

Prescription Drugs Terminology & Patterns of Use

The purpose of this document is to provide: 1) a brief background on the terminology used in the prescription drug (PD) empirical literature and 2) a summary of the nonmedical prescription drug usage patterns in the US, with a specific focus on the sub-populations of youth and older adults. While over-the counter (OTC) medications are sometimes included along with prescription drugs, this document does not cover OTC medications.

Prescription Drugs: Terminology

Nonmedical use of prescription drugs (NMUPD) is often broken down into 4 categories: pain relievers, stimulants, tranquilizers, or sedatives (SAMHSA, 2011). Pain relievers or opioid analgesics are commonly prescribed for the management of acute or chronic pain, including post-surgical pain. Commonly prescribed pain relievers include hydrocodone (e.g., Percocet), oxycodone (e.g., OxyContin, Vicodin), methadone and codeine. Stimulants are frequently prescribed for Attention Deficit Hyperactivity Disorder, narcolepsy, as well as depression that does not respond to typical medication. Examples of commonly prescribed stimulants include Adderall, Ritalin and Concerta. Sedative and Tranquilizers both fall under the category of Central Nervous System (CNS) depressants. These classes of drugs are commonly prescribed for sleep problems (e.g., insomnia), anxiety, panic disorders, and seizure disorders. Examples of sedatives include Nembutal, Mebaral, and Quaaludes. Common tranquilizers include **Valium**, **Xanax**, **Ativan**, and **Klonopin** (Hernandez & Nelson, 2010; NIDA Report, 2005).

There is no standard definition of nonmedical use of prescription drugs in the empirical literature and terms used to describe this phenomenon include: nonmedical use of prescription drugs, prescription drug misuse, prescription drug abuse or dependence, and misuse of psychotherapeutics¹. In some cases, the assessment of NMUPD is not distinguished from other illicit drug use and caution should be used when considering the overall category of “illicit drugs.”

Substance abuse: An intentional, maladaptive pattern of use of a medication (whether legitimately prescribed or not) leading to significant impairment or distress—such as repeated failure to fulfill role obligations, recurrent use in situations in which it is physically hazardous, multiple legal problems, and recurrent social and interpersonal problems—occurring over a 12-month period (DSM-IV; American Psychiatric Association, 1994).

¹ The majority of these definitions were included in (Gilson & Kreis, 2009).

Substance dependence: A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by 3 or more symptoms, occurring at any time in the same 12 month period. The symptoms include: tolerance; withdrawal; the substance is often taken in larger amounts or over a longer period of time than was intended; there is a persistent desire or unsuccessful efforts to cut down or control substance use; a great deal of time spent in activities trying to obtain the substance or recover from its effects; important social, occupational, or recreational activities given up or reduced because of substance use; and substance use continued despite knowledge of persistent or recurrent physical or psychological problem caused or exacerbated by substance (DSM-IV; American Psychiatric Association, 1994).

Addiction: A primary, chronic, neurobiological disease, with genetic, psychological, and environmental factors influencing its development and manifestations. Addiction is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving (Federation of State Medical Boards of the United States Inc., 2004).

Nonmedical Use of Prescription Drugs: National surveys use slightly different definitions of nonmedical use of prescription drugs:

- *National Survey on Drug Use and Health (NSDUH)*: use of a prescription drug without a prescription from a physician or simply for the experience or feeling the drugs caused (SAMHSA, 2011).
- *Monitoring The Future (MTF) and Youth Behavior Risk Survey (YRBS)*: use of a prescription drug (such as Oxycontin, Percocet, Vicodin, Codeine, Adderall, Ritalin, Xanax) without a doctor's prescription.

Prescription Drug Misuse: The intentional or unintentional use of a prescribed medication in a manner that is contrary to directions, regardless of whether a harmful outcome occurs (Hertz & Knight, 2006).

Recent Prescription Drug Use Usage Patterns

Current Use Rates

Prescription drugs are now the second most common class of drug after marijuana among adolescents (SAMHSA, 2011). In 2010, 10.1% of youth aged 12 to 17 reported current use (past 30-day) use of illicit drugs, with 7.4 % of adolescents reporting current marijuana use and 3% reporting current nonmedical use of prescription drugs (NMUPD). The average rate of past year NMUPD, as defined by use without a prescription or for the feeling the drugs caused, between 2002 and 2004 was 9.1% for youths (aged 12-17), 14.5% for young adults (aged 18-25), and 4.4% for adults aged 26 or older (Colliver, Kroutil, Dai, & Gfroerer, 2006).

Current Use Rates for Older Adults

According to the 2007 and 2008 National Survey of Drug Use and Health (NSDUH), 0.8 and 0.9 percent respectively of adults aged 65 and older were estimated to have engaged in past year NMUPD; 0.6 and 0.8% were estimated to have engaged in past year nonmedical use of pain

relievers. (SAMHSA, 2009). The NMUPD is projected to increase from 1.2% (911,000) in 2011 to almost 2.4% (2.7 million) in 2020 based on the growth of the older adult population as the baby boomers age and based on the higher usage of illicit and legal psychoactive drugs by the baby boomers (Colliver, Compton, Gfroerer, & Condon, 2006).

Trend Data on Initiation of Use

According to national epidemiological survey data within the past 10 years, the gap between new users of marijuana and new users of prescription drugs for nonmedical purposes is shrinking. Trends over the first half of the past decade suggest that while other substance use (e.g., alcohol, tobacco, marijuana) among adolescents decreased (Johnston, O'Malley, Bachman, & Schulenberg, 2006), prescription drug misuse increased from 2000-2004 and then rates remained relatively steady (Johnston et al., 2006; SAMHSA, 2009). However, there has been a slight decline in rates of current NMUPD in the last few years with rates declining from 4% in 2002-2003 to 3% in 2010 (SAMHSA, 2011). NMUPD was the most commonly abused illicit drug for 12-13 year olds (SAMHSA, 2006) and 12 to 17 year olds were more likely to start abusing prescription drugs compared to older adults (Office of the National Drug Control Policy, 2007; SAMHSA, 2006). Rates of past month NMUPD among young adults aged 18-25 (5.9%) did not change significantly across the past decade (SAMHSA, 2011). In a longitudinal study of adolescents from grade 10 through age 20, the majority (69.5%) of participants who used prescription drugs non-medically reported starting use in high school (Catalano, White, Fleming, & Haggerty, 2011). When focusing on the non-medical use of pain relievers, data demonstrate that most initiates (73.8%) report past year use of another illicit drug (e.g., marijuana, cocaine, or another prescription drug used non-medically) prior to initiation of the nonmedical use of pain relievers (SAMHSA, 2005).

Access

More than half of individuals aged 12 and older who report NMUPD obtained the prescription drugs for free from a friend or relative (SAMHSA, 2011). Monitoring the Future data from 2009-2010 confirms that the majority of 12th graders who endorse use of amphetamines, tranquilizers, or narcotics other than heroin reported that they were given them for free from a friend or relative (57-64% across the 3 classes of drugs). Buying the prescription drug from friend or relative was also common (38-50%). However, when examined separately, youth are more likely to report being given or buying prescription drugs from a friend compared to being given or buying prescription drugs from a relative. Additionally, 12th graders reported that they obtained narcotics drugs (e.g., pain relievers) from their own left over prescription (33%) compared to amphetamines (19%) or tranquilizers (14%) (Johnston et al., 2011). Taken together, friend networks and to a lesser extent family networks provide a common sources of prescription drug access for youth. Additionally, left over medication from prescriptions, particularly for the pain reliever class of drugs, is another source of access for youth. Recent data suggests that purchasing prescription drugs from a drug dealer or stranger or through the internet are less common methods of obtained prescription drugs for nonmedical purposes (SAMHSA, 2011; Johnston et al., 2011).

References

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders*. Washington, DC: American Psychiatric Association.

- Catalano, R. F., White, H. R., Fleming, C. B., & Haggerty, K. P. (2011). Is nonmedical prescription opiate use a unique form of illicit drug use? *Addict Behav*, 36(1-2), 79-86.
- Colliver, J., Kroutil, L., Dai, L., & Gfroerer, J. (2006). Misuse of prescription drugs: Data from the 2002, 2003, and 2004 National Surveys on Drug Use and Health (DHHS Publication No. SMA 06-4192, Analytic Series A-28) Rockville, MD: *Substance Abuse and Mental Health Services Administration, Office of Applied Studies*.
- Colliver, J. D., Compton, W. M., Gfroerer, J. C., & Condon, T. (2006). Projecting drug use among aging baby boomers in 2020. *Annals of epidemiology*, 16(4), 257-265.
- Federation of State Medical Boards of the United States Inc. (2004). Model policy for the use of controlled substances for the treatment of pain. Dallas, TX: Federation of State Medical Boards of the US.
- Gilson, A. M., & Kreis, P. G. (2009). The burden of the nonmedical use of prescription opioid analgesics. *Pain medicine*, 10(Suppl 2), S89-100.
- Hernandez, S. H., & Nelson, L. S. (2010). Prescription Drug Abuse: Insight Into the Epidemic. *Clinical Pharmacology & Therapeutics*, 88(3), 307-317.
- Hertz, J. A., & Knight, J. R. (2006). Prescription drug misuse: A growing national problem. *Adolesc Med Clin*, 17(751-769).
- Johnston, L. D., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2006). Monitoring the Future national survey results on drug use, 1975-2005. Volume I: Secondary school students *NIH Publication No. 06-5883*. Bethesda, MD: National Institute on Drug Abuse.
- NIDA Report. (2005). Prescription Drugs: Abuse and Dependence *NIDA Research Report Series*: National Institute on Drug Abuse.
- Office of the National Drug Control Policy. (2007). Prescription Drugs. An Analysis of Recent Trends on the Emerging Drug Threat.
- SAMHSA. (2006). Results from the 2005 National Survey on Drug Use and Health: National Findings *Office of Applied Studies, NSDUH Series H-30, DHHS Publication No. SMA 06-4194*. Rockville, MD.
- SAMHSA. (2005). Results from the 2004 National Survey on Drug Use and Health: National findings. *Office of Applied Studies, NSDHU Series H-28, DHHS Publication SMA 05-4062*. Rockville, MD.
- SAMHSA. (2009). Results from the 2008 National Survey on Drug Use and Health: National Findings *Office of Applied Studies, NSDUH Series H-36, HHS Publication No. SMA 09-4434*. Rockville, MD.
- SAMHSA. (2011). Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings *NSDUH Series H-41, HHS Publication No. (SMA) 11-4658*. Rockville, MD: Substance Abuse and Mental Health Services Administration.

Consequences of the Non-Medical Use of Prescription Drugs (NMUPD)

The purpose of this document is to describe the adverse (including both short and long-term) consequences associated with nonmedical use of prescription drugs (NMUPD).

Physical Consequences: Nonmedical Use of Prescription Drugs

Increased Risk of Overdose, Injury, and Death

Non-medical use of prescription drugs is associated with an increased number of Emergency Department (ED) visits. A review of 5 years of SAMHSA's Drug Abuse Warning Network (DAWN) data (2004–2008) of ED visits involving NMUPD estimated that the number of ED visits for the nonmedical use of opioid analgesics increased 111% (from 144,600 to 305,900 visits) during this 5-year period and increased 29% during the last year of data studied (2007–2008). Oxycodone, hydrocodone, and methadone were the most common prescription drugs involved in these ED visits. The estimated number of ED visits involving nonmedical use of benzodiazepines, which result in sedative or anxiolytic effect, increased 89% during 2004–2008 (from 143,500 to 271,700 visits) and 24% during 2007–2008 (MMWR, 2010). Data on ED visits involving the nonmedical use of other types of prescription drugs (e.g., stimulants, tranquilizers) were not available. Data could not be located on drugged driving or on-the-job accidents specific to NMUPD.

