as the presence of a past-year DSM-IV diagnosis for abuse and/or dependence on prescription medications, but the respondent did not report receiving substance abuse treatment. Due to the complex sampling design of the NSDUH, all descriptive and inferential analyses were conducted with SUDAAN release 10.0 (RTI, 2009).

Disorders	Definition
Substance Use Disorders	
Substance Dependence	A maladaptive pattern of substance use with adverse clinical consequences. The DSM-IV has widened the concept of dependence to include the association of substance use with uncontrolled use or with use in spite of adverse consequences.
Substance Abuse	A maladaptive pattern of substance use that causes clinically significant impairment, not meeting dependence criteria. This may include impairments in social, family, or occupational functioning, in the presence of a psychological or physical problem, or in satiations in which use of the substance is physically hazardous, such as driving while intoxicated.
Substance Induced Disorders	
Substance Intoxication	Reversible, substance-specific physiological and behavioral changes due to recent exposure to a psychoactive substance. Produced by all substances.
Substance Withdrawal	A substance-specific syndrome that develops following cessation of or reduction in dosage of a regularly used substance. Occurs with chronic use of all substances, except perhaps cannabis and hallucinogens.
Substance Induced Delirium (confusion, psychosis)	Occurs with overdose of many substances
Substance Induced Psychotic Disorder (psychosis)	May occur with phenylcyclidine (PCP) and hallucinogens, stimulants, cannabis, and alcohol.
Substance Induced Mood Disorder (depression, mania) **Anxiety**	Common with many substances, especially alcohol and stimulants. Disorder must be distinguished from primary psychiatric disorder that preceded drug use.
Substance Induced Sleep Disorder	A sleep disturbance attributable to acute or chronic substance use. Common with alcohol, sedatives, and stimulants.
Substance Induced Sexual Dysfunction	Alcohol, benzodiazepines, and opioids commonly reduce sexual responsiveness and performance.
Substance Induced Persisting Disorders	Substance-specific syndromes that persist long after drug use ceases (e.g., hallucinogen "flashbacks," memory impairments, or dementia).

* dsm-iv criteria (american psychiatric association, 1994)

Table 3. Classification of Substance Use and Substance Induced Disorders*

3. Patterns of prescription drug use and disordered use in the United States

Although trend data indicate that the prevalence of nonmedical use of prescription drugs has nearly doubled over the past two decades (Blanco, et al., 2007), the rate of nonmedical

use remained fairly consistent over the past 5 years (Figure 1). Among youth (aged 12-17), the NSDUH showed that approximately 8 percent (8,000 per 100,000) used any class of prescription medication in the prior year. Among those that used, about 16% met the criteria for abuse or dependence (Figure 2). The rate of use far exceeds that of adults (aged 18 or older) where approximately 6% used any prescription medication non-medically and the
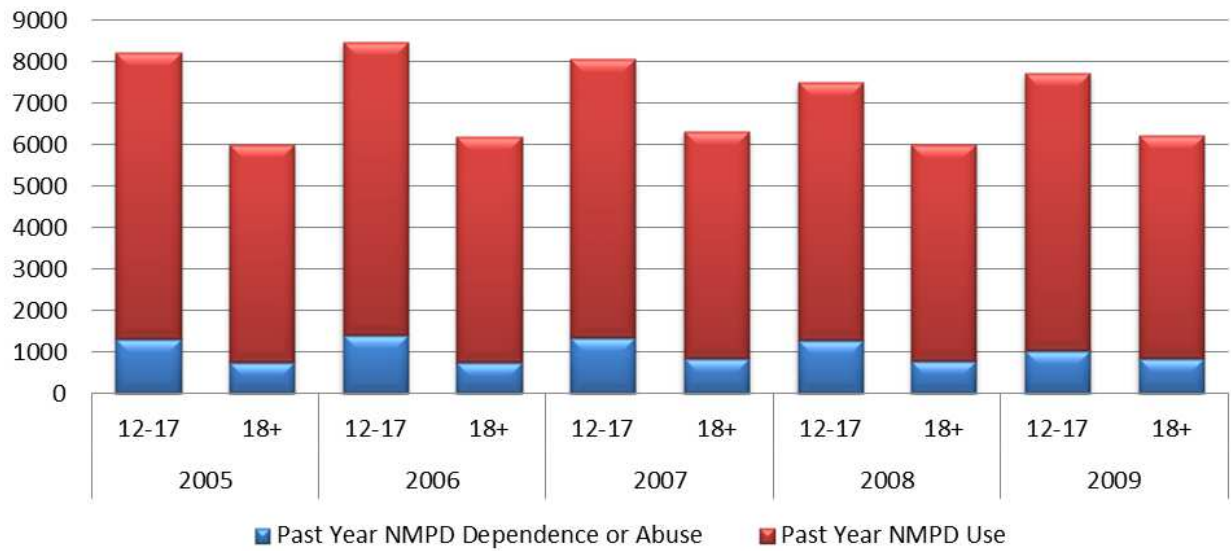

