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Prescription Opioid Policy and Illicit Drug Use

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Prescription Opioid Policy and Illicit Drug Use

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TABLE OF CONTENTS

ABSTRACT

Opioids have become a major public health concern in recent years with non-medical use of both prescription opioids and heroin on the rise. There have been increases in opioid related overdoses, accidental deaths, treatment admissions, and sales associated with the increased illicit use of opioids. The following capstone project uses the three paper model to explore some of the issues associated with this rising epidemic including prescription opioid policies enacted in recent years, the populations these policies impact, and potential effects they may have on drug use behavior, as well as additional factors that potentially influence opioid user behavior. Paper one explores prescription opioid policy and reviews the literature evaluating these policies. Paper two focuses on the non-medical prescription opioid using population and explores how the demographic and drug use characteristics of the population differ across time, specifically the past decade. Finally, paper three examines heroin use in subgroups of prescription opioid users, with the main focus on non-medical OxyContin users compared to other non-medical prescription opioid users across the past decade.

Keywords: Prescription opioids, heroin, opioid policy, prescription drug monitoring programs, abuse-deterrent formulations, illicit drug use

CHAPTER I: OVERVIEW

Opioids have become a major public health concern in recent years. These substances include drugs such as morphine, oxycodone, and heroin.[1–3] Opioids bind to opioid receptors and act on the central nervous system to relieve pain by reducing the intensity of pain signals to the brain.[1–3] They are typically used and prescribed in medical settings for the relief of pain. Additional effects of opioids may include euphoria, sedation, respiratory depression, and nausea, among others.[2]

Over the past few decades, non-medical use of both prescription opioids and heroin has been on the rise in the U.S.[4–6] Parallel to this have been increases in opioid related overdose, accidental death, treatment admissions, and prescription opioid sales.[7–10] Additionally, several policies and programs have been developed and implemented to address the growing problem, including prescription drug monitoring programs and abuse-deterrent formulations of prescription opioids.[11–16] These programs have been shown to alter drug use behavior among the prescription opioid using population.[17–22]

The following capstone project uses the three paper model to explore some of these policies in detail, the populations they impact, and potential effects they may have on drug use behavior, as well as additional factors that potentially influence opioid user behavior.

In the first paper, I explore two types of policies that target access to and the abuse potential of prescription opioids: a) prescription drug monitoring programs and b) abuse-deterrent formulations. In this paper, I explore the characteristics of these intervention efforts, research that has been conducted to evaluate them, and make recommendations for future evaluation research. The aim of the study is to provide a background of what research has been

conducted to examine how these policies have impacted the non-medical prescription opioid using population and areas where further research may prove useful.

The second paper focuses on the non-medical prescription opioid using population. Here, I explore how the demographic and drug use characteristics of the population differ across time, specifically in the past decade. The aim of this study is to investigate how the non-medical prescription opioid using population has changed across demographic and drug use characteristics given the substantial increase in prescription opioid policy. The goal is to make inferences about the source of these changes and what additional research may help elucidate the issue.

Finally, in paper three, I examine a subgroup of prescription opioid users, non-medical OxyContin users, and compare them to other non-medical prescription opioid users. I investigate heroin use in this population and how it has differed over the same time period used in the second paper, comparing the differences over time. The aim in this study is to determine if the changes in heroin use over time in the OxyContin using population are more pronounced at any certain point in time and if those differences appear to be larger when compared to the other groups. Additionally, the paper aims to describe the demographic and drug use characteristics of the OxyContin using population.

Further justification for each of the papers can be found in the introduction section of each. In addition to the three papers, a final chapter discusses the three papers and capstone as a whole in terms of public health and policy implications and future directions for research. Finally, references, tables, figures, and appendices for all papers are included in a single respective section for each, as indicated in the table of contents; these sections are not organized by paper in this document.

CHAPTER II: PAPER 1

TITLE: A review of policies targeting illicit access to and non-medical use of prescription opioids

INTRODUCTION

The U.S. has been facing a growing prescription opioid epidemic in recent decades. Estimates from the Substance Abuse and Mental Health Services Administration (SAMHSA)* show that in 2013 there were approximately 4.5 million current non-medical prescription pain reliever (NMPR) users, which represented 1.7% of the U.S. population.[23] Additionally, between 1999 and 2008, sales of prescription drugs and related overdose death rates quadrupled.[24] During this time, treatment admissions for prescription drugs grew by nearly 500%, the majority of which were for opioid prescription drugs.[24]

Several studies indicate that prescription opioids may function as "gateway" drugs to heroin use.[25–27] The most commonly abused prescription drugs are opioids, such as hydrocodone (Vicodin) and oxycodone (OxyContin).[1] Given the similar euphoric and other effects that heroin and prescription opioids share, users may turn to heroin when faced with reduced access and rising costs of prescription opioids.[28]

NMPR use frequently precedes heroin initiation; one study found that four out of five recent heroin initiates between 2002 and 2011 reported having used NMPRs before heroin.[29] In the same study, only 1% of recent NMPR initiates reported having ever used heroin.[29] Another study found that early NMPR use in childhood was a significant predictor of heroin initiation in

* See APPENDIX A for full acronym guide

young adulthood.[30] A qualitative study conducted in Philadelphia and San Francisco found that the most commonly reported reasons for transitioning from prescription opioids to heroin were cost and ease-of-access to supply after becoming dependent on prescription opioids.[26] Another study found an association between past year NMPR use and past year heroin use, but did not include consideration of each group's NMPR or heroin use history.[31] One study of NMPR users found that those at greatest risk of recent heroin initiation between 2002 and 2011 lived in metropolitan areas (84.6%), identified as non-Hispanic white (74.0%), and had household incomes less than $50,000 per year (56.5%).[29]

Many efforts have been made to curb the increased access to and non-medical use of prescription drugs, including development of prescription drug monitoring programs by many states and development of abuse-deterring formulations by pharmaceutical companies.[11–16] Some of these interventions, especially the introduction of abuse-deterring formulations of highly abused prescription opioids, have been successful in reducing prescription opioid misuse and overdose rates.[17–22] However, there are potential externalities that may occur when these large scale policies are implemented that were not considered during development of the policies.

Studies evaluating the impact of prescription opioid misuse policies on drug use behavior are essential in order to improve future approaches. However, it is important to first identify what research has already been conducted in order to expand on the existing literature and to identify areas where there is need for further understanding. This article focuses on two major types of policies that have been implemented in recent years across the U.S. to reduce access to and misuse of prescription opioids: a) development of prescription monitoring programs; and b) development of abuse-deterrent formulations of prescription opioids. An overview of each policy

is provided, along with previous research evaluating the impact of these policies, and finally recommendations for future research.