Rates of US deaths involving the overdose of prescription drugs increased rapidly during 1999–2006 (Warner, Chen, & Makuc, 2009). The number of US deaths due to poisoning doubled between 1999–2005 from about 20,000 to 37,000. This increase is largely attributed to deaths involving prescription opioid analgesics—this coincided with a nearly 4 fold increase in use of prescription opioids nationally (Hernandez & Nelson, 2010; Paulozzi, Budnitz, & Xi, 2006). Opioid pain relievers were involved in 73.8% of the 20,044 prescription drug overdose deaths which occurred in 2008 (MMWR, 2011).

Acute Medication Side Effects and Withdrawal Symptoms

Prescription drugs all have potential acute (side) effects that range from mild symptoms to more severe reactions that can lead to significant morbidity and potentially death (see above). Effects vary by type of medication misused.

- Common acute side effects of opioid prescription drugs include nausea, sedation/drowsiness, depressed respiration, euphoria, dysphoria, constipation and itching. Termination or reduction in opioid use can lead to withdrawal symptoms including restlessness, muscle and bone pain, insomnia, diarrhea, vomiting, cold flashes with goose bumps, and involuntary leg movements (Manchikanti & Singh, 2008; NIDA Report, 2005).
- CNS depressant (sedatives, tranquilizers) side effects include increased drowsiness or sedation. CNS depressants can slow heart rate and respiration when combined with prescription pain

medications, some types of OTC cold/allergy medications, or alcohol. Rapid discontinuation of sedatives or tranquilizers can lead to seizures, some of which can be life-threatening (NIDA Report, 2005).

- Effects of stimulant medications include increases in alertness, attention and energy; physiologic effects also include elevated heart rate, blood pressure, increased respiration, suppressed appetite, and sleep deprivation. Frequent use of stimulants during a short period of time can lead to feelings of hostility or paranoia. Large doses can lead to irregular heartbeat and high body temperature, as well as potential for heart failure or seizures. Stimulant withdrawal symptoms can include fatigue, depression, and disrupted sleep cycles (NIDA Report, 2005).

Other adverse consequences associated with regular NMUPD over a long period of time include hormonal & immune system effects, physiological dependence, and increased sensitivity to pain. These long-term effects can lead to an increase in physical disability related to these subsequent medical conditions (Manchikanti & Singh, 2008).

Dependence

NMUPD is associated with a greater likelihood of developing dependence (Blanco et al., 2007; Colliver, Kroutil, Dai, & Gfroerer, 2006; McCabe, West, Morales, Cranford, & Boyd, 2007; SAMHSA, 2011), particularly for adolescents who begin use earlier in adolescence, some data suggest age 16 (Colliver et al., 2006), others suggest age 13 (McCabe et al., 2007). Opioid analgesics, which are in the pain reliever category of prescription drugs, are more likely to lead to dependence. In 2004, 1 in 3 adolescents in drug treatment had a diagnosis of prescription drug abuse or dependence (Colliver et al., 2006). National survey data suggest that adolescent females may be at greater risk of dependence on prescription drugs compared to their male counterparts. There are several hypothesized reasons for this difference, including potentially greater pharmacologic sensitivity in females, as well as greater access to prescription drugs by females since they are more likely to be prescribed medications (Cotto et al., 2010).

Association with Psychiatric Conditions

NMUPD is associated with increased risk of developing psychiatric and other medical conditions (Hernandez & Nelson, 2010; Strassels, 2009), including depression, anxiety, ADHD and mania. Hall and colleagues (2010) found that among a sample of 723 adolescents in residential care for antisocial behavior, those who endorsed high levels of anxiety and depression also reported significantly greater amount of sedative/anxiolytic misuse compared to adolescents who did not report high levels of anxiety and depression. Several studies have demonstrated a link between major depressive disorder and greater NMUPD (Havens, Young, & Havens, 2011; Manchikanti & Singh, 2008; Schepis & Krishnan-Sarin, 2008; Subramaniam & Stitzer, 2009); however it is unknown if this indicates a directional relationship, or whether another factor might account for both conditions. Research has found an association between illicit drug use and increased risk of suicide, however, however this has not been directly linked with NMUPD (Bohnert, Roeder & Ilgen, 2010). A study of treatment-seeking opiate dependent adolescents found that prescription drug opioid users endorsed higher rates of ADHD and manic episodes compared to adolescent heroin users. Both groups of adolescents reported high scores on a measure of depression (Subramaniam & Stitzer, 2009). Additional research is needed to determine whether certain classes of prescription drugs are related to different types of psychiatric or other medical conditions.

Cognitive Changes

Evidence from a study using functional Magnetic Resonance Imaging (fMRI) with 10 individuals with PD opioid dependence and 10 matched healthy controls found that opioid dependence was associated with structural and functional changes in the brain. The regions that appear to be affected include brain regions responsible for the regulation of affect and impulse control, as well as the centers of the brain involved in reward and motivation functions (Upadhyay et al., 2010). The sample sizes used in fMRI studies are typically small and therefore the generalizability of the findings is not known.

Psychosocial Consequences: Nonmedical Use of Prescription Drugs

Delinquency/and or Violent Behavior

Several studies have demonstrated a link between violent or delinquent behavior (Catalano, White, Fleming, & Haggerty, 2011; Hall, Howard, & McCabe, 2010; Harrell & Broman, 2009; McCauley et al., 2010; Sung, Richter, Vaughan, Johnson, & Thom, 2005) and NMUPD. The direction of the relationship (e.g., NMUPD leads to increased violent/delinquent behavior; delinquent behavior leads to future NMUPD) has not been established. However, in a longitudinal study of adolescents assessed from grade 10 to age 20, the only unique predictor of nonmedical opiate prescription drug use was violent behavior. This relationship remained significant after accounting for licit (alcohol, tobacco) and illicit (marijuana, cocaine/crack, psychedelics, heroin) drug use (Catalano et al., 2011).

Academic Functioning

Greater misuse of prescription drugs is associated with lower levels of educational attainment (Harrell & Broman, 2009). Adolescents reporting greater rates of NMUPD also demonstrate poorer academic performance (McCabe & Boyd, 2005; Schepis & Krishnan-Sarin, 2008), and a greater likelihood of school drop-out (Havens et al., 2011; Wu, Pilowsky, & Patkar, 2008). Due to the cross-sectional design of these research studies it is not possible to rule out that poorer academic functioning occurs prior to the onset of NMUPD or that another factor is associated with both poor academic functioning and NMUPD.

Economic Burden

The economic burden of NMUPD has been estimated to be \$9.5 billion for 2005 (Hernandez & Nelson, 2010). These costs include arrests, legal and adjudication costs, as well as correctional facilities costs associated with NMUPD. Economic loss associated with decreased work productivity due to disability, death and withdrawal from the workforce is also included. Additionally, NMUPD users are more likely to use medical services than non-users (Hernandez & Nelson, 2010; Strassels, 2009).

References

- Blanco, C., Alderson, D., Ogburn, E., Grant, B. F., Nunes, E. V., Hatzenbuehler, M. L., & Hasin, D. S. (2007). Changes in the prevalence of non-medical prescription drug use and drug use disorders in the United States: 1991-1992 and 2001-2002. *Drug Alcohol Depend*, 90(2-3), 252-260.
- Bohnert A, Roeder K., & Ilgen M.A. (2010). Unintentional overdose and suicide among substance users: A review of overlap and risk factors. *Drug and Alcohol Dependence*, 110 (3), 183-192.
- Catalano, R. F., White, H. R., Fleming, C. B., & Haggerty, K. P. (2011). Is nonmedical prescription opiate use a unique form of illicit drug use? *Addict Behav*, 36(1-2), 79-86.
- Colliver, J., Kroutil, L., Dai, L., & Gfroerer, J. (2006). Misuse of prescription drugs: Data from the 2002, 2003, and 2004 National Surveys on Drug Use and Health (DHHS Publication No. SMA 06-4192, Analytic Series A-28) Rockville, MD: *Substance Abuse and Mental Health Services Administration, Office of Applied Studies*.
- Cotto, J. H., Davis, E., Dowling, G. J., Elcano, J. C., Staton, A. B., & Weiss, S. R. (2010). Gender effects on drug use, abuse, and dependence: a special analysis of results from the National Survey on Drug Use and Health. *Gend Med*, 7(5), 402-413.
- Hall, M. T., Howard, M. O., & McCabe, S. E. (2010). Subtypes of adolescent sedative/anxiolytic misusers: A latent profile analysis. *Addict Behav*, 35(10), 882-889.
- Harrell, Z. A., & Broman, C. L. (2009). Racial/ethnic differences in correlates of prescription drug misuse among young adults. *Drug Alcohol Depend*, 104(3), 268-271.

- Havens, J. R., Young, A. M., & Havens, C. E. (2011). Nonmedical prescription drug use in a nationally representative sample of adolescents: evidence of greater use among rural adolescents. *Arch Pediatr Adolesc Med*, 165(3), 250-255.
- Hernandez, S. H., & Nelson, L. S. (2010). Prescription Drug Abuse: Insight Into the Epidemic. *Clinical Pharmacology & Therapeutics*, 88(3), 307-317.
- Manchikanti, L., & Singh, A. (2008). Therapeutic opioids: a ten-year perspective on the complexities and complications of the escalating use, abuse, and nonmedical use of opioids. *Pain Physician*, 11(2 Suppl), S63-88.
- McCabe, S. E., & Boyd, C. J. (2005). Sources of prescription drugs for illicit use. *Addict Behav*, 30(7), 1342-1350.
- McCabe, S. E., West, B. T., Morales, M., Cranford, J. A., & Boyd, C. J. (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.
- McCauley, J. L., Danielson, C. K., Amstadter, A. B., Ruggiero, K. J., Resnick, H. S., Hanson, R. F., Smith, D. W., Saunders, B. E., & Kilpatrick, D. G. (2010). 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*, 51(1), 84-93.
- MMWR. (2010). Emergency department visits involving nonmedical use of selected prescription drugs - United States, 2004-2008. *MMWR Morb Mortal Wkly Rep*, 59(23), 705-709.
- MMWR. (2011). Vital Signs: Overdoses of Prescription Opioid Pain Relievers — United States, 1999–2008. *MMWR Morb Mortal Wkly Rep*, 60(43), 1487-1492.
- NIDA Report. (2005). Prescription Drugs: Abuse and Dependence *NIDA Research Report Series*: National Institute on Drug Abuse.
- Paulozzi, L. J., Budnitz, D. S., & Xi, Y. (2006). Increasing deaths from opioid analgesics in the United States. *Pharmacoepidemiol Drug Saf*, 15(9), 618-627.
- SAMHSA. (2011). Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings *NSDUH Series H-41, HHS Publication No. (SMA) 11-4658*. Rockville, MD: Substance Abuse and Mental Health Services Administration.
- Schepis, T. S., & Krishnan-Sarin, S. (2008). Characterizing adolescent prescription misusers: a population-based study. *J Am Acad Child Adolesc Psychiatry*, 47(7), 745-754.
- Strassels, S. A. (2009). Economic burden of prescription opioid misuse and abuse. *J Manag Care Pharm*, 15(7), 556-562.
- Subramaniam, G. A., & Stitzer, M. A. (2009). Clinical characteristics of treatment-seeking prescription opioid vs. heroin-using adolescents with opioid use disorder. *Drug Alcohol Depend*, 101(1-2), 13-19.
- Sung, H. E., Richter, L., Vaughan, R., Johnson, P. B., & Thom, B. (2005). Nonmedical use of prescription opioids among teenagers in the United States: trends and correlates. *J Adolesc Health*, 37(1), 44-51.
- Upadhyay, J., Maleki, N., Potter, J., Elman, I., Rudrauf, D., Knudsen, J., Wallin, D., Pendse, G., McDonald, L., Griffin, M., Anderson, J., Nutile, L., Renshaw, P., Weiss, R., Becerra, L., & Borsook, D. (2010). Alterations in brain structure and functional connectivity in prescription opioid-dependent patients. *Brain*, 133(Pt 7), 2098-2114.
- Warner, M., Chen, L. H., & Makuc, D. M. (2009). Increase in fatal poisonings involving opioid analgesics in the United States, 1999-2006. *NCHS Data Brief*(22), 1-8.
- Wu, L. T., Pilowsky, D. J., & Patkar, A. A. (2008). Non-prescribed use of pain relievers among adolescents in the United States. *Drug Alcohol Depend*, 94(1-3), 1-11.