Fig. 1. Past Year Nonmedical Prescription Drug Use and Meeting Criteria for Dependence or Abuse of Nonmedical Prescription Drugs, by Age and Year: 2005-2009 NSDUH (per 100,000)
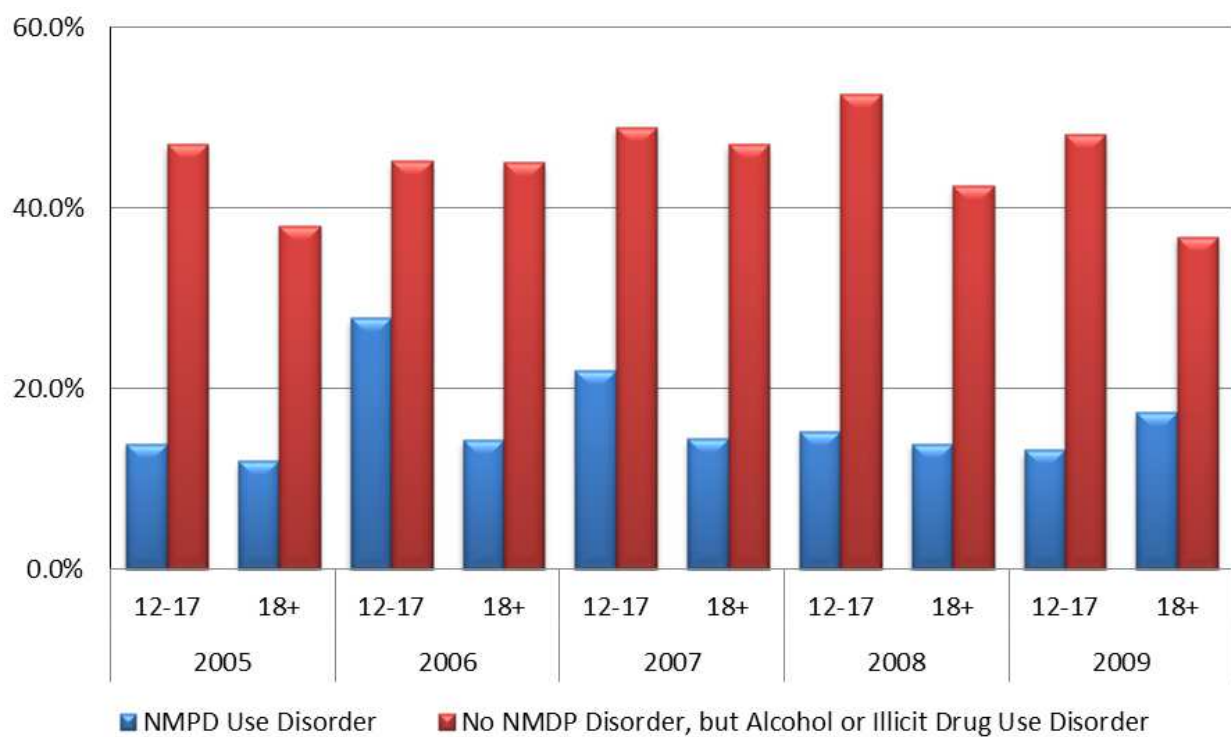
Fig. 2. Past Year Substance Use Disorder among Persons Receiving Drug Treatment in the Past Year, by Age and Year: 2005-2009 NSDUHs (In Percent)

rates of disordered use was about 16%, similar to adolescents. These data suggest that problematic levels of abuse are developing far earlier in lifecourse, especially compared to other drugs, such as heroin and cocaine where the median age of disordered use is in the mid 20s (SAMSHA, 2006). Additional data (Figure 2) indicate that adolescent females are progressing to abuse/dependence more rapidly than males. Among those that received any form of treatment for a substance use disorder in the United States (about 2.3 million in 2009), Figure 3 reveals that approximately 15% to 18% met the criteria for a prescription drug disorder. A concern about drug treatment is that care usually focuses on eliminating the most harmful substance in the client's drug-taking repertoire, so prescription drug disorders often go unrecognized and untreated compared to illicit drugs such as cocaine and heroin. When broken down by the amount of co-occurring disorders among those in treatment, Figure 4, shows that of those in drug treatment that have a prescription drug disorder, about 70% have a co-occurring drug and/or alcohol use disorder as well.