PRESCRIPTION DRUG MONITORING PROGRAMS

Prescription drug monitoring programs (PDMPs) have been implemented across the U.S. at the state-level and are designed to allow health care providers and others to prevent doctor shopping, diversion and drug misuse by providing information on individuals' prescription histories.[32,33] The Harold Rogers Prescription Drug Monitoring Program and the National All Schedule Prescription Electronic Reporting Act of 2005 (NASPER) were designed to facilitate the development of PDMPs by state governments and the number of PDMPs has since increased significantly.[28,33–35]

Characteristics of PDMPs

To date, 49 states have some form of an operational PDMP in place, with Missouri being the only state without an operational PDMP.[33] The characteristics of PDMPs can vary significantly from state to state. For instance, not all prescription drugs are monitored by states in the same way. The U.S. Drug Enforcement Agency (DEA) categorizes drugs into schedules ranging from I to V.[11] Schedule I drugs are illegal and defined as "drugs with no currently accepted medical use and a high potential for abuse".[36] Schedules II through V are drugs that can be prescribed legally in the U.S.[11] Drugs are categorized into one of these schedules based on their potential for abuse, with schedule I substances having the greatest potential and schedule V the least.[36] All state PDMPs monitor schedule II through IV substances, with thirty six also monitoring schedule V substances.[33]

The administering agency also varies across state PDMPs.[37] The most common administering agencies are boards of pharmacy and departments of health, which do so in 20 and 13 states, respectively.[37] Other administering agencies include professional licensing (6 states), law enforcement (7 states) and substance abuse agencies (3 states).[37]

States also vary in which types of agencies and individuals have access to the information within their respective PDMP. Most states provide access to their PDMP information for health care practitioners and pharmacists, as these are the gate keepers to prescription drug access for the general population.[37] Some states, however, also allow agencies such as law enforcement, licensing and regulatory boards, Medicaid programs, research organizations, and medical examiners to access their PDMP data.[37] The purpose of allowing law enforcement access is so they can use the information for criminal investigations of either patients or practitioners engaging in illegal or suspicious activity. Similarly, giving licensing and regulatory boards and Medicaid programs access to the data allows them to monitor and investigate health care practitioners who prescribe drugs monitored by the PDMP. Research organizations can use the information to investigate prescription drug trends and research other important topics associated with PDMPs, while state medical examiners can use the information to help in investigation of cause of death in suspicious cases. Involving additional agencies helps to broaden the scope of access to PDMP data and may increase the effectiveness and utility of PDMP programs. However, this benefit must be weighted and balanced with the protection and security of patient privacy and records.

Another important characteristic of PDMPs is the frequency of data collection. The frequency at which data are reported and entered into the PDMP database can range from daily to monthly.[37] Daily frequencies are ideal as they allow practitioners and others using the systems

to obtain up-to-date information on their patients and thus are likely the most effective in preventing illegal and harmful activities and behavior like doctor shopping. Monthly reporting, on the other hand, may result in a time gap in obtaining patient prescription behavior during which individuals may be able to circumvent the system.

An important factor in regard to promotion of PDMP effectiveness is prescriber and dispenser mandates for registration/enrollment with their state's PDMP and use of PDMP data when appropriate. Mandating registration and use promotes increased participation and in turn reduces opportunity for abuse of the system by both practitioners and patients. To date, 25 states have legislation in place that mandates registration by health care practitioners prescribing monitored drugs and/or dispensers with their PDMP.[38] Twenty eight states have mandates requiring queries into PDMPs by prescribers and dispensers when monitored substances are being provided to patients.[38]

A relatively new outcome of PDMPs is interstate information sharing.[37] Given that PDMPs are operated on a state-by-state basis, doctor shopping and other illegal activities may be more easily conducted in border regions between states. Having data sharing agreements can aid in preventing cross-border activity. As of March 2016, thirty fives state PDMP programs were engaged in some form of interstate data sharing, while nine were in the process of implementing plans for interstate data sharing.[37]

Evaluation and Impact of PDMPs

There have been several evaluations of PDMPs showing an association with improved outcomes related to prescription drug use.[28,34,39–45] Studies have found that PDMPs were related to slowed growth in the supply of prescription drugs to consumers; decreased prescription-drug-

related treatment rates, prescription rates and poison center calls; and reduced prescription drug-related costs, such as medical claims and workers' compensation.[28,34,39–45]

A study conducted in 2006 by Simeone Associates, Inc., a public policy consulting firm, evaluated the impact PDMPs have had on supply of prescription drugs and misuse.[28] The study used the Automation of Reports and Consolidated Orders System (ARCOS) to estimate the supply of schedule II controlled substances. They also used the Treatment Episode Data Set (TEDS) as a proxy to estimate prescription drug misuse.[28] Additionally, they factored in program characteristics in the analysis, for example the "proactivity" of the PDMP. Proactive was defined in the study as a state having a PDMP in place that generates unsolicited reports when they are determined to be warranted.[28] The authors found that states with PDMPs in place had reductions in the per capita supply of prescription pain relievers and stimulants over time, after implementation of the PDMP.[28] They also found that admissions rates to substance abuse treatment facilities for each type of drug were positively associated with supply.[28] The analysis also indicated that states with "proactive" PDMPs, as defined by the authors, may be reducing the supply of prescription drugs, specifically prescription pain relievers and stimulants, at a greater rate than those states that have "non-proactive" PDMPs.[28]

The findings of the study are useful as they indicate that PDMPs do have an effect on supply of prescription drugs and, in turn, treatment admission rates for prescription pain relievers and stimulants. However, admissions represent only a fraction of the prescription drug abusing population and thus may not give an accurate representation of what is occurring in the entire population. Other data sets, such as the National Survey on Drug Use and Health (NSDUH), which measures substance use behavior in the United States annually, could be used in similar analyses to estimate the effect of supply of prescription drugs on drug use behavior.[46]

In 2006, an article published in *Health Services Research* investigated geographic variation in opioid use in various patient populations nationally.[40] They used an outpatient prescription claims database to determine the prevalence of opioid prescriptions among the sample.[40] They aggregated data at both the state and county level.[40] The authors investigated a range of explanatory factors, one of which was presence of a prescription drug monitoring program.[40] In the study, one model showed a negative association between presence of a prescription monitoring program and claims rates for controlled-release oxycodone.[40]

The findings indicate that PDMPs may reduce the number of prescriptions of controlled-release oxycodone. Although this finding can't be generalized to all prescription drugs, the indication does warrant further investigation into other prescription drugs. However, the study did not find the same results in two additional models which included other explanatory variables, thus the results must be taken with caution.