Risk and Protective Factors Associated with Nonmedical Use of Prescription Drugs: Literature Review (2006-2011)

GOAL: To explore the risk and protective factors associated with the nonmedical use of prescription drugs (NMUPD), identifying those with the strongest, most consistent links to use, and therefore those that may serve as the strongest levers of change. Using a social-ecological framework, this document describes some of the most commonly researched risk and protective factors related to NMUPD based on published research from 2006-2011. The review of the empirical literature focused on US samples of adolescents and older adults. While all classes of prescription drugs were examined, specific focus was given to opioid/pain reliever class of prescription drugs (PD), the most common class of prescription drug used for nonmedical purposes.

METHODS: A literature search was conducted using PSYCHINFO, PUBMED, and EBSCO for articles published between 2006 and 2011. Search terms included “prescription drugs”, “opioid,” “opiates” “sedatives” “tranquilizers” “stimulants” in combination with these additional terms: “adolescents,” “older adults,” “elderly,” “consequences,” “Risk and protective factors,” “Availability,” “Access,” “Community,” “Norms,” “Family,” “Parental,” “Mental Health,” “pain,” “chronic pain,” and “school”.

Article selection was based on the following criteria:

- Full text was available.
- Studies had clearly identified methodologies and results, or were well-researched meta-analyses.
- At least one of the main findings was specifically related to prescription drugs

For the purposes of this review, studies needed to focus specifically on risk and protective factors or include a section of the review on factors associated with NMUPD. Literature around consequences and interventions are discussed in a separate document. A Ph.D.-Level reviewer examined studies for methodological quality, including only those studies that accounted for well-known confounds, applied appropriate statistical tests, and used well-defined measures.

ORGANIZATION: This paper is organized into 5 global domains (i.e., Community/Neighborhood, School, Family, Peer, and Individual). Risk and protective factors associated with each domain are further divided into the following categories:

- **STRONG:** These factors have a **clear, direct relationship** to use/intention to use that **consistently persists even after accounting for a host of other variables** that have been shown to relate to use. The relationship has been supported with little to no inconsistency by:
 - At least one peer-reviewed, published, meta-analysis¹ demonstrating an effect size larger than $d = .20$ or $r = .10$ (Cohen's 1988 benchmarks for a small effect size) OR
 - At least 2 peer-reviewed, published longitudinal studies OR
 - At least 1 peer-reviewed, published longitudinal study AND at least 2 peer reviewed, published cross-sectional studies².
- **MODERATE:** The relationship of these factors to use/intention to use **appears significant in some studies, but may drop out after accounting for other factors in others**. The “moderate” category also contains factors that provide some evidence of a significant relationship, but have not been as well studied, including those with:
 - Only one peer-reviewed, published longitudinal study and fewer than 2 peer reviewed, published cross-sectional studies, OR
 - More than 2 peer-reviewed, published cross-sectional studies, but no peer-reviewed, published longitudinal studies.
- **SUBPOPULATION ONLY:** Two or more peer-reviewed, published studies suggest that the factor **is significantly related to use only for a subset of the population** (e.g., younger adolescents, older adults).
- **INSUFFICIENT RESEARCH:** Research connecting these factors to use/intention to use may be poorly designed. Included in this category are factors that have been **inadequately studied** (i.e., fewer than 1-2 peer reviewed, published studies on the factor, no longitudinal analyses), particularly from 2006- present. Outstanding questions may be identified in the “Level of Evidence/Supporting Literature” column.
- **WEAK:** Two or more peer-reviewed, published studies agree that these factors are not related to use after accounting for other variables.

¹ NOTES: No Meta-analyses have been conducted specifically for NMUPD, and the reviews that have been written do not necessarily summarize the existing literature in a systematic way, such as weighting methodologically rigorous studies more strongly than other methodologically weaker studies. The majority of the studies are cross-sectional designs that use self-report surveys to assess either the concurrent relationship between two variables (e.g., current other illicit substance use and current NMUPD, but does not specify which comes first), or are retrospective designs that ask participants to report behavior or conditions that have occurred in the past and examine how these retrospective histories are associated with current, past year or lifetime NMUPD. Neither of these designs are as rigorous as perspective, longitudinal study designs. Less research has been conducted specifically examining NMUPD and therefore drawing strong conclusions regarding relationships between risk and protective factors and NMUPD is challenging. A well designed, representative longitudinal study found that there was a large degree of overlap between nonmedical use of prescription opioids and other licit and illicit drugs (Catalano et al, 2011). The study concluded that nonmedical use of opioids, one class of prescription drug, does not represent a unique form of illicit drug use with substantially different negative outcomes compared to other illicit drugs. This finding suggests that the risk and protective factors may be similar for nonmedical use of opioids/pain relievers and illicit drugs.

² Although “study counting” is clearly limited by publication bias, it can provide a useful way to talk about convergence of findings.

COMMUNITY DOMAIN			
Risk Factor	Evidence Level	Justification for Evidence Level	Level of Evidence/Supporting Literature
Availability/ Opportunities to Use: Social Access	MODERATE	<p><i>Surveys have shown a significant relationship between greater perceived availability or ease of access of prescription drugs and NMUPD. This factor was rated as moderate due to the cross-sectional design of the studies identified.</i></p> <p><i>For other areas of substance use, greater social availability has been consistently related to greater substance use (tobacco, alcohol, illicit drugs).</i></p>	<p>According to national and local surveys, the most common method for obtaining PD for nonmedical purposes is through social sources (SAMHSA, 2011). Over half of respondents aged 12 and older who report NMUPD reported that they got PD for free from a friend or relative. Nearly 80% of these respondents indicated that the friend or relative originally got the PD from one doctor. Among respondents reporting past year use of pain relievers for nonmedical purposes--55% obtained the pain relievers most recently from a friend or relative for free, 11.4% bought them from a friend or relative, and 4.8% took them from a friend or relative without asking (SAMHSA, 2011). These percentages are similar to those reported in NSDUH data from 2006-2009. Surveys completed in a college age sample found a similar pattern of access, with the majority of respondents reporting parents and friends as the most common source of PD. The internet had the lowest prevalence of use for obtaining PD for nonmedical use (0.2%) (McCabe, Cranford, Boyd, & Teter, 2007).</p> <p>A systematic review of the literature for misuse of stimulant medication identified one study of junior and senior high students that showed that students were more likely to report obtaining stimulants not prescribed to them if there was a student in their classroom who was prescribed stimulants, suggesting that greater access to stimulant medication is an important risk factor for nonmedical use (Wilens et al., 2008).</p> <p>A recent study examining factors associated with NMUPD among students grades 5 through 11 in Tennessee, a state with high rates of NMUPD, found a significant association between perceived availability of prescription drugs and reported NMUPD (Collins, Abadi, Johnson, Shamblen, & Thompson, 2011). According to a recent CASA survey, for the first time adolescents reported that it was easier to get PD than buy beer (National Center on Addiction and Substance Abuse at Columbia University, 2008).</p>
Availability/ Opportunities to Use: Retail Access	MODERATE/ INSUFFICIENT RESEARCH	<p><i>Several review articles identified an association between greater availability as an important factor in the increase in NMUPD. This factor was rated MODERATE/Insufficient since these reviews did not provide a systematic review</i></p>	<p>Several reviews of the literature argue that one of the primary factors associated with the increase in opioid analgesic use and misuse is the increase in availability, which is due in part to the development of new medications as well as changes in physician's prescribing practices, especially around pain management (Compton & Volkow, 2006; Sung, Richter, Vaughan, Johnson, & Thom, 2005; Twombly & Holtz, 2008). None of these reviews, however, provide evidence of a direct causal link between increased availability and increased use. Trombley & Holtz's (2008) review identifies one study examining national prescribing practices which showed that between 1992 to 2002, the number of prescriptions for the pain relievers' hydrocodone and</p>

		<i>of existing empirical studies. However, substantial evidence suggests that increases in NMUPD mirrors the increase in the availability of PD.</i>	oxycodone increased 376% and 380%, respectively, highlighting the increase in availability of opioids/pain relievers. These large increases are in contrast to an increase of only 61% for prescription drugs overall, and an increase in US population growth of 12% (Twombly & Holtz, 2008). Prescriptions for other pain medications have shown similar increases (Compton & Volkow, 2006).
Community Norms Favorable for Drug Use	INSUFFICIENT RESEARCH	<i>Only one cross-sectional study demonstrated a relationship with NMUPD.</i>	One study was identified in the last 5 years that examined the association between community norms favorable towards drug use and nonmedical use of prescription drugs. Collins and colleagues (2011) found a significant association between greater community norms against substance use and less reported NMUPD among youth in grades 5-11.
Neighborhood quality, disorganization, community attachment, mobility	INSUFFICIENT RESEARCH	<i>No studies were identified for this risk factor category.</i>	No research studies were identified that examined the association between these community factors and NMUPD.
SCHOOL DOMAIN			
Risk Factor	Evidence Level	Justification for Evidence Level	Level of Evidence/Supporting Literature
Academic Failure/Low Educational Attainment	MODERATE	<i>Four of these studies are cross-sectional designs that utilize large, representative US samples (sample size ranged from 4,882 to 36,992).</i>	Several cross-sectional studies using nationally representative samples of adolescents have demonstrated a significant relationship between poorer academic performance (McCabe & Boyd, 2005a; Schepis & Krishnan-Sarin, 2008), school drop-out (Havens, Young, & Havens, 2011; Wu, Pilowsky, & Patkar, 2008) and PD misuse. Additionally, lower educational attainment in a sample of US adults, was associated with greater misuse of PD (Harrell & Broman, 2009). However, Collins (2011) failed to find a significant relationship between school grades and NMUPD. The cross-sectional designs of these studies make it difficult to determine the temporal ordering of NMUPD or poor academic performance.
Low Bonding to School	MODERATE	<i>Two cross-sectional studies examined school bonding/commitment variables and NMUPD. One study utilized a large, nationally representative sample of adolescents, while the other examined a smaller (n=890), geographically limited sample.</i>	Ford (2009) utilized 2005 NSDUH national data to examine the relationship between school bonding and past year NMUPD among adolescents aged 12-17. Adolescents with stronger bonds to school had decreased odds of past year NMUPD. Collins (2011) also demonstrated an inverse relationship between greater commitment of school and less NMUPD in a smaller, local sample of youth.