■ NMPD Use Disorder Only

■ NMPD and Alcohol Use Disorder, No Other Illicit Drug Use Disorder

■ NMPD and Other Illicit Drug Use Disorder, No Alcohol Use Disorder
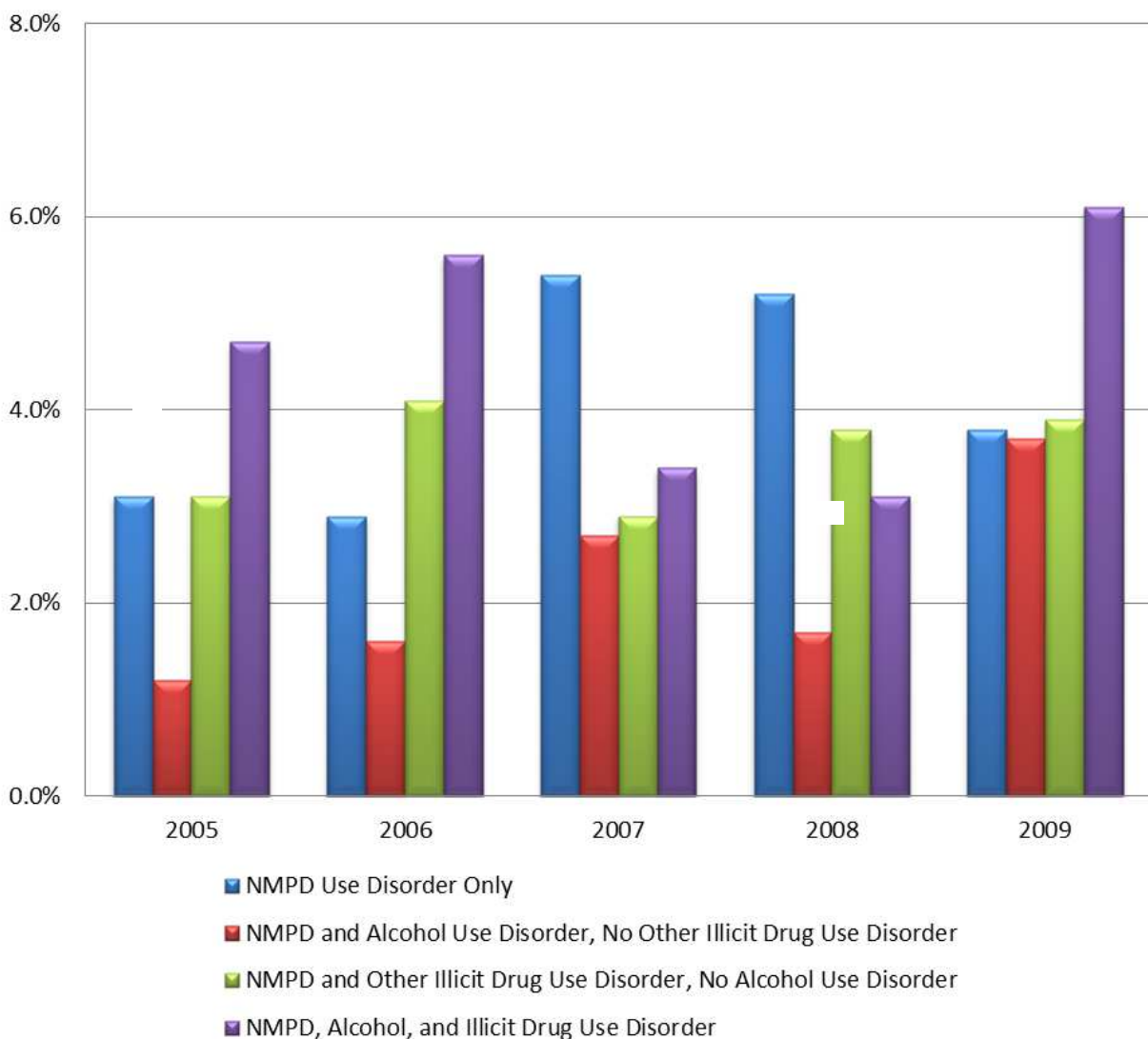
■ NMPD, Alcohol, and Illicit Drug Use Disorder

Fig. 3. Past Year Substance Use Disorders Among Persons Aged 18 or Older Receiving Past Year Drug Treatment, by Year: 2005-2009 NSDUHs
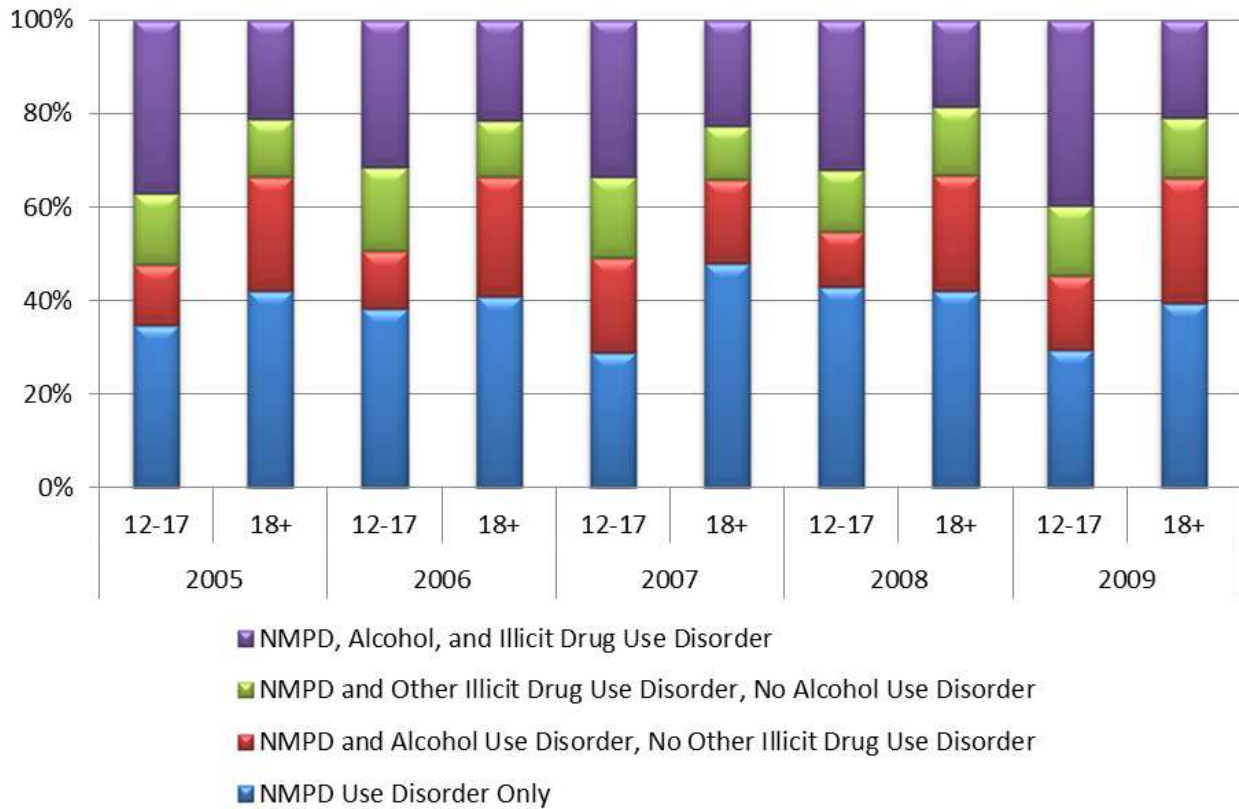
Fig. 4. Poly Drug Use Disorder among Persons with NMPD Use Disorder, by Age and Year:
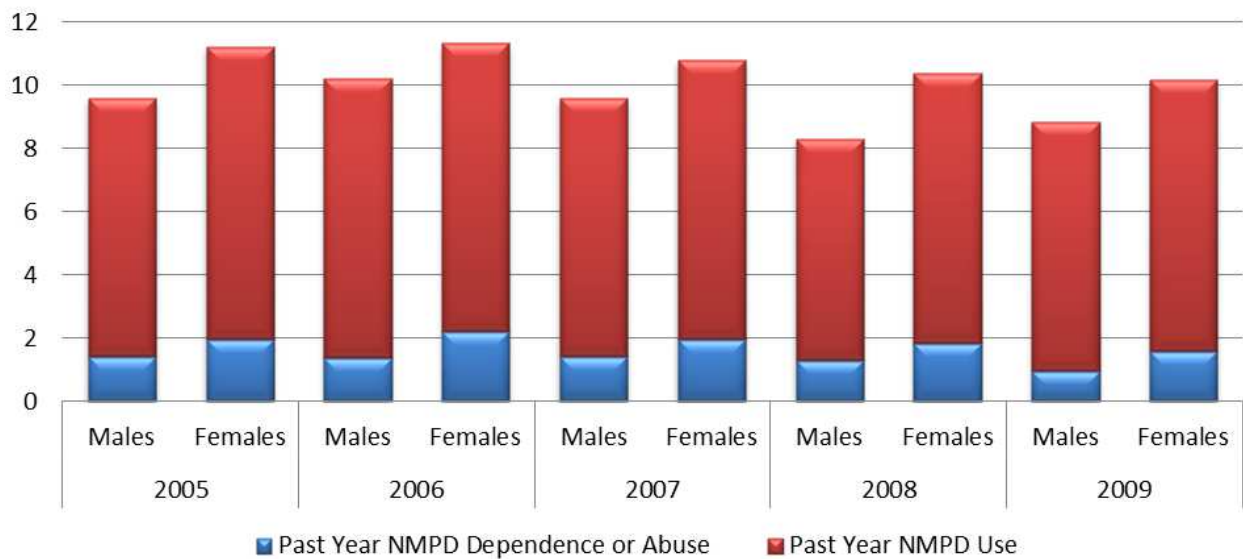2005-2009 NSDUHs