A study from 2009 looked at the association between state shipments of prescription opioids and prescription opioid treatment admission rates, and the impact of PDMPs on prescription opioid treatment admission rates.[44] The authors found that increases in state shipments of prescription opioids were associated with increased treatment admissions.[44] They also found that states with PDMPs had lower shipment rates and slower increases in prescription opioid admissions over the study period compared to those without.[44] This study is another example of research indicating reduced access to prescription drugs associated with PDMPs.

A 2010 evaluation of the Kentucky All Schedule Prescription Electronic Reporting System (KASPER), which is Kentucky's PDMP, investigated opinions by program utilizers on the effectiveness of KASPER.[34] The study focused on pharmacists, prescribers and law enforcement agents as these were viewed as the "key user groups".[34] Surveys were given in two

formats: mailed survey packets and online surveys.[34] Pharmacists and prescribers were given the choice between the two methods, although law enforcement agents were only presented with the online survey option.[34] The authors found that more than 90% of pharmacists, prescribers and law enforcement agents perceived KASPER as effective in preventing drug abuse and diversion, and reducing doctor shopping.[34] The study also found that substance abuse admission rates for prescription opioid abuse have risen significantly in the years after the KASPER system was established.[34]

The study is beneficial in providing insight into the effects that KASPER is having on the prescription drug epidemic in the Commonwealth. The system appears to be perceived as effective by stakeholders and the study shows an increase in admissions rates for prescription opioids, which may indicate that at least some drug misusers are turning toward treatment for their addiction as access to prescription drugs is reduced. For future research, it may be beneficial to investigate access to substance abuse treatment and if the state is meeting the new demand that may be driven by the KASPER system. Additionally, it may be helpful to monitor the success of prescription drug addiction treatment and what recovering substance abusers do after treatment. Following these individuals overtime may give insight as to the characteristics that promote successful treatment outcomes, which programs work best, and what types of drugs these individuals use when/if they relapse.

A 2012 study evaluated state trends in opioid abuse associated with PDMPs.[43] The study used a prescription drug abuse surveillance system known as RADARS (Researched, Abuse, Diversion and Addiction-Related Surveillance) to determine opioid abuse across states between 2003 and 2009. States were grouped into three categories: (a) PDMP in place during the entire study period; (b) No PDMP in place during the entire study period; and (c) PDMP became

operational during the study period.[43] The findings of the study indicated that PDMPs were associated with a reduction in growth rates of opioid abuse and misuse over time.[43] This was true for both the general population and the population seeking treatment for substance abuse (analyses were conducted for each).[43]

The study provided important insight in that PDMPs appear to be associated with change in behavior. They were shown to be associated with reductions in opioid abuse and misuse. It should be cautioned when interpreting the results that these findings are only for abuse and misuse of prescription opioids. They do not consider factors such as shifts in drug use and misuse to other substances that are not monitored by PDMPs. Research investigating the overall changes in drug abuse and misuse associated with PDMPs for all drug categories may give a better picture of what is actually occurring in states post PDMP implementation in terms of overall drug abuse and misuse.

Recommendations for Future Evaluations

Although the above studies provide great insight into the effectiveness of PDMPs, there are several areas of research that have not been investigated that could prove very important in terms of understanding the effects of these programs on substance use and related outcomes. First, programs vary significantly in terms of frequency of data collection, mandate, authorized users, and other factors described in the previous characteristics section of this paper. None of the national studies take all or often any of these factors into account in their analyses. Understanding which characteristics of PDMPs are associated with the greatest positive impact on relevant outcomes is important in moving forward and establishing these systems nationally.

This will allow states with weaker PDMPs to model after other states with better PDMP models and in turn put in place the most effective system possible.

Another interesting area of research that has not received much attention is regional variation in the impact of PDMPs within a state. Certain regional characteristics such as proximity to state borders, rural vs. urban settings, etc. may play a role in how effective PDMPs are and may be worth investigation. It may be that individuals who are closer in proximity to state borders are more easily able to circumvent their state's PDMP by going to practitioners in neighboring states.

It may also be beneficial for future evaluations of PDMPs to consider the impact they may have on illicit substance use, such as heroin and cocaine. The most commonly abused prescription drugs are opioids, such as hydrocodone (Vicodin) and oxycodone (OxyContin).[1] Given the similar euphoric and other effects that heroin and prescription opioids share, addicts may turn to heroin due to a reduction in access to prescription opioids associated with implementation of PDMPs.[28] Heroin is an illicit substance and thus obtained in forms that are unregulated, may contain toxic contaminants, and vary in purity or concentration.[3,47] The shift from prescription opiates to heroin could result in worse health outcomes and other costs to the drug abusing population and society as a whole. Additionally, ignoring these effects may lead to evaluations that overestimate the benefit of PDMPs and fail to address the need for concurrent programs that prevent drug abuse shift from prescription to illicit substances. Future evaluations should be conducted to determine these effects and incorporate them into the evaluations of PDMPs with recommendations for policies that may help avert this shift.

Finally, many of the studies evaluating PDMPs used the TEDS data set for their analyses, likely because the state level data are public and easily accessed for this data set. It would be

interesting, however, if other data sets were used to attempt to understand the impact that PDMPs have on prescription-related overdoses, mortality, and crime rates. The topic area is currently relevant and additional national studies need to be conducted to determine the full effect of these programs. Research in this topic area will not only help understand the policy implications of PDMPs, but also under what circumstances and implementation strategies PDMPs are most effective.