FAMILY DOMAIN			
Risk Factor	Evidence Level	Justification for Evidence Level	Level of Evidence/Supporting Literature
Poor Parental Monitoring/Supervision/ Parental Involvement	MODERATE	<p><i>Two studies were found a significant relationship between parenting variables and NMUPD. Twombly & Holtz (2008) review also reports findings from earlier studies using NSDUH data. One study failed to find a significant relationship.</i></p> <p><i>Data from other substances support a strong and consistent protective relationship between strong parental monitoring behaviors and high parental attachment and decreased risk of substance use.</i></p>	<p>Studies examining NMUPD have also demonstrated a significant relationship between poor parental monitoring and lack of parental involvement with past year misuse of prescription opioids (Sung et al., 2005; Twombly & Holtz, 2008). A study of 781 ethnically diverse adolescent girls and their mothers found that parental monitoring and parental involvement were protective factors for NMUPD (Schinke, Fang, & Cole, 2008). One study identified over the past 5 years failed to find an association between parental monitoring and NMUPD (Collins et al., 2011).</p> <p>Parents may also represent a source of access to prescription drugs, with 60% of adolescents reporting that prescription pain relievers are “easy” to obtain from parents or friends (SAMHSA, 2006).</p>
Parental Disapproval of Use	MODERATE	<i>Two cross-sectional studies identified over the past 5 years found a significant relationship between disapproval of use and less NMUPD.</i>	College students who reported more tolerant parental attitudes towards substance use were more likely to endorse NMUPD (Ford, 2008). Collins (2011) found that parent disapproval of NMUPD also demonstrated a significant correlation with NMUPD among youth (Grades 5-11).
Parental Substance use	INSUFFICIENT RESEARCH	<i>Only one review article cited evidence that a family history of substance abuse is associated with NMUPD.</i>	The research literature on alcohol and other illicit drugs have demonstrated a strong relationship between family history of substance abuse and dependence and adolescent substance misuse (Latimer & Zur, 2010). There is evidence that a family history of drug or alcohol abuse is associated with a greater risk of prescription opioid abuse (Gilson & Kreis, 2009), but more research is needed to determine whether this risk factor differs by type of substance of abuse/dependence or by class of prescription drug used for nonmedical purposes.
Sibling Substance Use	INSUFFICIENT RESEARCH	<i>There were no empirical studies in the past 5 years that specifically explored sibling use of alcohol, illicit drugs, or PD as a risk factor for NMUPD.</i>	

PEER DOMAIN			
Risk Factor	Evidence Level	Justification for Evidence Level	Level of Evidence/Supporting Literature
Peer Norms: Peer Approval of Use	MODERATE	<i>Two cross-sectional study found a significant relationship between peer approval of use and NMUPD. Additionally, many research studies have demonstrated this significant relationship with other substances.</i>	Having peers who either approve or neither approve or disapprove of marijuana use is associated with greater risk of NMUPD (Sung et al., 2005). Having friends who report more tolerant attitudes towards substance use was associated with greater NMUPD in a college-age sample of young adults (Ford, 2008).
Number of Friends who use (PD, other substances)	MODERATE	<i>Three cross sectional studies have examined this specifically with NMUPD, but there are many studies that have demonstrated this relationship with other substances.</i>	Close friends use of substances is one of the strongest and most consistent risk factors for substance use. Research supports this same conclusion for peer substance use being associated with adolescent NMUPD (Collins et al., 2011; Schinke et al., 2008; Sung et al., 2005).
Normative Misperceptions of Peer Use	INSUFFICIENT RESEARCH	<i>Only one cross-sectional study was identified over the past 5 years that examined this risk factor for NMUPD.</i>	A sample of college students found that the majority of students overestimated the prevalence of NMUPD among their peers. For example, perceived rates of nonmedical use of opioids was 18.2%, which was more than double the actual rates of use (7.4%). Past year nonmedical users of prescription stimulants and opioids perceived peers prevalence rates of NMUPD to be significantly higher than non-users (McCabe, 2008).
Association with Delinquent Peers	INSUFFICIENT RESEARCH	<i>Only one cross-sectional study was identified over the past 5 years that examined this risk factor for NMUPD.</i>	Having more friends who engaged in delinquent behavior and less prosocial behavior was associated with greater likelihood of nonmedical use of Ritalin, tranquilizers, and narcotic (e.g., opioids) prescription medications by youth aged 11-18 (Fleary et al 2011).

INDIVIDUAL DOMAIN			
Risk Factor	Evidence Level	Justification for Evidence Level	Level of Evidence/Supporting Literature
Perception Risk/Harm	STRONG	<i>One longitudinal and several studies using cross-sectional analyses support an inverse association between perceived risk or harm and NMUPD.</i>	<p>NMUPD has been characterized by adolescents as “responsible, controlled, or safe” (Friedman, 2006). Forty percent of adolescents report the belief that NMUPD is safer than illegal drugs, even without a prescription. One-third of adolescents reported that there was “nothing wrong” with occasional NMUPD; the same percentage also believe that painkiller medications are “not addictive” (Twombly & Holtz, 2008).</p> <p>Cross-sectional studies have demonstrated an inverse relationship between the level of perceived risk or harm and likelihood of NMUPD (Arria, Caldeira, Vincent, O’Grady, & Wish, 2008; Collins et al., 2011; Johnston, O’Malley, Bachman, & Schulenberg, 2006; Quintero, Peterson, & Young, 2006). A study utilizing the national Motoring the Future annual survey of 8th, 10th and 12th graders found that an increase in sedative use among 12th graders occurred alongside a decrease in perceived risk of use. During this same time period, an increase in peer group disapproval of marijuana use was correlated with decreased rates of use of marijuana (Johnston et al., 2006) supporting a causal link between perceptions of risk and rates of use. A longitudinal study of undergraduates also found that lower perceived harmfulness of PD was associated with an increased risk of NMUPD, after controlling for relevant demographic factors (Arria et al., 2008).</p>
Personality Characteristics: Sensation Seeking	STRONG	<i>One longitudinal and three cross-sectional studies, (two adolescent, one college age sample) found a significant association between sensation-seeking and NMUPD.</i>	Three studies have found that high sensation seeking aspect of personality is associated with a greater risk of NMUPD, after controlling for demographic factors (Arria et al., 2008; Collins et al., 2011; Schepis & Krishnan-Sarin, 2008). Similarly, Fleary and colleagues (2011) found that youth reporting greater risk-taking was associated with a greater likelihood of nonmedical use of Ritalin and tranquilizers, but risk-taking was not associated with likelihood of nonmedical prescription opioid use.
Early onset of use	MODERATE	<i>Studies across all licit and illicit drugs support that association between earlier onset and increased risk of later substance use problems, including abuse and dependence. Two studies identified over the past 5 years looked at early onset of NMUPD.</i>	Earlier onset of NMUPD (one study reported use at or before age 13 while another reported use at or before age 16) put adolescents at greater risk of developing prescription drug abuse or dependence compared to those individuals who start NMUPD at or after age 21 (Colliver, Kroutil, Dai, & Gfroerer, 2006; McCabe, West, Morales, Cranford, & Boyd, 2007). The odds of developing lifetime PD abuse among non-medical users decreased by 5% for each year NMUPD was delayed, while the odds of developing PD dependence decreased by 2% with each year onset was delayed (McCabe, West, et al., 2007).

Alcohol or illicit Drug use/abuse/dependence	STRONG	<i>One longitudinal, one systematic review and numerous cross-sectional studies demonstrate a significant association between substance use, abuse and dependence and NMUPD.</i>	Many studies have demonstrated the association between NMUPD and alcohol, tobacco, and other illicit drug use, abuse, and dependence (Benotsch, Koester, Luckman, Martin, & Cejka, 2011; Blanco et al., 2007; Catalano, White, Fleming, & Haggerty, 2011; Daniulaityte, Falck, Wang, & Carlson, 2009; Fleary, Heffer, & McKyer, 2011; Ford, 2009; Hall, Howard, & McCabe, 2010; Levine, 2007; McCabe, Boyd, & Young, 2007; McCabe, Cranford, Morales, & Young, 2006; McCauley et al., 2010; Schepis & Krishnan-Sarin, 2008; Wilens et al., 2008; Wu, Ringwalt, Mannelli, & Patkar, 2008). Previous histories of alcohol use or other drug use disorders are associated with increased odds of NMUPD (Blanco et al., 2007). Adolescents own use of illicit drugs was found to be the strongest risk factor for nonmedical use of prescription opioids (Sung et al., 2005). Some studies have shown that individuals who use their PD as prescribed are not at an increased risk of other substance use than non-users (Boyd, McCabe, & Teter, 2006; McCabe, Teter, & Boyd, 2004), while other studies have found that medical users of PD are more likely to report illicit drug use (Collins et al., 2011; McCabe, Boyd, et al., 2007).
Motivations for Nonmedical Use	INSUFFICIENT EVIDENCE	<i>Several studies have examined motivations for NMUPD, and one study found a significant relationship between sensation-seeking motives (e.g., use to get high) and NMUPD compared to those who endorses self-treating motivations, such as to treat pain.</i>	Evidence also suggests that some motives for NMUPD put adolescents at greater risk of abuse/dependence on PD. Reasons for NMUPD have been to gain a pharmacologic effect of the medication (e.g., treat pain, relax, perform better), or to feel good/high. One study found that “relieve pain” was the most common single reason given for NMUPD (40%), while the other 60% reported more than one motive for NMUPD. Boyd et al (2009) found that adolescents who reported NMUPD for sensation-seeking motives rather than self-treating motives were more likely to report other illicit drug use, gambling, and binge drinking (Boyd, Young, Grey, & McCabe, 2009).
Mental Health Diagnoses	MODERATE	<i>Many studies support the link between other mental health diagnoses, particularly depression and anxiety and NMUPD, however, these studies are all cross-sectional.</i>	Mental health problems are associated with NMUPD (Blanco et al., 2007; Braden et al., 2009; Havens et al., 2011; Herman-Stahl, Krebs, Kroutil, & Heller, 2006; McCauley et al., 2011; Schepis & Krishnan-Sarin, 2008; Sung et al., 2005). Having a history of major depressive and/or anxiety disorders is associated with greater odds of NMUPD (Blanco et al., 2007). Individuals diagnosed with depression or anxiety disorders were more likely to be prescribed opioids and prescribed them at higher doses compared to individuals not diagnosed with mental health disorders (Braden et al., 2009). Personality disorders and bipolar disorder has also been associated with greater NMUPD (Gilson & Kreis, 2009). A study of college age stimulant misuse found that students reporting greater psychological distress and internal restlessness were more likely to report nonmedical use of prescription stimulants (Weyandt et al., 2009). Additionally, individuals reporting recent contact with a mental health professional also report higher rates of NMUPD (Sung et al., 2005; Wu, Pilowsky, et al., 2008; Wu, Ringwalt, et al., 2008).

			A study comparing treatment seeking adolescent opioid prescription drug users found that these adolescents reported higher rates of psychiatric disorders compared to adolescents seeking treatment for heroin dependence. In particular, opioid PD users presented with higher rates of Attention-deficit Hyperactivity Disorder and manic episodes (Subramaniam & Stitzer, 2009).
Delinquent/ Antisocial Behavior	STRONG	<i>Two reviews (one was a systematic review of the literature on prescription stimulants) and three cross-sectional studies support this relationship. One cross-sectional study failed to find a significant relationship with NMUPD.</i>	<p>Antisocial behavior as well as a history of delinquent behaviors have been associated with higher rates of NMUPD (Gilson & Kreis, 2009; Harrell & Broman, 2009; McCauley et al., 2010; Sung et al., 2005). Conduct disorder, which includes delinquent and antisocial behavior as clinically relevant symptoms, has been shown to be associated with nonmedical use of prescription stimulants (Wilens et al., 2008). It should be noted that substance use in adolescence is often classified as delinquent behavior which introduces a potential confound into this relationship, however substance use alone is not sufficient for a diagnosis of conduct disorder.</p> <p>Collins (2011) failed to find a significant relationship between antisocial behavior and NMUPD, however, it is important to note that this study utilizes a geographically limited sample which limits the generalizability of its findings.</p>
Chronic Pain (non-cancer)	MODERATE (for PD misuse) and INSUFFICIENT RESEARCH (for abuse)	<i>One systematic review of articles between the years of 1966-2006 for abuse/addiction, one cross-sectional diagnostic interview study using DSM-IV abuse/dependence criteria, and three cross-sectional studies of indicators of misuse support an associated between chronic pain and NMUPD.</i>	<p>Estimates of abuse or dependence of prescription opioids among chronic pain patients prescribed opioids vary from 3.27% to 25.8%. In terms of opioid misuse, estimates range from 11.5% to 41.8%. A systematic review including 24 studies determined an abuse/addiction rate of 3.27% (Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008), which is greater than rates of dependence or abuse of prescription pain relievers (less than 1%) in national samples of individual aged 12 and older (SAMHSA, 2011). Diagnostic interviews keyed to DSM-IV criteria with a random sample of pain patients (n=705) reported that 25.8% met criteria for opioid dependence (Boscarino et al., 2010). Multiple studies have considered aberrant urine toxicology screens (UTS) or drug behaviors (such as early refills) among pain patients as indicators of potential misuse. In a systematic review including 5 UTS studies, aberrant use averaged 20.4% and including 17 behavior studies aberrant use was 11.5%. In a retrospective medical record review of UTS (n=938,586), 26.6% of patients had higher than expected and 15.2% lower than expected opioid levels (Couto, Romney, Leider, Sharma, & Goldfarb, 2009). A smaller prospective study of UTS and behavior (n=196) reported that 36% of patients met a broad definition of opioid misuse (Ives et al., 2006). Another prospective study found that 34.1% of patients (n=455) were positive for aberrant drug behavior (Jamison, Butler, Budman, Edwards, & Wasan, 2010). These studies should be interpreted cautiously due to varying definitions of abuse and aberrant use, varying methodology, and the lack of evidence relating aberrant UTS and behaviors to abuse/dependence.</p>
Attendance at Religious services	INSUFFICIENT RESEARCH/ SUBPOPULATION	<i>Only two studies were identified over the past 5 years that examined religious</i>	<p>Infrequent religious attendance was found to be associated with increased PD use (Sung et al., 2005). Greater religious attendance was a protective factor for African-American adolescents grades 7 to 12 (Harrell & Broman, 2009).</p>

	ONLY	<i>attendance and NMUPD. One study only found evidence of a protective effect for African American youth.</i>	
Self-efficacy	INSUFFICIENT RESEARCH	<i>One cross-sectional study demonstrated a significant cross-sectional relationship between the risk factor and some classes of prescription drugs.</i>	Lower self-efficacy, as measured by less mastery of the external world, was associated with nonmedical use of Ritalin, tranquilizers, and narcotic prescription medications (Fleary et al., 2011).