Fig. 5. Percent of Past Year Nonmedical Prescription Drug Use and Meeting Criteria for
Dependence or Abuse of Nonmedical Prescription Drugs among 12-17 years olds, by Sex
and year: 2005-2009 NSDUHs

4. Prescription pain relievers

Therapeutic Indications: Pain relievers as a therapeutic medication class are also referred to as analgesics. They are distinguished by the ways in which they act in the peripheral or central nervous system. Analgesics that are non-steroidal anti-inflammatory drugs (NSAIDS) are used to treat mild pain and act by reducing inflammation at the site of an injury or disease in the body. NSAIDS typically do not require a prescription in the United States and are available "over-the-counter" (OTC) at local pharmacies, drug stores, and even gas stations. Other types of (OTC) analgesics are not NSAIDS (e.g., acetaminophen), but act on the same physiological pathways to reduce the neuro-chemical sensation of pain.

Narcotic analgesics are used to treat moderate to severe pain, in many instances require a prescription from a prescriber that is licensed by the Drug Enforcement Agency (DEA). Perhaps the most widely used class of pain reliever in the United States is opioids, which can be subdivided into three types. First, naturally occurring (e.g., morphine or codeine) opioids are derived from the opium poppy plant. These drugs are typically altered into pro-drugs during the pharmaceutical manufacturing process, meaning that they are chemically converted to opioids as they are metabolized into the body. This manufacturing strategy is preferable to leaving the chemical structure unaltered (i.e., free base) because it increases the bioavailability of the drugs during metabolization and therefore maximizes their efficacy. Naturally occurring opioids are also used as chemical building blocks for semi-synthetic opiates (e.g., hydrocodone, oxycodone). Both naturally occurring and semi-synthetic opioids attach to specific opioid receptors in the brain (e.g., Mu, Kappa, Delta, and Epsilon). Heroin is a semi-synthetic opioid that is similar in chemical structure to morphine and was primarily developed as a legitimate treatment for pain in the 1800s. However, it was discovered to have high affinity to abuse because it quickly activates the brain's opioid neuro-receptors, thus producing a quick euphoric flush that is highly desirable by recreational abusers. Fully synthetic opioids (e.g., methadone, tramadol, dextropropoxyphene) are fully manufactured drugs and are not chemically related to opiates in structure, other than they selectively bind to the same neural receptors in the brain. There is controversy regarding the degree to which fully synthetic opioids have the same abuse liability as naturally occurring or semi-synthetic opioids (Aldworth, et al., 2010; Dasgupta, et al., 2011; Wu, Woody, Yang, Mannelli, et al., 2011). Overall, these drugs are known as exogenous opioids in that they are external stimuli, whereas endogenous opioids are produced internally (e.g., endorphins) in response to high levels of physical or emotional activity, and are secreted from the pituitary glands and attach to the opioid-like receptors in the brain.