ABUSE-DETERRENT FORMULATIONS

Abuse-deterrent formulations of prescription opioids are designed to deter potential abusers from consuming these medications in ways unintended by the manufacturer. Many abusers of prescription opioids prefer to use non-oral routes, such as inhalation, smoking and injection, to consume prescription opioids because this allows for faster and more intense onset of euphoria and other desired effects.[14,48] Therefore, abuse-deterrent formulations typically attempt to make it more difficult for abusers to effectively use the drug in non-oral routes and achieve the desired effects. There are two main approaches to abuse-deterrent formulation used in prescription opioids currently on the market. These are a) opioid agonist/antagonist combinations and b) formulations with agents that make crushing and dissolving more difficult.[49,50]

Characteristics of Abuse-Deterrent Formulations

Development of formulations of prescription opioids that also contain opioid antagonists work to prevent abuse by blocking the euphoric effects of the drugs when used in ways other than those intended by the manufacturer.[51] Opioid agonists are drugs that bind to opioid

receptors in the brain and activate them, resulting in the pain relieving and other effects that are felt when these drugs are taken[51]. Opioid antagonists bind to the same receptors as opioid agonists, however, they do not activate the receptors and typically block opioid agonists from binding.[51] Manufacturers of this type of abuse-deterrent formulation design the drugs so that the antagonist is only absorbed into the users systems if the drug is tampered with, such as being crushed, chewed, or dissolved. When tampered with, the antagonist is absorbed into the users system and blocks the positive effects of the agonist. Conversely, if the drug is taken properly the agonist is absorbed and the antagonist passes through the users system with no or minimal absorption, allowing the agonist to operate as intended. Examples of prescription opioid using this type of abuse-deterrent formulation that are currently on the market include: Targiniq ER, a formulation of extended-release oxycodone and the opioid antagonist naloxone; and Embeda, an extended-release morphine that contains the opioid antagonist naltrexone.[50,52]

The other method of abuse-deterrent formulation currently used in the market is formulations with agents that make crushing and dissolving more difficult. Typically, these formulations contain agents that make it more difficult to crush the drug into powder for snorting or smoking, and when crushed and/or dissolved creates a viscous gel that is difficult to inject. Examples of this type of abuse-deterrent formulation are OxyContin ER (extended-release oxycodone), Hysingla ER (extended-release hydrocodone), and Zohydro ER (extended-release hydrocodone).

Evaluation and Impact of Abuse-Deterrent Formulations

Although all new drugs marketed as abuse-deterrent formulations are required to conduct research on the association between the new formulation and clinical outcomes associated with

abuse, these formulations are relatively new and therefore fewer studies have been published that evaluate their impact on drug use behavior.[50,52] One abuse-deterrent formulation that is of particular interest due to high abuse potential and the significant body of literature examining it relative to other abuse-deterrent formulations is the reformulation of extended-release OxyContin (ER-OC) introduced in August 2010.[15,17] Due to the significant amount of literature associated with the introduction of this abuse-deterrent formulation and the lack of literature available for other abuse-deterrent formulations, this section focuses on the introduction of this specific abuse-deterrent formulation.

OxyContin was introduced into the U.S. market in 1996 and was aggressively marketed and promoted for use in treating moderate to severe pain.[53–55] Sales of OxyContin grew quickly and by 2004 OxyContin had become the most abused prescription drug in the U.S.[54,56] Abuse by non-oral routes, such as snorting, smoking and injecting, is common among OxyContin abusers.[57–59]

The introduction of the abuse-deterrent form of ER-OC, which made use of the drug by non-oral routes more difficult, has been shown to be successful in reducing abuse of ER-OC.[19–22] One study found that within two years of the introduction of reformulated ER-OC, non-oral abuse decreased by 66% and oral abuse decreased by 41% among individuals assessed for substance abuse treatment.[21] Another study found that reported fatalities involving ER-OC decreased by 82% within three years of the introduction of reformulated ER-OC.[22] A study of OxyContin users in a rural county in Kentucky found that prevalence of abuse of reformulated ER-OC was significantly lower than that of the original formulation of ER-OC (33% vs. 74%).[19] Finally, a poison control centers study found that reports of ER-OC abuse exposures decreased by 32% after the introduction of reformulated ER-OC.[20]

These studies indicate that it is likely, at least for ER-OC, that the introduction of abuse-deterrent formulations can have the desired effect of deterring abuse of the specific prescription opioids in question. However, the narrow focus of these studies also leaves the question of whether users are actually reducing overall abuse of prescription opioids or shifting their use to alternative substances.

A few studies have investigated whether the introduction of reformulated ER-OC has been associated with increases in abuse of other opioids such as heroin and buprenorphine among OxyContin users. One study showed that since the introduction of reformulated OxyContin, the level of reported heroin exposures to poison centers increased by 37% by 2012, while ER-OC exposures decreased by 26%.[17] Another study of opioid users entering substance abuse treatment found that reporting OxyContin as the primary drug of abuse decreased from 35.6% before the introduction of reformulated ER-OC to 12.8% after, while past 30 day heroin use to get high doubled during the same study period.[18] Additionally, a study of opioid users entering substance abuse treatment showed a significant reduction in past month OxyContin abuse after the introduction of ER-OC (45% to 26%), while past month use of heroin rose from less than 30% to 50% during the study period.[12] Finally, a time-series analysis of patients presenting for treatment found significant increases in abuse of buprenorphine after introduction of reformulated ER-OC.[60]

These studies indicate that there may be some shift occurring when abuse-deterrent formulations are introduced into the market. However, they generally focus on a subset of the prescription opioid-using population. Most of these studies take advantage of substance abuse treatment data, which likely does not give a depiction of the impact of abuse-deterrent

formulations on the prescription opioid using population as whole, as only a small portion of opioid users actually seek treatment.

Recommendations for Future Evaluations

Few studies have evaluated the impact of abuse-deterrent formulations on drug use behavior other than examining the impact these policies have on abuse of the specific prescription opioid targeted by each new formulation. There is still debate as to whether or not the introduction of various abuse-deterrent formulations, such as ER-OC, actually result in shifts to other opioids, particularly heroin.[61] A recent study comparing past year users of heroin and/or prescription painkillers found that heroin users were more likely to be involved in criminal activity, have poorer mental and physical health, and were less economically stable.[27] This implies that if shifting from prescription opioids to heroin or increasing the frequency of heroin use among opioid users is occurring, this may result in negative health and other consequences on users. Examining the population of non-medical prescription opioid users over time would prove beneficial to understand how the population changes after the introduction of these formulations.

Additionally, previous studies have focused on opioid users entering or being evaluated for treatment, which only represents a small proportion of opioid users.[62] No studies have used a nationally representative sample to evaluate the impact of introducing abuse-deterrent formulations on prescription opioid users in terms of shifts in patterns of opioid use other than the targeted prescription opioid. Future research should take a broad approach and consider patterns of use of multiple types of opioids and other commonly abused substances in the

prescription opioid-using population before and after introduction of abuse-deterrent formulations.

CONCLUSION

The need for further understanding of the prescription opioid population is abundantly clear. This population is difficult to follow over time and the current atmosphere of introducing many different policies to avert the prescription opioid epidemic makes determining how these policies impact overall opioid use difficult. Efforts to curb prescription opioid use such as development of PDMPs and abuse-deterrent formulations are likely influencing drug use behavior in prescription opioid users beyond just how they use prescription opioids. Narrowing down a change in a population and associating it with a single specific policy is difficult. However, even if this cannot be achieved, it may still be beneficial to study the patterns of substance use among prescription opioid users since the beginning of the increased introduction of these types of policies in order to better understand the drug use patterns in this population and how they have changed during this time period.