The following identified risk and protective factors, many of them demographic characteristics, are not changeable. However, knowledge regarding these factors may be useful in order to identify and select appropriate individuals and/or groups into prevention programs.

Gender: Evidence is mixed regarding gender differences and nonmedical use of prescription drugs. Some studies have found that adolescent females are more likely to report nonmedical use of prescription drugs (Ford, 2009; Sung et al., 2005; Wu, Ringwalt, et al., 2008). In particular, females may be more likely to report nonmedical use of opioids or sedatives/anxiolytics (McCabe, Boyd, et al., 2007; McCabe, Cranford, et al., 2007), and are more likely to report nonmedical use for the purpose of “self-treating” compared to males who tend to report more “sensation-seeking” reasons (e.g., get high) (Boyd et al., 2009). However one study found that males reported more nonmedical use of opioid analgesics compared to females (McCabe & Boyd, 2005). Another study examining 2006 NSDUH data of all individuals aged 12 and older found that males were more likely to report lifetime and past year nonmedical use of prescription opioids, but there were no gender differences for rates of abuse or dependence on prescription opioids. Additionally males and females may gain access to PD for nonmedical purposes differently. Adolescent females are more likely to obtain opioids prescription drugs for free or to steal them from a friend or relative, while adolescent males are more likely to purchase prescription drugs or acquire them from a physician (Collins et al., 2011; Schepis & Krishnan-Sarin, 2009).

Ethnicity/Race: Research has consistently found higher rates of NMUPD among individuals who identify as White (Benotsch et al., 2011; Collins et al., 2011; Ford, 2009; McCabe & Boyd, 2005; McCabe, Boyd, et al., 2007; Wu, Ringwalt, et al., 2008) after accounting for other risk factors (e.g., availability, peer use). A larger percentage of white respondents reported sensation-seeking motives for NMUPD compared to non-white respondents (Boyd et al., 2009).

Socioeconomic Status: Several studies have demonstrated a relationship between lower socioeconomic status and increased risk for NMUPD (Ford, 2009; Sung et al., 2005), however, additional research is needed in this area in order to determine whether other factors (e.g., availability, family factors) may account for this significant relationship.

Summary/ Overview of Findings

Global Domain	Risk or Protective Factor	Evidence Level
Individual	Perception Risk/Harm	STRONG
Individual	Personality Characteristics: Sensation Seeking	STRONG
Individual	Alcohol or Illicit Drug Use/Abuse/ Dependence	STRONG
Individual	Delinquent/ Antisocial Behavior	STRONG
Community	Availability/ Opportunities to Use: Social Access	MODERATE
School	Academic Failure/Low Educational Attainment	MODERATE
School	Low Bonding to School	MODERATE
Family	Poor Parental Monitoring or Supervision/ Low Parental Attachment or Involvement	MODERATE
Family	Parental Disapproval of Substance Use	MODERATE
Peer	Peer Norms: Peer Approval of Use	MODERATE
Peer	Number of Friends who use (PD, other substances)	MODERATE
Individual	Early onset of use	MODERATE
Individual	Mental Health Diagnoses	MODERATE
Community	Availability/ Opportunities to Use: Retail Access	MODERATE/ INSUFFICIENT RESEARCH
Individual	Chronic Pain (non-cancer)	MODERATE (for PD misuse) and INSUFFICIENT RESEARCH (for abuse)
Community	Community Norms Favorable for Drug Use	INSUFFICIENT RESEARCH
Community	Neighborhood quality, disorganization, community attachment, mobility	INSUFFICIENT RESEARCH
Family	Parental Substance use	INSUFFICIENT RESEARCH
Family	Sibling Substance Use	INSUFFICIENT RESEARCH
Peer	Normative Misperceptions of Peer Use	INSUFFICIENT RESEARCH
Peer	Association with Delinquent Peers	INSUFFICIENT RESEARCH
Individual	Motivations for Nonmedical Use	INSUFFICIENT RESEARCH
Individual	Attendance at Religious services	INSUFFICIENT RESEARCH/ SUBPOPULATION ONLY
Individual	Self-efficacy	INSUFFICIENT RESEARCH

References

- Arria, A. M., Caldeira, K. M., Vincent, K. B., O'Grady, K. E., & Wish, E. D. (2008). Perceived harmfulness predicts nonmedical use of prescription drugs among college students: interactions with sensation-seeking. *Prev Sci*, 9(3), 191-201.
- Benotsch, E. G., Koester, S., Luckman, D., Martin, A. M., & Cejka, A. (2011). Non-medical use of prescription drugs and sexual risk behavior in young adults. *Addict Behav*, 36(1-2), 152-155.
- Blanco, C., Alderson, D., Ogburn, E., Grant, B. F., Nunes, E. V., Hatzenbuehler, M. L., & Hasin, D. S. (2007). Changes in the prevalence of non-medical prescription drug use and drug use disorders in the United States: 1991-1992 and 2001-2002. *Drug Alcohol Depend*, 90(2-3), 252-260.
- Boscarino, J. A., Rukstalis, M., Hoffman, S. N., Han, J. J., Erlich, P. M., Gerhard, G. S., & Stewart, W. F. (2010). Risk factors for drug dependence among outpatients on opioid therapy in a large US healthcare system. *Addiction*, 105(10), 1776-1782.
- Boyd, C. J., Young, A., Grey, M., & McCabe, S. E. (2009). Adolescents' nonmedical use of prescription medications and other problem behaviors. *J Adolesc Health*, 45(6), 543-550.
- Braden, J. B., Sullivan, M. D., Ray, G. T., Saunders, K., Merrill, J., Silverberg, M. J., Rutter, C. M., Weisner, C., Banta-Green, C., Campbell, C., & Von Korff, M. (2009). Trends in long-term opioid therapy for noncancer pain among persons with a history of depression. *Gen Hosp Psychiatry*, 31(6), 564-570.
- Catalano, R. F., White, H. R., Fleming, C. B., & Haggerty, K. P. (2011). Is nonmedical prescription opiate use a unique form of illicit drug use? *Addict Behav*, 36(1-2), 79-86.
- Collins, D., Abadi, M. H., Johnson, K., Shamblen, S., & Thompson, K. (2011). Non-Medical Use of Prescription Drugs Among Youth in an Appalachian Population: Prevalence, Predictors, and Implications for Prevention. *Journal of Drug Education* 41(3), 309 - 326.
- Colliver, J., Kroutil, L., Dai, L., & Gfroerer, J. (2006). Misuse of prescription drugs: Data from the 2002, 2003, and 2004 National Surveys on Drug Use and Health (DHHS Publication No. SMA 06-4192, Analytic Series A-28) Rockville. MD: *Substance Abuse and Mental Health Services Administration, Office of Applied Studies*.
- Compton, W. M., & Volkow, N. D. (2006). Abuse of prescription drugs and the risk of addiction. *Drug Alcohol Depend*, 83 Suppl 1, S4-7.
- Couto, J. E., Romney, M. C., Leider, H. L., Sharma, S., & Goldfarb, N. I. (2009). High rates of inappropriate drug use in the chronic pain population. *Population Health Management*, 12(4), 185-190.
- Daniulaityte, R., Falck, R. S., Wang, J., & Carlson, R. G. (2009). Illicit use of pharmaceutical opioids among young polydrug users in Ohio. *Addict Behav*, 34(8), 649-653.
- Fishbain, D. A., Cole, B., Lewis, J., Rosomoff, H. L., & Rosomoff, R. S. (2008). What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review. *Pain Medicine*, 9(4), 444-459.
- Fleary, S. A., Heffer, R. W., & McKyer, E. L. (2011). Dispositional, ecological and biological influences on adolescent tranquilizer, Ritalin, and narcotics misuse. *J Adolesc*, 34(4), 653-663.
- Ford, J. A. (2008). Social Learning Theory and Nonmedical Prescription Drug Use among Adolescents. *Sociological Spectrum*, 28(3), 299-316.
- Ford, J. A. (2009). Nonmedical Prescription Drug Use Among Adolescents. *Youth & Society*, 40(3), 336-352.
- Gilson, A. M., & Kreis, P. G. (2009). The burden of the nonmedical use of prescription opioid analgesics. *Pain medicine*, 10(Suppl 2), S89-100.
- Hall, M. T., Howard, M. O., & McCabe, S. E. (2010). Subtypes of adolescent sedative/anxiolytic misusers: A latent profile analysis. *Addict Behav*, 35(10), 882-889.

- Harrell, Z. A., & Broman, C. L. (2009). Racial/ethnic differences in correlates of prescription drug misuse among young adults. *Drug Alcohol Depend*, 104(3), 268-271.
- Havens, J. R., Young, A. M., & Havens, C. E. (2011). Nonmedical prescription drug use in a nationally representative sample of adolescents: evidence of greater use among rural adolescents. *Arch Pediatr Adolesc Med*, 165(3), 250-255.
- Herman-Stahl, M. A., Krebs, C. P., Kroutil, L. A., & Heller, D. C. (2006). Risk and protective factors for nonmedical use of prescription stimulants and methamphetamine among adolescents. *J Adolesc Health*, 39(3), 374-380.
- Ives, T., Chelminski, P., Hammett-Stabler, C., Malone, R., Perhac, J. S., Potisek, N., Shilliday, B., DeWalt, D., & Pignone, M. (2006). Predictors of opioid misuse in patients with chronic pain: a prospective cohort study. *BMC health services research*, 6(1), 46.
- Jamison, R. N., Butler, S. F., Budman, S. H., Edwards, R. R., & Wasan, A. D. (2010). Gender differences in risk factors for aberrant prescription opioid use. *The Journal of Pain*, 11(4), 312-320.
- Johnston, L. D., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2006). Monitoring the Future national survey results on drug use, 1975-2005. Volume I: Secondary school students *NIH Publication No. 06-5883*. Bethesda, MD: National Institute on Drug Abuse.
- Latimer, W., & Zur, J. (2010). Epidemiologic Trends of Adolescent Use of Alcohol, Tobacco, and Other Drugs. *Child and adolescent psychiatric clinics of North America*, 19(3), 451-464.
- Levine, D. A. (2007). "Pharming": the abuse of prescription and over-the-counter drugs in teens. *Curr Opin Pediatr*, 19(3), 270-274.
- McCabe, S. E. (2008). Misperceptions of non-medical prescription drug use: a web survey of college students. *Addict Behav*, 33(5), 713-724.
- McCabe, S. E., & Boyd, C. J. (2005). Sources of prescription drugs for illicit use. *Addictive behaviors*, 30(7), 1342-1350.
- McCabe, S. E., Boyd, C. J., & Young, A. (2007). Medical and nonmedical use of prescription drugs among secondary school students. *Journal of Adolescent Health*, 40(1), 76-83.
- McCabe, S. E., Cranford, J. A., Boyd, C. J., & Teter, C. J. (2007). Motives, diversion and routes of administration associated with nonmedical use of prescription opioids. *Addictive behaviors*, 32(3), 562-575.
- McCabe, S. E., Cranford, J. A., Morales, M., & Young, A. (2006). Simultaneous and concurrent polydrug use of alcohol and prescription drugs: prevalence, correlates, and consequences. *J Stud Alcohol*, 67(4), 529-537.
- McCabe, S. E., West, B. T., Morales, M., Cranford, J. A., & Boyd, C. J. (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.
- McCauley, J. L., Amstadter, A. B., Macdonald, A., Danielson, C. K., Ruggiero, K. J., Resnick, H. S., & Kilpatrick, D. G. (2011). Non-medical use of prescription drugs in a national sample of college women. *Addict Behav*, 36(7), 690-695.
- McCauley, J. L., Danielson, C. K., Amstadter, A. B., Ruggiero, K. J., Resnick, H. S., Hanson, R. F., Smith, D. W., Saunders, B. E., & Kilpatrick, D. G. (2010). 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*, 51(1), 84-93.
- National Center on Addiction and Substance Abuse at Columbia University. (2008). National Survey of American Attitudes on Substance Abuse XIII: Teens and Parents. New York, NY: National Center on Addiction and Substance Abuse at Columbia University.
- Quintero, G., Peterson, J., & Young, B. (2006). Exploratory Study of Socio-Cultural Factors Contributing to Prescription Drug Misuse Among College Students *Journal of Drug Issues*, 36(4), 903-932.
- SAMHSA. (2006). Results from the 2005 National Survey on Drug Use and Health: National Findings *Office of Applied Studies, NSDUH Series H-30, DHHS Publication No. SMA 06-4194*. Rockville, MD.
- SAMHSA. (2011). Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings *NSDUH Series H-41, HHS Publication No. (SMA) 11-4658*. Rockville, MD: Substance Abuse and Mental Health Services Administration.