Epidemiology of Nonmedical and Disordered Use: The United States has one of the highest levels per capital consumption of prescription opioids (United Nations, 2004). While the use of narcotic opioids is recognized as an important weapon in the physician's arsenal to combat mild to severe pain, studies have correlated high levels of exposure to nonmedical use and problematic levels to dependence (Dasgupta et al, 2006). Prescription pain relievers are the have the highest prevalence of nonmedical use, especially among youth aged 12-17 (Figure 6). Between 2005 to 2009, approximately 6.5% of youth (pop est. 6,000 per 100,000) used a prescription pain reliever non-medically in the prior year. About 1/6 of those who abused also used at levels consistent with DSM-IV abuse and/or dependence. Among adults aged 18 or older, the rates of nonmedical use were lower, approximately 4.5% (pop est. 4,500 per 100,000). The rates of disordered use were similar to youth, with about 16 percent reporting symptoms of abuse and/or dependence.
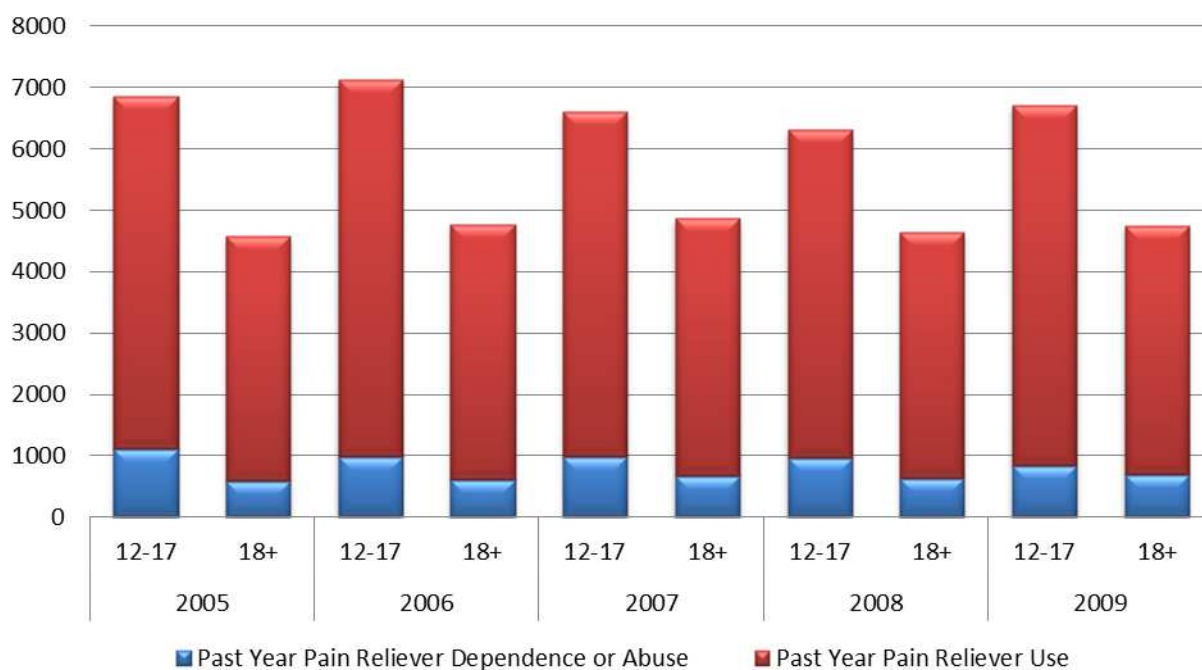
Fig. 6. Past Year Pain Reliever Use and Meeting Criteria for Dependence or Abuse of Pain Relievers, by Age and Year: 2005-2009 NSDUHs (Per 100,000)

Treatment: Treatment for opioid pain medications tend toward the pharmacological spectrum, although some behavioral therapies do exist. The most common pharmacological treatment therapies for opioid pain medications include methadone, Buprenorphine, and Naltrexone or buprenorhpine/suboxone. Of the three, methadone is the oldest and most frequently used pharmacology (Amato et al., 2005), although limited evidence has shown that Buprenorphine may be slightly advantageous to methadone in terms of lessening withdrawal symptoms faster and overall completion of treatment (Gowing, Ali, & White, 2004). In contrast, a systematic review of Naltrexone indicates that the treatment may not be very effective on treatment retention or abuse relapse rates (Minozzi et al., 2006). Although pharmacotherapies are popular with clinicians, trials on behavioral therapies have shown to be effective in the treatment of opioid pain medication abuse. These therapies have been found to increase treatment adherence as well as increase social support variables known to increase positive outcomes (Amato et al., 2008). Specific behavioral therapies like motivational interventions among prescription drug abusers have been shown to reduce use by 25% in over half of users (Zahradnik et al., 2009).

5. Sedatives/tranquilizers

This class of therapeutic medications is primary used to treat used to treat anxiety and sleep disorders. They are also a major source of drug overdoses and adverse drug reactions (DAWN, 2008). The effects of most sedative medications are mediated through the GABA-chloride receptor complex, and there have been specific neural-receptors that have a high affinity to benzodiazepines. These effects are potentiated with co-ingestion with other depressants, such as alcohol. At extremely high levels of use, sedatives/hypnotics produce a loss of coordination, euphoria, dyskinesia, and even hallucinations. There are primarily two classes of medications. Barbiturates are among the

oldest sedative/hypnotics and are sub-classified into their mechanism of duration (ultrashort acting, short acting, and long acting pharmacokinetics). The second major class is benzodiazepines. Unlike barbiturates, benzodiazepines are not useful for producing deep sedation and therefore are considered less powerful and of lower addictive potential. Because sedative/hypnotic drugs reduce neural excitability in the brain, neural adaption may occur after a period of weeks or months of prolonged use. Therefore, tapering rather than immediate withdrawal is recommended for patients who may develop physical tolerance after long-term exposure.