CHAPTER III: PAPER 2

TITLE: Changes in Demographic Characteristics and Drug Use among Non-Medical Prescription Opioid Users, 2005-2014

INTRODUCTION

Use of prescription opioids for non-medical purposes has become a major problem in the U.S in recent decades.[4–7] Between 1999 and 2007, the number of opioid analgesic associated unintentional overdose deaths rose from less than 4,000 to nearly 12,000 annual deaths, while during the same time period treatment admissions for prescription opioids nearly quadrupled.[7,8] Drug overdose deaths are now the number one cause of accidental death in the U.S., with 40% of all accidental deaths being a result of prescription opioid use.[9]

The growth in the problem of nonmedical use of prescription opioids is, at least in part, a result of the rise in the number of prescriptions for opioids that occurred in the 1990s and early 2000s.[7,63,64] In response to the growing epidemic, several intervention efforts have been developed to prevent overprescribing and decrease access to and/or the potential abuse of prescription drugs. One intervention is the development of prescription drug monitoring programs (PDMPs). These programs monitor prescribing behaviors of doctors and patients and are designed and implemented at the state level.[13,33] PDMPs help health care professions and monitoring organizations prevent doctor shopping, overprescribing, diversion and drug abuse.[13,33] Several studies have shown PDMPs to be associated with improved prescription drug use outcomes, including slowed growth in prescription drug supply, and decreased treatment rates, prescription rates and poison center calls.[28,34,39–45] Since 2000, the number of states with

PDMPs has increase substantially and currently all but one state has some form of PDMP in place.[33]

Another important effort in the prevention of non-medical use of prescription opioids has been the development of abuse-deterrent formulations of prescription drugs. Many non-medical users of prescription opioids consume the drugs using non-oral routes, such as inhalation, smoking and injection.[14,48] Abuse-deterrent formulations are designed to make non-oral use of prescription drugs more difficult.[14,48] Typical methods include: a) combining an opioid antagonist with the prescription opioid that only activates when efforts to use the drug non-orally are made; and b) formulations with agents that make crushing and dissolving the drug more difficult.[48,50–52] These formulations have become very common in the past five to ten years and examples include extended-release (ER) OxyContin, Hysingla ER, Zohydro ER, Targiniq ER, and Embeda.[48,50–52] Many of these drugs are relatively new and substantial research evaluating their impact on prescription drug use does not exist for most.

One reformulation that has been studied extensively is ER OxyContin. Studies have associated the introduction of ER OxyContin with significant decreases in both non-oral and oral misuse of the drug and decreases in reported fatalities.[19–22] Several studies have also indicated that the introduction of the formulation may be associated with increases in use of other drugs, in particular heroin.[12,17,18,60]

In addition to the growing problem of non-medical prescription opioid use, the past decade or so has seen increases in heroin access and use. The Substance Abuse and Mental Health Services Administration (SAMHSA) estimates that the number of individuals using heroin in the past 12 months nearly doubled between 2007 and 2013, while heroin dependence more than doubled in the same time frame.[65] Increases in perceived ease of availability of heroin

were also shown among heroin users in the same study.[65] Other studies have also indicated that the concentration of heroin in the U.S. illicit market has been on the rise and prices of heroin on the decline in recent years.[66,67]

The combination of increased prescription opioid related policy and availability of illicit substance alternatives, especially heroin, may have had an influence on the prescription opioid using population in terms of demographic makeup and drug use behavior, as the policies create barriers to access to prescription opioids and access to heroin provides a viable alternative. Certain populations may be more or less likely to continue prescription opioid use when faced with policies that reduce access to them. Additionally, some users may begin using other drug alternatives, such as heroin, to compensate for the reduced access to prescription opioids. This means that the demographic composition and drug use patterns of the prescription opioid using population may be very different now than they were a decade ago.

Recent studies of the prescription opioid population have shown increases in prescription opioid use disorder, frequency of prescription opioid use, drug overdose deaths, and increased heroin use in recent years.[6,68,69] However, no studies to the authors' knowledge have investigated the non-medical prescription opioid using population in terms of changes in a variety of demographic characteristics and alternative drug use, over the past decade. Increased heroin use in recent years has been indicated in some previous studies.[31,69] However, other potential substitute substances, such as cocaine and alcohol, have not been examined across time. It may be beneficial to understand how the demographic characteristics and drug use behavior differ in recent years in order to better understand the target population for interventions and policies targeting non-medical users of prescription opioids. Examining these factors may also

inform and give insight into the potential influence current opioid policies have on the prescription opioid using population and areas where further research may be needed.

In order to better understand the prescription opioid using population and how it has changed in recent years, this study aims to: a) describe the demographic characteristics and use of various categories of drugs among prescription opioid users; and b) compare these differences from year-to-year over the past decade.

METHODS

Data

Data on substance use were obtained from the National Survey on Drug Use and Health (NSDUH) public use files for years 2005 through 2014. The NSDUH is an annual survey conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA).[70] The survey can be used to estimate drug use and mental health status at both the national and state level. The survey involves approximately 70,000 in-person, computer assisted interviews with a random sample of the civilian, non-institutionalized population of the U.S. that is 12 years of age or older. The overall response rate for each year included in the study was between 70% and 80%.

Each public use file contains data for a single year of survey data. Public use files were grouped in two year intervals for ease of comparison of data from different time periods, as the goal of the study was to identify trends in demographic and drug use over time in the non-medical opioid using population. The combinations were: 2005-2006, 2007-2008, 2009-2010, 2011-2012, and 2013-2014.

Non-medical pain reliever (NMPR) is the term used in the NSDUH to refer to prescription opioids, as well as a few prescription drugs used to treat pain symptoms that do not act on the same receptors as opioids. However, the vast majority of those reporting NMPR use reported opioid NMPR use. In a previous study using the NSDUH it was shown that those reporting only non-opioid NMPR use represented n=36 across six years of survey data (2002-2004 and 2008-2010) which represented a little more than 0.001% of the total sample of NMPR users.[31] For this reason, the NMPR population is considered in this study to represent the non-medical prescription opioid using population.

Inclusion Criteria

The NSDUH collects data on past 12 month use of various substances, including NMPR use. In order to be included in the analysis the respondent must have reported using NMPRs within the past 12 months. Further explanation of how this variable was calculated is provided below under the variables section. The final total sample size was 39,090, with year group sample sizes of 8,620 (2005-2006), 8,551 (2007-2008), 8,415 (2009-2010), 7,633 (2011-2012), and 5,871 (2013-2014).