- Schepis, T. S., & Krishnan-Sarin, S. (2008). Characterizing adolescent prescription misusers: a population-based study. *J Am Acad Child Adolesc Psychiatry*, 47(7), 745-754.
- Schepis, T. S., & Krishnan-Sarin, S. (2009). Sources of prescriptions for misuse by adolescents: differences in sex, ethnicity, and severity of misuse in a population-based study. *J Am Acad Child Adolesc Psychiatry*, 48(8), 828-836.
- Schinke, S. P., Fang, L., & Cole, K. C. (2008). Substance use among early adolescent girls: risk and protective factors. *J Adolesc Health*, 43(2), 191-194.
- Subramaniam, G. A., & Stitzer, M. A. (2009). Clinical characteristics of treatment-seeking prescription opioid vs. heroin-using adolescents with opioid use disorder. *Drug Alcohol Depend*, 101(1-2), 13-19.
- Sung, H. E., Richter, L., Vaughan, R., Johnson, P. B., & Thom, B. (2005). Nonmedical use of prescription opioids among teenagers in the United States: trends and correlates. *J Adolesc Health*, 37(1), 44-51.
- Twombly, E. C., & Holtz, K. D. (2008). Teens and the misuse of prescription drugs: evidence-based recommendations to curb a growing societal problem. *J Prim Prev*, 29(6), 503-516.
- Weyandt, L. L., Janusis, G., Wilson, K. G., Verdi, G., Paquin, G., Lopes, J., Varejao, M., & Dussault, C. (2009). Nonmedical Prescription Stimulant Use Among a Sample of College Students. *Journal of Attention Disorders*, 13(3), 284-296.
- Wilens, T. E., Adler, L. A., Adams, J., Sgambati, S., Rotrosen, J., Sawtelle, R., Utzinger, L., & Fusillo, S. (2008). Misuse and Diversion of Stimulants Prescribed for ADHD: A Systematic Review of the Literature. *Journal of the American Academy of Child & Adolescent Psychiatry*, 47(1), 21-31.
- Wu, L. T., Pilowsky, D. J., & Patkar, A. A. (2008). Non-prescribed use of pain relievers among adolescents in the United States. *Drug Alcohol Depend*, 94(1-3), 1-11.
- Wu, L. T., Ringwalt, C. L., Mannelli, P., & Patkar, A. A. (2008). Prescription pain reliever abuse and dependence among adolescents: a nationally representative study. *J Am Acad Child Adolesc Psychiatry*, 47(9), 1020-1029.

Strategies/Interventions for Reducing Non-Medical Use of Prescription Drug (NMUPD)

The Substance Abuse and Mental Health Services Administration's (SAMHSA) Center for Substance Abuse Prevention (CSAP) has highlighted three considerations in determining which interventions provide the best fit for a community's comprehensive prevention plan¹:

1. Conceptual fit: Is the intervention relevant and logically connected to identified risk factors and outcomes?
2. Practical fit: Is the intervention appropriate given the culture of a particular community, taking into account community readiness, the community's population, and general local circumstances?
3. Strength of evidence: Is there sufficient documented evidence to support the strategy's efficacy?

The current document summarizes the strength of evidence found in the literature for strategies that may affect the initiation, escalation and consequences of prescription drug use.

¹ From SAMHSA's "Identifying and Selecting Evidence-Based Interventions", published in January, 2009. (Available at: http://www.ncspfsig.org/Project_Docs/2009%20Evidence-based%20guidance%20document.pdf).

Methods

A search of the empirical literature was conducted using PSYCHINFO, and PUBMED, to look for articles published between 2006 and 2011. Initial search terms included “prescription drugs” “opioids” “stimulants” “sedatives” “tranquilizers”, in combination with “adolescents,” “older adults,” “elderly,” “strategy”, “intervention”, “prevention”. Additionally, a search of The Substance Abuse Mental Health Service Administration’s National Registry of Evidence Based Prevention Programs (NREPP) was conducted to look for programs with reported effects on nonmedical use of prescription drugs. Different components of these programs were examined and separate component parts were included in search terms with “prescription drugs” and “nonmedical use of prescription drugs.” Only two NREPP programs report outcomes separately for PD.

A Ph.D.-Level reviewer examined studies for methodological quality, including only those studies that accounted for well-known confounds, applied appropriate statistical tests, and used well-defined measures.

Document Organization

This paper is organized into 5 global domains (i.e., Community/Neighborhood, School, Family, Peer, and Individual). The first column under each domain identifies common risk and protective factors. The document is organized by these risk factors because each of these factors can provide a unique point of entry for intervening. The second column (“Related Strategies”) points to various strategies that may relate to the identified risk factor.

The third column (“Justification for Evidence Level”) summarizes existing literature by ranking the strategy into one of the following categories:

- Evidence of direct effects on ATOD use in general, and NMUPD specifically.
 - *Supported by at least 2 studies from the peer-reviewed prevention literature. At least one of these studies reported results specifically for prescription drugs.*
- Little or no evidence of direct effect
 - *At least one peer reviewed study in the prevention literature shows that this strategy does not impact use. This finding was not contradicted by other published research.*
- Theoretical support, insufficient evidence
 - *The specific application of the strategy to PD is untested and/or has not been published in the peer-reviewed prevention literature, particularly during the past 5 years. Existing research may be inconsistent (reaching significance in some studies, but not significant in others).*

The “Supporting Research” column provides more in-depth analysis of available literature.

COMMUNITY DOMAIN			
Risk Factor	Related Strategy	Justification for Evidence Level	Supporting Research
Availability: Social Access	Restrict availability in home through education/communication strategy	<p>Theoretical Support, Insufficient Evidence</p> <p><i>This intervention was given this label since there is evidence from other substances (e.g., alcohol) that restricting social access to substances results in reduced rates of substance use. Preliminary evidence suggests support for NMUPD.</i></p>	<p>Parents may represent a source of access to prescription drugs, with 60% of adolescents reporting that prescription pain relievers are “easy” to obtain from parents or friends (SAMHSA, 2006). A multi-component intervention designed to restrict access to harmful legal products, including prescription drugs was implemented across 4 communities in Alaska (Gruenewald, Johnson, Shamblen, Ogilvie, & Collins, 2009; Johnson et al., 2007). The intervention included a school-based prevention program and retail, home and school-based environmental strategies. Students’ surveyed reported significant decreases in perceived availability at the end of this multi-component intervention, although changes in the use of harmful legal products, including NMUPD were not reported. While some aspects of these environmental strategies do not apply to prescription drugs (e.g., restricting legal products from retail vendors, such as inhalants, glues), one strategy focused on having parents take an inventory of high-risk products in their home, including prescription drugs, and then take appropriate steps to restrict the availability of these products from youth. The parent environmental strategy included 2-3 family night events held in each of the 4 intervention communities and data was collected on parents who attended these family nights. No outcome data were presented (Johnson et al., 2007).</p>
Availability: Retail Access	Change prescriber practices (e.g., education programs aimed at improving appropriate prescribing practices to limit nonmedical use/abuse)	<p>Theoretical Support, Insufficient Evidence</p> <p><i>Only one study was located that examined outcomes of an academic detailing intervention with physicians, but lack of follow-up data limit conclusions that can be drawn from this study. Other studies from the medical literature address physician training interventions, but they are not specific to NMUPD.</i></p>	<p>Improving prescribing practices of health care providers, particularly for opioids, has been proposed as a method for reducing availability of PD for misuse. Physician training strategies include 1) academic detailing, 2) training to recognize the cardinal features of patients trying to obtain PD for non-medical purposes, 3) adapting prescribing drug writing habits to more safely provide appropriate interventions, 4) providing Screening, Brief Intervention and Referral to Treatment (SBIRT) training to new physicians/trainees (Manchikanti, 2007; Twombly & Holtz, 2008). While many articles identify physician training as a potential effective strategy for reducing NMUPD, few empirical studies have examined the effects of these training interventions.</p> <p>“Academic Detailing” interventions aim to educate physicians regarding the appropriate prescribing of prescription drugs, particularly opioid pain relievers. One study provided 1 hour presentations to physicians that contained information about the consequences of prescription pain medicines (e.g., increase in deaths due to opioid poisoning) as well as safe prescribing practices. The majority of physicians (90%) indicated greater knowledge of PD consequences and confidence in ability to adopt appropriate practices. Low follow-up rates at 1 and 6 months limit findings regarding actual changes in safe prescribing practices (Cochella & Bateman, 2011).</p> <p>Several states have begun initiatives to promote safer PD prescribing practices. For</p>

			<p>example, North Carolina launched the Safer Opioid Prescribing (SOP) initiative in 4 counties across the state which includes a 4-pronged approach: outreach and education to physicians, education to patients regarding appropriate storage and disposal of PD, community building around NMUPD, and TA to physicians to implement safer prescribing practices. Initial results suggest that the intervention led to increased physician registration for and usage of the state's Prescription Drug Monitoring Program compared to physicians in other counties in the state (Governor's Institute on Alcohol and Substance Abuse, 2010). However, descriptions of the intervention components were not provided and it is not possible to determine the relative impact of each component of the intervention on changing physicians' behaviors.</p> <p>Guidelines for appropriate clinical management of chronic non-cancer pain with opioids have been available for longer than a decade, however, more recent evidence-based guidelines have been created (Chou et al., 2009; Paulozzi, Weisler, & Patkar, 2011). Additionally, different assessment tools have been used to assess 1) abuse potential among patients being considered for long-term opioid therapy, 2) degree of misuse/abuse among patients taking opioids for some length of time, and 3) current abuse/dependence of prescription opioids. A few of these assessment tools have been adapted for use with adolescents (Passik, Kirsh, & Casper, 2008). Researchers have recommended the use of these guidelines and tools to prevent NMUPD, however it is difficult to assess whether these tools translate into changes in NMUPD.</p>
Availability: Retail Access	State-level Prescription Drug Monitoring Programs	<p>Evidence of Direct Effects</p> <p><i>According to several state and national evaluations, there is evidence that PMPs are associated with decreased availability of PD. Some evidence suggests that this occurs through changed prescribing practices. However, a large observational study comparing US states with and without PMP found no differences in opioid use rates or overdose deaths by PMP status. Additional evidence is needed to determine if more recently implemented PMPs are linked with overall</i></p>	<p>Currently 44 states have enacted Prescription Drug Monitoring Programs (PMP), although only 35 states have operational PMPs (Paulozzi, Weisler, et al., 2011). PMPs typically collect data from pharmacies on dispenses controlled substance prescriptions and can be an important tool to reduce availability of PD through reducing PD diversion (e.g., prescription fraud, forgeries, doctor-shopping, inappropriate/illegal prescription practices by some physicians). A report summarizing the outcomes of states PMPs found that states without PMP were more likely to experience higher rates of PD diversion (PMP Center of Excellence at Brandeis University, 2011). For example, since 2004 oxycodone distribution in Kentucky, a state with an active PMP, rose at a much lower rate compared to two states (Florida and Tennessee) which did not have PMPs during that time. Additionally, a national evaluation comparing states with and without PMPs found that states with proactive PMP had less availability of prescription pain relievers and stimulants compared to states without proactive PMP (availability measured by slower growth per capita in these classes of PD)(PMP Center of Excellence at Brandeis University, 2011). Data from 6 different state reports demonstrated that physicians found that being provided data from their state's PMP was useful and that a proportion of physicians reporting changing their prescribing practices based on the information provided (Baehren et al., 2010; PMP Center of Excellence at Brandeis University, 2011).</p> <p>However, an observational US study between the years of 1999-2005 examined</p>