Epidemiology of Nonmedical and Disordered Use: The rate of nonmedical use and disordered use is far lower for sedative/hypnotics than prescription pain relievers. As shown in Figure 7, approximately 2% of youth and adults reported nonmedical use in the prior year. Use also appeared stable between 2005 to 2009. Among those reporting use in the past year, approximately 16% of youth and adults met the criteria for abuse and/or dependence.
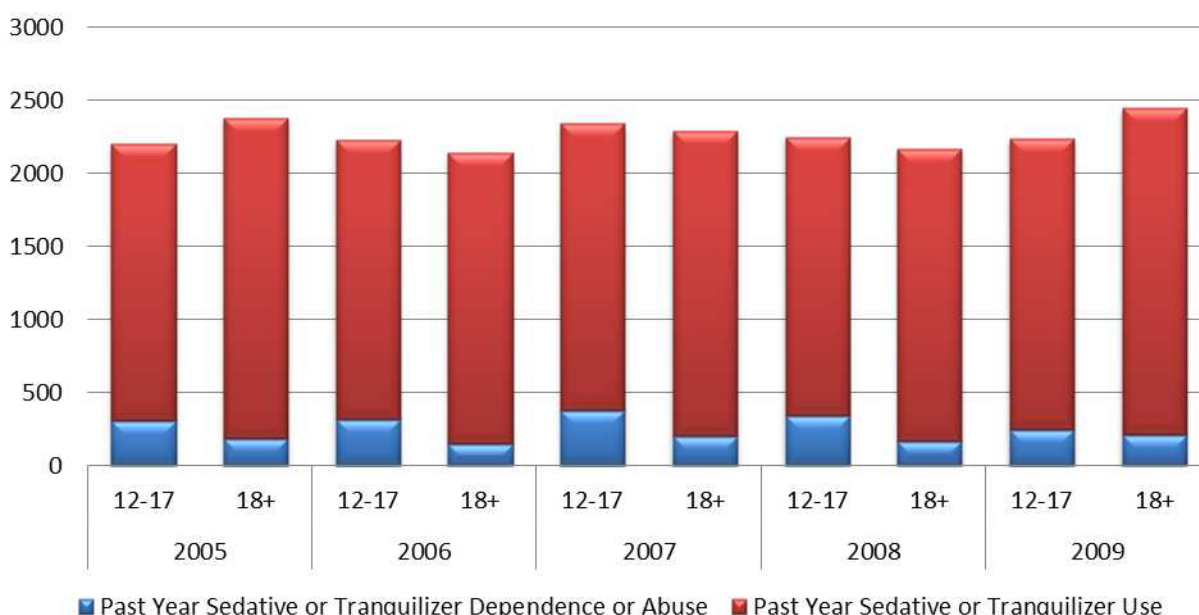

Fig. 7. Past Year Sedative and Tranquilizer Use and Meeting Criteria for Dependence or Abuse of Sedatives and Tranquilizers, by Age and Year: 2005-2009 NSDUHs (Per 100,000|)

Treatment: Other than tapering, many types of treatment seem to be effective in treating benzodiazepine abuse. Minimal intervention, such as receiving physician advice or a form letter from a physician as well as treatment programs led by physicians or counselors are two effective treatments (Voshaar, Couvee, van Balkom, Mulder, & Zitman, 2006). Tailored behavioral interventions have also been found to be particularly effective in benzodiazepine abusers (Ten Wolde et al., 2008; Tyrer et al., 1996). Behavioral therapy programs augmented with pharmacotherapies, such as imipramine also help to reduce use among abusers. Other pharmacotherapies such as Carbamazepine have also significantly improved drug abstinence among benzodiazepine abusers (Voshaar, Couvee, et al., 2006; Voshaar et al., 2006; Voshaar et al., 2003). Behavioral interventions, such as cognitive behavioral therapy has also shown promise in reducing dependence (Denis, Fatseas, Lavie, & Auriacombe, 2006).

6. Psychostimulants

These drugs are typically used to treat attentional disorders (e.g., attention deficit disorder) and sleep disorders (e.g., narcolepsy). They are also compounds used in cold-medications because they are used to expand the nasal and esophageal airways and assist breathing (e.g., Ephedra). Ironically, low dosages of amphetamines actually produce a calming effect in those with attentional disorders. Drugs in this class are structurally related to a wide range of drugs that increase activation of the central nervous system. These include legitimate drugs such as caffeine and nicotine as illicit such as crack cocaine. Prescription stimulants are typically referred to as amphetamines, and available in two chemical forms: l-amphetamine (e.g., Benzedrine) and d-amphetamine (aka dextroamphetamine). Amphetamines have a high resemblance to the dopamine (DA) transmitter in their chemical structure, therefore have a high affinity to DA receptors in binding. Methamphetamine is perhaps the most potent form of amphetamine in its effects on the central nervous system. Illicit forms of methamphetamine (e.g., crystallize methamphetamine or crystal meth) are manufactured using processes to increase the speed of uptake in the brain because amphetamine is first metabolized in the liver and has a slow uptake and a long half life (about 7-30 hours depending upon the formulation).