Variables

Demographic variables compared across the years of survey data included metropolitan status, race/ethnicity (white non-Hispanic, black non-Hispanic, Hispanic of any race, and other), education, income, sex, age, health insurance (any health insurance vs. none), and marital status (currently married or living as married vs. single). Metropolitan status was defined in the NSDUH using the Office of Management and Budget (OMB) definitions.[71] Education was

grouped by highest achievement with categories including: less than high school, high school, some college, and a category for 12-17 year olds, as they likely would not have had the opportunity to obtain any education other than less than high school.

Variables describing past 12 month drug use of a variety of drug types were included in the study. These included: non-medical pain relievers, non-medical OxyContin, heroin, alcohol, cocaine, crack, stimulants, marijuana, sedatives, hallucinogens, and inhalants. The NSDUH asked respondents to choose the easiest way to describe the total number of days they used each substance in the past 12 months and gave them the options of days per week, days per month, or days per year. The survey included a variable for each substance which was created from the responses to these questions and defined the total number of days in the past 12 months the substance was used. These created variables were used to create a new variable that categorized the past 12 month use of each substance into four categories: none, 1-29 days, 30-89 days, and 90+ days. A variable for injection drug use, defined as ever injecting any drug, was also included in the analysis.

Analysis

Demographic and drug use variables were compared across year groupings. Chi-square was used to test for differences in each variable, with weighted percentage distributions and standard errors reported. Each year group was compared to the year group immediately preceding it, i.e. 2013-2014 vs. 2011-2012, and to the first year group in the study, i.e. 2005-2006. All analyses were conducted using SAS 9.4. In order to adjust for the multi-stage complex survey design of the NSDUH, survey commands were used (PROC SURVEYFREQ) to allow strata, cluster and weight variables to be included in the analysis, providing appropriately

weighted estimates. Additionally, the DOMAIN statement was used to identify and account for the NMPR subpopulation within the NSDUH.

RESULTS

Table 1 describes the demographic characteristics of past 12 month non-medical pain reliever (NMPR) users. Both the 2011-2012 and the 2013-2014 year groups differed significantly at the $\alpha = 0.05$ level from the 2005-2006 year group, with both appearing to have a smaller proportion of white non-Hispanics and greater proportions of the other race/ethnicity categories than the 2005-2006 year group. Additionally, the 2011-2012 year group differed significantly from the 2009-2010 year group in race/ethnicity, similarly with a smaller proportion of white non-Hispanics and a greater proportion of all other race/ethnicity categories. **Figure 1** further describes these differences by showing the percentage of the population reporting any race/ethnicity other than white non-Hispanic. In this graph, a possible trend appears across year groups with the proportion of those reporting any race/ethnicity other than white non-Hispanic increasing with time (26.8% in 2005-2006 and 34.9% in 2013-2014).

Table 1 also shows a statistically significant difference in age for all year groups when compared to 2005-2006. **Figure 2** further portrays this difference, with a pattern of older individuals representing a greater proportion of the NMPR using population in later years (the 50+ age group represented 9.8% in 2005-2006 and 17.6% in 2013-2014). It also appears that there may be a pattern in the education variable with those with any college making up a greater percentage of the population in later years (39.8% in 2005-2006 vs. 46.4% in 2013-2014).

Table 2 describes past 12 month drug use for several categories of drugs among NMPR users. Significant differences were found in the number of days of NMPR use in the past 12

months, with the percentage of the population using for 30-89 days or 90+ days appearing to be greater in both the 2011-2012 (19.7% and 18.1%, respectively) and 2013-2014 (20.9% and 19.8%, respectively) groups when compared to the 2005-2006 group (18.8% and 15.2%, respectively). These differences are shown graphically in **Figure 3**.

OxyContin use also appeared to have significant differences among some year groups, with 2009-2010, 2011-2012, and 2013-2014 year groups all differing significantly from the 2005-2006 year group. **Figure 4** shows graphically the percentage of NMPR users using OxyContin one or more days in the past 12 months. The figure shows an initial increase from 10.5% in the 2005-2006 year group to a peak in the 2009-2010 year group of 14.5% and then a decline in the following year groups to 12.3% in the 2013-2014 year group.

Several other drugs were also shown to have significant differences among at least some year groups. Two noticeable patterns appear among these drugs. First, heroin use is significantly more common among NMPR users in the 2009-2010, 2011-2012, and 2013-2014 year groups (3.7%, 4.0%, and 5.4%, respectively) when compared to the 2005-2006 (2.5%). **Figure 5** shows this pattern further. Although the majority of NMPR users still do not appear to use heroin, the difference between 2.5% in 2005-2006 and 5.4% in 2013-2014 is more than a two-fold increase in the proportion using heroin. A similar pattern appears with marijuana use, although to a lesser degree, with 2009-2010, 2011-2012, and 2013-2014 year groups all showing greater percentages of the population using marijuana (51.2%, 51.2%, and 50.7%, respectively) when compared to 2005-2006 (48.4%).

The second distinguishable pattern is that the percentage of NMPR users also using cocaine and/or crack appears to be smaller in all later year groups when compared to the 2005-2006 year group. **Figure 6** shows the trend in cocaine use among NMPR users. A steep drop

appears between 2005-2006 and 2009-2010, with any cocaine use in the past 12 months dropping from 20.2% to 16.0%. It appears that after this point the percentages stay similar in subsequent year groups, with 15.1% in 2011-2012 and 16.0% in 2013-2014. Finally, the percentage of NMPR users ever injecting drugs in the 2011-2012 and 2013-2014 year groups (8.8% and 9.4%, respectively) were significantly greater than the 2005-2006 group (6.9%). **Figure 7** further shows this pattern.

DISCUSSION

The results of the study indicate that when comparing the population of non-medical pain reliever (NMPR) users over the past decade, racial and ethnic diversity has increased, users are now older, frequency of NMPR use has increased, non-medical OxyContin use peaked around the middle of the study period and then began to drop, heroin use increased, cocaine use decreased, and injection drug use became more common.

There are a several possible factors that may contribute to the changes in distribution of the population's characteristics and drug use across time. It is easiest to think of this in terms of use and non-use of NMPRs and how certain subgroups of users move from one of these states to the other. This is not a longitudinal study and therefore is not following the population over time. However, each year is assumed to be a nationally representative sample, and therefore the idea is that comparing the estimates from time period to time period gives us insight into these movement patterns.