		<i>reductions in availability of PD.</i>	differences between the 19 states with operational PMP and those that did not. There were no differences between rates of drug overdose mortality, opioid overdose mortality or opioid consumption by PMP status. However, the study found that mortality rates and consumption patterns were significantly lower among the 3 states (CA, NY, TX) that required the use of special prescribing forms (Paulozzi, Kilbourne, & Desai, 2011). While PMP hold promise, additional data is needed to determine whether these programs lead to actual changes in consumptions or consequences of PD use.
Availability: Retail Access	Restrict Internet Availability	Theoretical Support, insufficient evidence <i>The internet has the lowest prevalence of use for obtaining PD for nonmedical use.</i>	According to national and local surveys, the most common method for obtaining PD for nonmedical purposes is through social sources (SAMHSA, 2011). Over half of respondents aged 12 and older who report NMUPD reported that they got PD for free from a friend or relative. Nearly 80% of these respondents indicated that the friend or relative originally got the PD from one doctor. Among respondents reporting past year use of pain relievers for nonmedical purpose--55% obtained the pain relievers most recently from a friend or relative for free, 11.4% bought them from a friend or relative, and 4.8% took them from a friend or relative without asking (SAMHSA, 2011). These percentages are similar to those reported in NSDUH data from 2006-2009. Surveys completed in a college age sample found a similar pattern of access, with the majority of respondents reporting parents and friends as the most common source of PD. The internet had the lowest prevalence of use for obtaining PD for nonmedical use (0.2%) (McCabe, Cranford, Boyd, & Teter, 2007).
Community Norms Favorable for Drug Use	Using Mass media to increase public concern about use and change normative perceptions	Evidence of Direct Effects <i>One study examined a media intervention to increase community knowledge, norms and behaviors around PD. Results suggest limited reach of the intervention, however, some respondents report attitude and behavior changes as a result of the mass media campaign.</i>	One study examining the effects of a statewide educational media campaign in Utah targeting prescription drugs was conducted between 2008 and 2009. Results found low reach of the campaign, with only 48% of those surveyed who recalled seeing the campaign ads. Of those who recalled the campaign, 52% said that the media messages made them less likely to share medications, 51% reported that they were less likely to use PD not prescribed for them, and 29% reported a change in their understanding of prescription pain medication (PPM) dangers changed over the last year. There were no changes in reported beliefs regarding medical sharing or the burden of PPM misuse in the community. Among the fraction of respondents who were aware of the drug disposal issue, there was a significant increase in reported behaviors regarding disposal of PPM from pre to post-test, although only 18% reported they disposed of leftover medications as a result of the media messages. The number of respondents who were familiar with how to dispose of PPM remained unchanged (43%) (Johnson, Porucznik, Anderson, & Rolfs, 2011).
	Use of community coalitions to affect change	Theoretical Support, Insufficient Evidence <i>While there is evidence to suggest that community coalitions can be part of an effective intervention</i>	One study aimed at reducing opioid overdose deaths examined rates of overdose deaths before and after a 5 component intervention which included community activation and coalition building, in addition to monitoring and surveillance data, prevention of overdoses, use of rescue medications for reversing overdoses, and evaluating project components. Results support an unadjusted reduction in the overdose deaths rate from 43 per 100,000 in 2008 to 29 per 100,000 in 2010. Additionally, overdose rates in Wilkes county , North Carolina did not increase over this time, while nearly all other

		<i>targeting PD, it is not known what the relative contribution of this approach is for reducing NMUPD.</i>	counties in NC experienced an increase (Albert et al., 2011). The authors were not able to identify the relative contribution of coalition building to the decrease in overdose deaths.
	Community Mobilization	<p>Theoretical Support, Insufficient Evidence</p> <p><i>Community mobilization strategies have been found to be effective for reducing use of other substances, but there is not specific evidence for NMUPD. It is not clear whether the community mobilization strategies studied focused on NMUPD.</i></p>	<p>Previous research has supported the link between community interventions that include a community mobilization component and reductions in substance use outcomes. A long-term randomized controlled trial of the Communities that Care (CTC) model examined outcomes of this model, which seeks to mobilize community stakeholders to collaborate on the development and implementation of a science-based community prevention system. This study was the first randomized trial that examined outcomes 4 years after initial implementation. While there were significant reductions in alcohol, cigarette use by 10th grade within the 14 communities randomized to CTC condition compared to the 14 comparison communities, no significant differences were seen between CTC and comparison communities for prescription drugs misuse, smokeless tobacco, marijuana and, inhalant use by 10th grade (Hawkins et al., 2011). The difference in effects may be due to a greater focus on underage drinking and cigarette smoking strategies, and relatively less focus on illicit drugs, and PD misuse. Ogilvie and colleagues describe a community readiness strategy implemented in 4 Alaskan communities in order to increase community readiness to prevent abuse of inhalants and other harmful legal products, including PD. Each community increased their community readiness according to pre- and post- key informant survey data, although the amount of change was variable across communities. No data was provided to link changes in community readiness to changes in risk and protective factors or consumption patterns of NMUPD in these communities. No comparison communities were utilized (Ogilvie et al., 2008).</p>
Neighborhood quality, disorganization, community attachment, mobility	Altering the physical environment	Theoretical support, insufficient evidence.	<p>Altering the physical environment may include:</p> <ul style="list-style-type: none"> • Boarding up abandoned buildings • Cutting back shrubbery to make drug deals more visible • Installing surveillance cameras in lobbies of apartment buildings with severe drug problems. • Improving lighting in high-crime areas • Altering traffic patterns to make drive-by purchases more difficult. <p>Such measures are relatively easy for communities to implement, and evidence from the broader crime-prevention field has shown that they do deter some forms of crime (as cited in Birkmayer, Fisher, Holder, and Yacoubian, 2008). To date, no peer-reviewed, published research has evaluated the efficacy of such measures on disrupting sales of Prescription drugs. However, it is important to note that according to national and local surveys, the most common method for obtaining PD for nonmedical purposes is through social sources (SAMHSA, 2011), meaning that such public space interventions may not work for reducing NMUPD.</p>
Neighborhood quality,	Increasing Community	Theoretical Support, Insufficient Evidence	No intervention studies were identified in this area over the past 5 years.

disorganization, community attachment, mobility	Connection/Enhanced bonding/socialization	<i>No studies were identified to determine whether strategies designed to enhance community connection and bonding will lead to reduction in NMUPD.</i>	
SCHOOL DOMAIN			
Risk Factor	Related Strategy	Justification for Evidence Level	Supporting Research
Academic Failure/Low Educational Attainment	Academic Skills Enhancement (e.g., tutoring, vocational training, and college prep)	<p>Theoretical Support, Insufficient Evidence</p> <p><i>Academic enhancement is only one component of the CASASTART intervention, therefore it is difficult to determine the relative contribution of academic enhancement to reductions in NMUPD.</i></p>	No intervention studies were identified in this area over the past 5 years. A review of NREPP programs found that CASASTART resulted in greater school promotion after 3 years compared to controls who did not received the intervention. The program also resulted in less NMUPD compared to controls (Harrell, Cavanagh, & Sridharan, 1998).
Low Bonding to School	Enhance Connection and Bonding to School	<p>Theoretical Support, Insufficient Evidence</p> <p><i>No studies were identified to determine whether strategies designed to enhance school bonding will lead to reduction in NMUPD.</i></p>	No intervention studies were identified in this area over the past 5 years.

FAMILY DOMAIN			
Risk Factor	Related Strategy	Justification for Evidence Level	Supporting Research
Poor Parental Monitoring & Supervision/ Low Parental Involvement	Improve parental Monitoring	Evidence of Direct Effects <i>One longitudinal study of a web-based parent-child intervention led to improved parenting outcomes as well as reductions in NMUPD, however the intervention was designed and implemented with adolescent females only.</i>	A web-based prevention program for adolescent girls and their mothers resulted in girls in the intervention reporting more positive outcomes compared to girls in the control condition at a 2 year follow-up for: communication with their mothers, greater closeness to their mothers, more knowledge of family rules about substance use, and greater awareness of parental monitoring of their extracurricular activities. Mothers receiving the web-based program reported better 2-year follow-up outcomes on their observance of family rituals, communication and closeness with their daughters, establishment of family rules against their substance use, monitoring of out-of-home activities, and mothers own weekly alcohol consumption (Schinke, Fang, & Cole, 2008). The intervention condition also reported less NMUPD compared to control group who did not receive the intervention.
	Parent training in clear standard and consistent discipline	Evidence of Direct Effects	See Parental Monitoring.
Disapproval of Substance Use	Parental training/ Intervention aimed at improving clear communication of disapproval of use	Evidence of Direct Effects.	Evidence from a longitudinal, randomized trial of two prevention programs (Iowa Strengthening Families Program (ISFP), Preparing for the Drug Free Years (PFDY)) implemented in 7 th grade targeting parental nurturing/bonding, parent-child communication among other risk and protective factors, found long-term effects on NMUPD (Spoth, Trudeau, Shin, & Redmond, 2008). ISFP condition reported less past year narcotic misuse among 12 th graders and less narcotic and barbiturate misuse among young adults. PDFY reported less prescription drug misuse than controls, but the difference was only marginally significant. A longitudinal control trial of a web-intervention for adolescent girls and their mothers (see parental monitoring) also demonstrated positive outcomes (Schinke et al., 2008).
	Parent and Family training around family management and positive family interaction	Evidence of Direct Effects	See Parental Monitoring.
Parental Substance use	Parent education regarding use, social and personal competence skills, stress management	Evidence of Direct Effects	See Parental Monitoring.

PEER DOMAIN			
Risk Factor	Related Strategy	Justification for Evidence Level	Supporting Research
Peer Norms: Peer Approval of Use	Peer leadership, peer refusal skills, social and personal competence skills	Theoretical Support, Insufficient Evidence <i>Evidence is inconsistent for individually-focused prevention interventions for NMUPD.</i>	While some studies support individually-focused prevention programs designed to improve both social and personal competency skills thought to be important for reducing onset and use of substances among youth (Fang, Schinke, & Cole, 2010; Schinke, Fang, & Cole, 2009; Spoth et al., 2008), other studies have not found specific positive effects of these programs on NMUPD, or risk factors (peer approval of use, number of friends using harmful legal products) (Clark et al., 2010; Gruenewald et al., 2009; Johnson, Shamblen, Ogilvie, Collins, & Saylor, 2009).
Number of Friends who use (PD, other substances)	Peer leadership, peer refusal skills, social and personal competence skills	Theoretical Support, Insufficient Evidence	See Peer Norms.
Normative Misperceptions of Peer Use	Social Norm campaigns	Evidence of Direct Effects. <i>Evidence from other areas of substance use have shown that normative education strategies are effective for reducing rates of use, and one randomized controlled trial of a web-based program for mother and daughters showed reduced in normative misperceptions of NMUPD.</i>	Normative education strategies (e.g., school-based prevention programs) should correct the misperception that NMUPD is normative behavior among youth (Twombly & Holtz, 2008). Schinke (2008) reported significant reduction in normative beliefs regarding peer use among girls receiving a web-based prevention program with their mothers.
Association with Delinquent Peers	Peer leadership, peer refusal skills, social and personal competence skills	Theoretical Support, Insufficient Evidence	See Peer Norms.