Epidemiology of Nonmedical and Disordered Use

The recent rise of diagnoses for attentional disorders in the United States (Birnbaum, 2004) has placed an increased volume of amphetamine stimulants used to treat ADHD/ADD within the public domain. An estimated 4% of youth aged 17 or younger have been projected to meet the diagnostic criteria for AHDH/ADD. Of importance is that much of the data indicate that youth and adults who use ADHD/ADD stimulants non-medically do so for its purported therapeutic value rather than euphoria or to "get high." (McCabe, et al., 2007; Novak et al., 2009). Epidemiological surveillance data from NSDUH (Figure 8) show
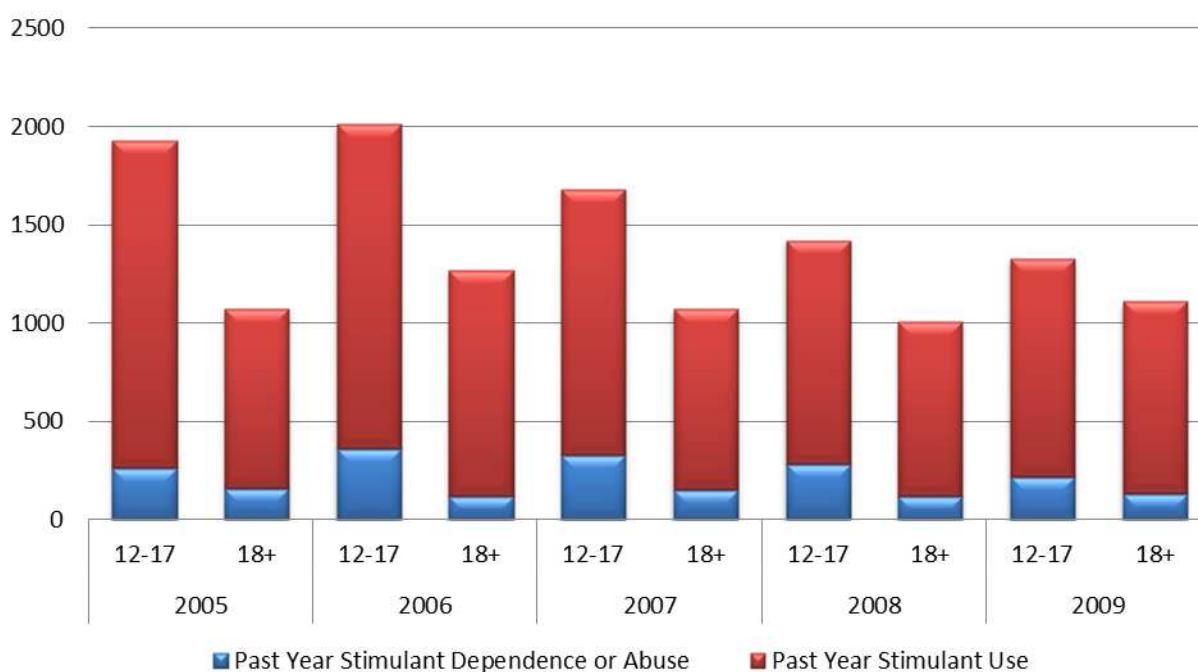

Fig. 8. Past Year Stimulant Use and Meeting Criteria for Dependence or Abuse of Stimulants, by Age and Year: 2005-2009 NSDUHs (Per 100,000)

that less than 2% of youth and 1% of adults reported nonmedical use, and of these, about 7% report levels consistent with abuse and/or dependence. Therefore, there may be a significant amount of nonmedical use of prescription psychostimulants, the level of problem use is far lower than prescription pain relievers and sedatives/hypnotics.

Treatment

Treatments for prescription stimulants and tranquilizers/sedatives are primarily limited to behavioral therapies (Rawson et al., 1995), though novel drug targets are being developed for cocaine and amphetamine use. Interventions such as cognitive behavioral therapy (CBT) and contingency management which have proven moderately effective for cocaine and methamphetamine use disorders in achieving drug abstinence can be applied to persons abusing or dependent upon prescription stimulants. Tapering can be used initially to begin treatment which will ease the symptoms of withdrawal, following by CBT and contingency management. An extensive review of the literature indicated that the behavioral therapies being applied to illicit stimulant abuse are currently the best options for treatment of prescription stimulant abuse (Vocci & Montoya, 2009). Currently, there is no Food and Drug Administration approved medication for the treatment of prescription stimulants.

7. Summary and future directions

Nonmedical prescription drug use had received a significant amount of policy and media attention in the past several years, with some using the term "epidemic" to describe the levels of use in the United States (Maxwell, 2011). In response, the Office of National Drug Control Policy (ONDCP), which is the policy arm of the President focused on substance abuse, issued a position statement in early 2011 (ONDCP, 2011). This policy release outlines the federal strategy for reducing nonmedical prescription drug abuse, and dictates various activities and a division of labor among federal agencies. The plan begins with patient and provider education programs across all federal health agencies. The content of which should focus on educating providers and patients on the safe and appropriate use of prescription medications, as well as the side effect profiles and the likelihood of abuse and diversion for nonmedical purposes. A more detailed understanding of the sequence of substance use initiation would help identify optimal points for prevention and treatment. For example, it is unknown how many persons develop a prescription drug disorder after long-term exposure to prescription medications used in the treatment of a legitimate medical condition. This pathway may be different in terms of etiology and treatment needs from a "garbage head" or poly-drug user who uses multiple illicit substances. For this latter type of user, prescription drugs are either substituted when illicit drugs are unavailable, used to self-treat withdrawal symptoms, or used concurrently to increase the feelings of euphoria. Research has shown differences in motivations to use based on therapeutic and euphoric reasons (McCabe, Cranford, Boyd, & Teter, 2007; McCabe, Teter, & Boyd, 2006; Novak, Kroutil, Williams, & Van Brunt, 2007; Novak, Reardon, & Buka, 2002), but additional knowledge is needed to articulate the pathways leading from initiation to regular use and dependence.