It may be that certain groups are being driven out of the NMPR using population at a faster rate than other. Studies have indicated that the rate of prescription opioid prescribing plateaued between 2010 and 2012, and abuse of NMPRs did the same between 2011 and

2013.[69,72,73] These studies indicate that either those entering the NMPR population have slowed or those exiting have increased, or a combination of the two. Obviously, some users will exit the NMPR user population due to death, either associated with NMPRs or not. However, as previous studies have shown, the pattern of drug overdose associated deaths typically follow that of non-medical drug use patterns, it is unlikely that this is the only explanation for possible increased exiting of the NMPR population.[24,62]

Some NMPR users may stop using due to decreased access to prescription opioids as a result of policies decreasing access or ability to abuse. Some of these users may be inclined to quit non-medical drug use entirely, either through treatment or other means, or begin using other drugs in place of NMPRs. This theory is consistent with several previous studies showing that after implementation of prescription drug monitoring programs there was slowed growth in the supply of prescription drugs, decreased NMPR associated treatment raters, poison center calls, and prescription rates.[28,34,39–44]

Similarly, studies have shown abuse-deterrent formulations to be associated with reductions in abuse of the targeted NMPR, decreased reporting of NMPR-associate fatalities, and fewer associated poison control center calls.[19–22] These studies indicate some users may also be driven out of the NMPR user population due to factors associated with these intervention efforts. Many of these policies were implemented during the study period and the previous literature supporting the influences of these policies on NMPR users. Therefore, it is logical to theorize that they, at least in part, contribute to the changing demographic and drug use patterns.

Additionally, certain groups may find it easier or more difficult to begin NMPR use in the changing prescription opioid environment. The results indicate that the age of users has increased from time period to time period in the study. It may be that as physicians prescribing NMPRs

have become more educated about the problems associated with NMPRs and addiction and programs like PDMPs force them to rethink their prescribing behavior. This may have led to increased hesitance to prescribe NMPRs and this hesitance may be more pronounced toward younger individuals than older, thus decreasing their ability to "doctor shop" and obtain NMPRs. Comparisons of time trends of prescribing of NMPRs stratified by age group would be beneficial in supporting or discrediting this theory.

Racial and ethnic diversity appeared significantly different when the 2011-2012 year group was compared to both the 2005-2006 and 2009-2010 year groups, with increased proportions of both black non-Hispanics and Hispanics represented in the 2011-2012 year group. This may be associated with the increased racial diversity in the U.S. population as a whole over the time period, or there may be some additional underlying factors that have yet to be identified that have had an influence. Further research to elucidate these factors is needed.

The study found that when compared to the 2005-2006 group, both the 2011-2012 and 2013-2014 groups showed significant increases in frequency of any NMPR use. This indicates that either users staying in the NMPR group long-term are using more frequently over time, those entering the NMPR group in later years of the study are using at higher frequencies than those entering the NMPR group in earlier years, less frequent NMPR users are more likely to exit in later years of the study, or some combination of these. Given the tightening of NMPR policy and changing prescribing behavior of providers, it may be that more casual users of NMPRs are decreasing in number. NMPR users that use more frequently may show more resistance to quitting NMPRs even when faced with greater challenges obtaining them. This explanation is logical as high frequency NMPR users would be more likely to be dependent and to have more consistent prescription sources.

Interestingly, non-medical OxyContin use peaked in the 2009-2010 year group and then showed declines afterword (**Figure 4**), though the declines in the subsequent year groups were not statistically different from the year group immediately preceding it. This peak coincides closely with the introduction of abuse-deterrent reformulation of OxyContin.[15,17] The findings cannot be attributed to or associated with the introduction of the abuse-deterrent OxyContin, however, they are worth noting.

Frequency of heroin use was shown to increase over the study period, which is consistent with a growing body of literature showing the increase in heroin use in the U.S. and the association between prescription opioid use and subsequent heroin initiation and use.[26,29–31,68,69,74,75] These two factors combined should lead one to predict that if heroin use is increasing and at the same time prescription opioid use typically precedes heroin initiation, then across the time period there would be growth in the proportion of NMPR users also using heroin. Coinciding with this increase in the frequency of heroin use was an increase in ever having injected drugs. These results are expected as heroin is frequently used via injection, while NMPR users use this route less often.[70,76]

Finally, both cocaine and crack showed declines in past 12 month use over the study period. It is difficult to discern the reasoning for such results given the scope of the study. Similar to the theory described above, it may be that casual multi-drug users have been more likely to exit or less likely to enter the NMPR using population over the study period due to barriers, while heavy opioid only users have been more likely to continue use. Further research examining classes of non-medical drug users across multiple drug types could aid in further explanation of these results.

Limitations

There are several limitations to the study. The cross-sectional design of the study is a hindrance to drawing conclusions about patterns across time. The study does not follow the same individuals across time and therefore change in individual behavior cannot be ascertained; only comparing distributions across time period for significant difference and making inferences about what those differences could potentially mean can be done with this study.

Additionally, we cannot say any particular policy was the cause of changes or is even associated with them, this can only be theorized about given the results. Also, no state-level variables were available in the public use files of the NSDUH and given that there are many factors across states that may impact NMPR users over time, none of these factors can be accounted for. Having state-level variables would also be beneficial to allow for studying drug policy implications within individual states, for example PDMPs, which are implemented at the state-level. Finally, there are likely confounding factors not accounted for in the study, given its descriptive nature.

Conclusion

The study indicated that the NMPR using population is evolving across demographic characteristics and drug use. Future analyses investigating drug use patterns in subgroups of prescription opioid users may be valuable as different subgroups may react differently to policies and other factors. Additionally, some policies or interventions like abuse-deterrent (re)formulations may be more or less successful in deterring non-medical use than others and thus evaluations of these policies separately would be valuable, but difficult unless planned in advance. Stratified analyses for different subgroups of prescription opioid users in terms of

quantity used may also prove valuable as it is likely that infrequent and frequent prescription opioid users are not the same across all factors and characteristics. Finally, studies looking at multiple opioid use and how this has changed over time and what opioids are commonly being used in conjunction with each other may give insight to which opioids should be targeted in future policy.