INDIVIDUAL DOMAIN			
Risk Factor	Related Strategy	Justification for Evidence Level	Supporting Research
Perception Risk/Harm	Either individual or environmental strategies designed to increase perceived risk/harm of NMUPD, alter norms from belief that PD “safer” alternative to other illicit drugs.	Evidence of Direct Effects <i>A few studies have demonstrated positive effects on perceptions of risk or harm, but these effects may disappear over time.</i>	A combination of individual (e.g., ThinkSmart curriculum) and environmental prevention strategies led to a significant increase in knowledge of the effects and problems associated with use of harmful legal products, including PD, as well as a decrease in perceived availability from baseline to follow-up (Gruenewald et al., 2009). Stay on Track, a school-based NREPP prevention curriculum program designed to reduce substance use by improving youth decision-making, goal-setting, communication and drug-resistance strategies indicated short-term gains in knowledge of risks/harms of substance use including PD following the prevention program, but their gains were not sustained at a 3 year follow-up (Osborne & Ross, 2006).
Personality Characteristics: Sensation Seeking	Personal competence skills	Theoretical Support, Insufficient Evidence	See Peer Norms.
Alcohol or illicit Drug use/abuse/dependence	Personal competence skills	Theoretical Support, Insufficient Evidence	See Peer Norms.
Motivations for Nonmedical Use	Education or environmental strategies to address misperceptions and increase risk associated with nonmedical use	Evidence of Direct Effects	See perception of risk/harm
Mental Health Diagnoses	Personal competence skills	Theoretical Support, Insufficient Evidence	See Peer Norms.
Delinquent/Antisocial Behavior	Mentoring /after-school activities, youth development programs	Theoretical Support, Insufficient Evidence <i>The intervention that was studied was a multi-component intervention and it is difficult to determine the relative contribution of each</i>	Results from a study examining the effects of CASASTART (NREPP program) found significant reductions in violence, delinquent behavior, such as drug trafficking and involvement with delinquent peers compared to the control condition (Harrell, Cavanagh, & Sridharan, 1998), the program also led to less reported NMUPD compared to controls. CASASTART is a multi-component community and school-based substance abuse and violence prevention program aimed at youth ages 8 -13 years of age with a number of identified risk factors for substance use.

		<i>of the components on outcomes (e.g., antisocial behavior, NMUPD).</i>	
Chronic Pain (non-cancer)	Improve Clinical Prescribing practices	Theoretical Support, Insufficient Evidence	See Retail Availability, Interventions aimed at physicians.
Attendance at Religious services	Alternative activities (including volunteering)	Theoretical Support, Insufficient Evidence <i>No studies were identified over the past 5 years that examined the effects of alternative activities, such as engagement in religious activities/programs on rates of NMUPD.</i>	No studies identified over the past 5 years.
Self-Efficacy	Personal Competence Skills	Theoretical Support, Insufficient Evidence	See Peer Norms.

Summary/Overview of Findings

Global Domain	Risk Factor	Related Strategy
Evidence of Direct Effect		
Community	Availability: Retail Access	State-level Prescription Drug Monitoring Programs
Community	Community Norms Favorable for Drug Use	Using Mass media to increase public concern about use and change normative perceptions
Family	Poor Parental Monitoring & Supervision/ Low Parental Involvement	Improve parental Monitoring
Family	Clear disapproval of substance use	Parental training/ Intervention aimed at improving clear communication of disapproval of use
Family	Disapproval of Substance Use	Parent and Family training around family management and positive family interaction
Family	Parental Substance use	Parent education regarding use, social and personal competence skills, stress management
Peer	Normative Misperceptions of Peer Use	Social Norm campaigns
Individual	Perception Risk/Harm	Either individual or environmental strategies designed to increase perceived risk/harm of NMUPD, alter norms from belief that PD “safer” alternative to other illicit drugs.
Individual	Motivations for Nonmedical Use	Education or environmental strategies to address misperceptions and increase risk associated with nonmedical use
Theoretical Support, Insufficient Evidence		
Community	Availability: Social Access	Restrict availability in home through education/ communication strategy
Community	Availability: Retail Access	Change prescriber practices (e.g., education programs aimed at improving appropriate prescribing practices to limit nonmedical use/abuse)
Community	Availability: Retail Access	Reduce Internet Availability
Community	Community Norms Favorable for Drug Use	Use of community coalitions to affect change
		Community Mobilization
Community	Neighborhood quality, disorganization, community attachment, mobility	Increasing Community Connection/ Enhanced bonding/ socialization

Community	Neighborhood quality, disorganization, community attachment, mobility	Altering the physical environment.
School	Academic Failure/Low Educational Attainment	Academic Skills Enhancement (e.g., tutoring, vocational training, and college prep)
School	Low Bonding to School	Enhance Connect and Bonding to School
Peer	Peer Norms: Peer Approval of Use	Peer leadership, peer refusal skills, social and personal competence skills
Peer	Number of Friends who use (PD, other substances)	Peer leadership, peer refusal skills, social and personal competence skills
Peer	Association with Delinquent Peers	Peer leadership, peer refusal skills, social and personal competence skills
Individual	Personality Characteristics: Sensation Seeking	Personal competence skills
Individual	Alcohol or illicit Drug use/abuse/dependence	Personal competence skills
Individual	Mental Health Diagnoses	Personal competence skills
Individual	Delinquent/Antisocial Behavior	Mentoring /after-school activities, youth development programs,
Individual	Chronic Pain (non-cancer)	Improve Clinical Prescribing practices
Individual	Attendance at Religious services	Alternative activities (including volunteering)
Individual	Self-Efficacy	Personal Competence Skills

References

- Albert, S., Brason Ii, F. W., Sanford, C. K., Dasgupta, N., Graham, J., & Lovette, B. (2011). Project Lazarus: Community-Based Overdose Prevention in Rural North Carolina. *Pain Medicine*, 12, S77-S85.
- Baehren, D. F., Marco, C. A., Droz, D. E., Sinha, S., Callan, E. M., & Akpunonu, P. (2010). A Statewide Prescription Monitoring Program Affects Emergency Department Prescribing Behaviors. *Annals of emergency medicine*, 56(1), 19-23.e13.
- Chou, R., Fanciullo, G. J., Fine, P. G., Adler, J. A., Ballantyne, J. C., Davies, P., Donovan, M. I., Fishbain, D. A., Foley, K. M., Fudin, J., Gilson, A. M., Kelter, A., Mauskop, A., O'Connor, P. G., Passik, S. D., Pasternak, G. W., Portenoy, R. K., Rich, B. A., Roberts, R. G., Todd, K. H., & Miaskowski, C. (2009). Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. *The Journal of Pain*, 10(2), 113-130.e122.
- Clark, H. K., Ringwalt, C. L., Hanley, S., Shamblen, S. R., Flewelling, R. L., & Hano, M. C. (2010). Project SUCCESS' effects on the substance use of alternative high school students. *Addictive behaviors*, 35(3), 209-217.
- Cochella, S., & Bateman, K. (2011). Provider Detailing: An Intervention to Decrease Prescription Opioid Deaths in Utah. *Pain Medicine*, 12, S73-S76.
- Fang, L., Schinke, S. P., & Cole, K. C. A. (2010). Preventing Substance Use Among Early Asian-American Adolescent Girls: Initial Evaluation of a Web-based, Mother-Daughter Program. *Journal of Adolescent Health*, 47(5), 529-532.
- Gruenewald, P. J., Johnson, K., Shamblen, S. R., Ogilvie, K. A., & Collins, D. (2009). Reducing adolescent use of harmful legal products: intermediate effects of a community prevention intervention. *Subst Use Misuse*, 44(14), 2080-2098.
- Harrell, A. V., Cavanagh, S., & Sridharan, S. (1998). Impact of the Children at Risk Program: Comprehensive final report II. Washington, DC: The Urban Institute.
- Hawkins, J. D., Oesterle, S., Brown, E. C., Monahan, K. C., Abbott, R. D., Arthur, M. W., & Catalano, R. F. (2011). Sustained Decreases in Risk Exposure and Youth Problem Behaviors After Installation of the Communities That Care Prevention System in a Randomized Trial. *Arch Pediatr Adolesc Med*, archpediatrics.2011.2183.
- Johnson, E. M., Porucznik, C. A., Anderson, J. W., & Rolfs, R. T. (2011). State-Level Strategies for Reducing Prescription Drug Overdose Deaths: Utah's Prescription Safety Program. *Pain Medicine*, 12, S66-S72.
- Johnson, K., Holder, H., Ogilvie, K., Collins, D., Ogilvie, D., Saylor, B., Courser, M., Miller, B., Moore, R., & Saltz, B. (2007). A community prevention intervention to reduce youth from inhaling and ingesting harmful legal products. *J Drug Educ*, 37(3), 227-247.
- Johnson, K., Shamblen, S., Ogilvie, K., Collins, D., & Saylor, B. (2009). Preventing Youths' Use of Inhalants and Other Harmful Legal Products in Frontier Alaskan Communities: A Randomized Trial. *Prevention Science*, 10(4), 298-312.
- Manchikanti, L. (2007). National drug control policy and prescription drug abuse: facts and fallacies. *Pain Physician*, 10(3), 399-424.
- Ogilvie, K. A., Moore, R. S., Ogilvie, D. C., Johnson, K. W., Collins, D. A., & Shamblen, S. R. (2008). Changing community readiness to prevent the abuse of inhalants and other harmful legal products in Alaska. *J Community Health*, 33(4), 248-258.
- Osborne, D., & Ross, D. (2006). The Stay on Track program evaluation. Final report of the longitudinal study: Prepared for the National Center for Prevention and Research Solutions.
- Passik, S. D., Kirsh, K. L., & Casper, D. (2008). Addiction-Related Assessment Tools and Pain Management: Instruments for Screening, Treatment Planning, and Monitoring Compliance. *Pain Medicine*, 9(S2).
- Paulozzi, L. J., Kilbourne, E. M., & Desai, H. A. (2011). Prescription Drug Monitoring Programs and Death Rates from Drug Overdose. *Pain Medicine*, 12(5), 747-754.

- Paulozzi, L. J., Weisler, R. H., & Patkar, A. A. (2011). A national epidemic of unintentional prescription opioid overdose deaths: how physicians can help control it. *J Clin Psychiatry*, 72(5), 589-592.
- PMP Center of Excellence at Brandeis University. (2011). Prescription Monitoring Programs: An Effective Tool in Curbing the Prescription Drug Abuse Epidemic: Bureau of Justice Assistance.
- SAMHSA. (2006). Results from the 2005 National Survey on Drug Use and Health: National Findings *Office of Applied Studies, NSDUH Series H-30, DHHS Publication No. SMA 06-4194*. Rockville, MD.
- Schinke, S. P., Fang, L., & Cole, K. C. (2008). Substance use among early adolescent girls: risk and protective factors. *J Adolesc Health*, 43(2), 191-194.
- Schinke, S. P., Fang, L., & Cole, K. C. (2009). Computer-delivered, parent-involvement intervention to prevent substance use among adolescent girls. *Prev Med*, 49(5), 429-435.
- Spoth, R., Trudeau, L., Shin, C., & Redmond, C. (2008). Long-term effects of universal preventive interventions on prescription drug misuse. *Addiction*, 103(7), 1160-1168.
- Twombly, E. C., & Holtz, K. D. (2008). Teens and the misuse of prescription drugs: evidence-based recommendations to curb a growing societal problem. *J Prim Prev*, 29(6), 503-516.