Tracking and enforcement are also primary goals outlined in the ONDCP Prescription Drug Control Strategy. While a large majority of the medications used for nonmedical purposes are obtained through friends and family, the highest volume consumers of prescription medications, who also meet the criteria for disordered use, obtain their medications through illicit channels such as doctor shopping, the internet, or theft (SAMHSA, 2009). There are a

number of initiatives to reduce the availability of prescription medications for diversion, such as "Medication Take Back Days" sponsored by local law enforcement in various states. In addition, drugs with even modest abuse liability, such as Tramadol—a non-opioid prescription pain reliever, are being rescheduled by several States so that prescribing and refilling practices by doctors and patients is more restrictive.

In response to the public health threat that prescription drug abuse poses, federal and state initiatives in the United States have earmarked more than $500 million toward reducing the supply of NMPD through prescription monitoring programs, regulations for prescribing and dosing, and physician education programs (Fischer, Bibby, & Bouchard, 2010; Fishman, 2011; Manchikanti, 2007). These programs are implemented in more than 40 states, with some form of legislation pending in the rest. Several screening instruments have also been developed to help clinicians identify potential abuse liability for their patient. Unfortunately, these programs and assessments have been developed and implemented in the absence of a strong scientific understanding of characteristics of prescription drug abuse. Medical professionals need guidance about types of NMPD to identify those with the greatest potential for abuse of a particular medication. It is also unknown whether individuals are aware of these monitoring systems and programs and if they have significantly affected drug procuring behaviors.

This chapter began with an important statement about the complexities of the national drug problem involving prescription medications in the United States. This chapter presented descriptive epidemiological data on prescription drug disorders and their treatment. Unlike other drugs of abuse, the body of knowledge around prescription drug abuse is in its relative infancy. Many unresolved questions remain regarding the degree to which the risk factors for alcohol and tobacco and marijuana in adolescence are similar to prescription drug abuse. Resolution of this question would help frame primary prevention efforts toward either universal or specialized prevention programming in schools and in the community. Moreover, there are also many unknown questions about how the bio-pharmacological properties of prescription medications contribute toward abuse liability. Prescription drug manufacturers are developing abuse deterrent formulations (ADFs) of commonly abuse drugs. For example, several drugs in the FDA pipeline (Phase I to III) employ sequestered naltrexone, an opioid antagonist, to limit the nonmedical use of opioid-based pain medications. When the pill is crushed or tampered, the naltrexone becomes activated and counteracts the effects of the opioid concentrated in the medication. However, these methods are only effective against abuse by tampering (e.g., crushing, snorting, injecting), so additional methods are needed to curb routes of abuse that include oral ingestion as well. The health care delivery system for behavioral health is also under going tremendous transformation, which has wide-ranging implications for the prevention and treatment of prescription drug abuse. While the final proposed structure is likely to stay under significant and prolonged debate, experts agree that behavioral health, which is largely responsible for the delivery of substance abuse treatment services, will have greater integration into the primary and specialized health care systems. Taken together, it appears that a multi-pronged approach that involves effects at multiple systematic levels will be needed to reduce the epidemic of prescription drug abuse over the next several years.

8. Acknowledgements

9. References

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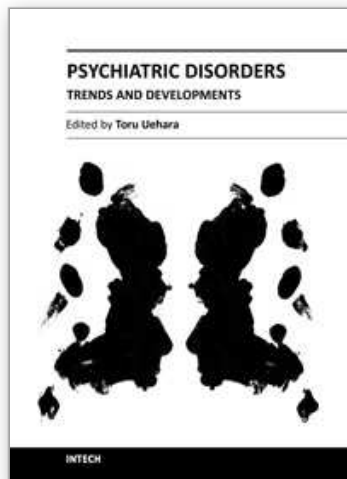
Psychiatric Disorders - Trends and Developments

Edited by Dr. Toru Uehara

Due to their prevalence, pervasiveness and burden inflicted on men and women of today, psychiatric disorders are considered as one of the most important, sever and painful illnesses. This impairment of cognitive, emotional, or behavioural functioning is in some cases tragic. Aside from knowing the physical organic factors, such as infections, endocrinal illnesses or head injuries, the aetiology of psychiatric disorders has remained a mystery. However, recent advances in psychiatry and neuroscience have been successful in discovering subsequent pathophysiology and reaching associated bio-psycho-social factors. This book consists of recent trends and developments in psychiatry from all over the world, presented in the form of multifarious and comprehensive articles. The first two sections of the book are reserved for articles on schizophrenia and depression, two major illnesses present in this field. The third section of the book is reserved for addiction psychiatry, related not only to socio-cultural but also biological alterations. The last section of the book, titled Biological Neuropsychiatry, consists of three topics - updated molecular biology, fundamental neuroscience and clinical neuropsychiatric conditions. Doubtlessly, this book will be fruitful for future developments and collaboration in world psychiatry.

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