CHAPTER IV: PAPER 3

TITLE: Trends in heroin use and initiation among non-medical prescription opioid users in the U.S., 2005-2014

INTRODUCTION

Opioid abuse, including both prescription opioids and heroin, has been become a major public health issue in recent decades. As of 2014, drug overdose is the leading cause of accidental death in the U.S.[9] Of the 47,055 lethal drug overdoses in 2014, 18,893 (40%) were related to prescription opioids, while 10,574 (22%) were related to heroin.[9] In addition to growing overdose deaths, sales of prescription pain relievers and substance use treatment admissions have been on the rise, with sales of prescription opioids seeing a four-fold increase between 1999 and 2010, and substance use disorder treatment admission rates six times larger in 2009 compared to 1999.[10] Finally, the concentration of heroin in the U.S. market has been on the rise, while the street price of heroin has been shown to be on the decline in recent years, and there has been increase in perceived availability of heroin among users.[65–67]

Several policies and programs have been developed in recent years to address the growing opioid problem in the U.S. These policies and programs have heavily focused on restricting access to prescription drugs (prescription drug monitoring programs) or decreasing the abuse potential of prescription drugs (i.e. development of abuse-deterrent formulations of prescription drugs).[11–16] Several studies have indicated that these programs are associated with reductions in non-medical prescription opioid use and related overdose rates.[17–22] Some studies

have also indicated that these policies may be driving at least some prescription opioid users to begin using heroin.[12,18,22]

Heroin and prescription opioids operate on the same receptors in the body and, in turn, produce similar euphoric effects.[28,51,77] Previous studies have suggested prescription opioids may function as "gateway" drugs to heroin; and prescription drug use typically precedes heroin initiation, whereas the reverse is far less common.[25,26,29,30,78,79] Given the decreased access to prescription opioids and barriers to non-medical use created by recent prescription drug policies, in conjunction with increased access and decreasing costs for heroin, there may now exist a stronger incentive for prescription opioid users to use heroin.

One prescription opioid of particular interest is OxyContin, which was introduced in 1996 for treatment of moderate to severe pain.[53–55] OxyContin rapidly became a popular drug and by 2004 was the most abused prescription drug in the U.S.[54,56] In response to this, an abuse-deterrent version of OxyContin was introduced in August 2010.[15,17] Literature has indicated that the reformulation has been associated with decreased reporting of OxyContin as the primary drug of abuse, increased heroin exposure calls to poison centers, and increased heroin use among those presenting at heroin treatment centers.[12,17,18,60]

The National Survey on Drug Use and Health (NSDUH) is an annual nationally representative survey of the civilian, non-institutionalized population of the U.S.,12 years of age or older.[70] The survey obtains information on respondents' mental health status, demographic characteristics, and drug use behavior over the past year for a broad spectrum of drugs, including prescription pain relievers and heroin. The NSDUH also includes a section devoted entirely to non-medical use of OxyContin that includes the same set of questions asked about in the other

drug sections. This provides a unique opportunity to study this subgroup of prescription opioid users separately from non-OxyContin non-medical prescription opioid users.

Since not all prescription opioids are the same in terms of potency, abuse potential, and risk, and because an OxyContin-specific reformulation has been developed, analyses investigating trends in demographic characteristics and drug use over time among non-medical OxyContin users may be beneficial. Studying this subgroup of NMPR users may provide some insight into how recent opioid policy and the changing opioid environment (access, cost, increased access to heroin, etc.) have influenced the characteristics and behaviors of the non-medical OxyContin using population.

Given the relationship between prescription opioid and heroin use, investigation of heroin use specifically and how it differs across time in the non-medical OxyContin using population may provide valuable information about the evolving opioid using population. Studies have evaluated heroin use among non-medical prescription opioid users.[29–31] However, no studies, to the authors' knowledge, have investigated how non-medical OxyContin users differ from other non-medical opioid users in terms of heroin use over time.

Investigating these factors over the past decade may not only inform intervention and treatment efforts, but also give insight into potential negative externalities associated with prescription opioid targeted policies that do not concurrently address the potential for users to begin use of more harmful substances. The findings may promote and inform development and implementation of policies that address substance abuse from a systems perspective rather than targeting individual categories of substances without consideration of other substances as potential replacements.

In order to address the issues described above, the following study aims to: a) describe heroin use behavior among non-medical OxyContin users compared to other non-medical prescription opioid users; and b) compare these differences from year-to-year over the past decade. The author hypothesizes that heroin use increased over the past decade for both non-medical OxyContin and other non-medical prescription opioid users. However, this growth is expected to be more pronounced among non-medical OxyContin users around the time of introduction of abuse-deterrent OxyContin.

METHODS

Data

The National Survey on Drug Use and Health (NSDUH) public use files for years 2005 through 2014 were used for all analyses. The NSDUH is an annual survey conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA) that obtains information on drug use and mental health status and can be used to calculate national and state level estimates.[70] The survey is given in-person with computer assistance annually to approximately 70,000 interviewees. The survey is designed to obtain a nationally representative random sample of the civilian, non-institutionalized population of the U.S. that is 12 years of age and older. Response rates for each year included in the study are 70% or greater.

A public use file was accessed and downloaded for each of the years 2005 through 2013 through the Inter-university Consortium for Political and Social Research (ICPSR) website.[80] ICPSR is the data stewardship organization currently used by SAMHSA to house their public use files. SAMHSA was contacted directly for the 2014 public use file because this public use file was not yet available through ICPSR at the time of the study. SAMHSA mailed the data,

codebook and other materials to the authors. A variable within each dataset identified the year of data and all public use files were combined using SAS to create a single dataset.

Non-medical pain reliever (NMPR) is the term used in the NSDUH to refer to prescription opioids and a few non-opioid prescription drugs that are also used to treat pain symptoms. The majority of those reporting NMPR use reported opioid NMPR use. In a previous study using the NSDUH, those reporting only non-opioid NMPR use represented n=36 across six years of survey data (2002-2004 and 2008-2010) which represents less than 0.002% of the total sample of NMPR users.[31] For this reason, the NMPR population is considered synonymous with the non-medical prescription opioid using population for the purposes of this study.

Inclusion Criteria

All observations within the dataset were used in the analyses. Respondents were stratified into one of three groups based on their response to questions about NMPR and non-medical OxyContin use in the past 12 months (detailed explanation provided in the **Variables** section below). The three groups were: NMPR users using OxyContin (NMPR-O), NMPR users not using OxyContin (NMPR-N), and those not using NMPRs of any kind in the past 12 months (NMPR-X). All analyses were conducted for each of the three separate groups. The total sample size was 558,372 for all years of combined data with the stratified groups having the following sample sizes: NMPR-O (N = 5,861), NMPR-N (N = 33,229), and NMPR-X (N = 519,282). Details of the sample size by year and NMPR group can be found in **Table 1**. The decision to include the NMPR-X group in the analysis was to provide the ability to identify heroin use trends in this population and make comparisons to those of NMPR users.

Variables

The NSDUH asks respondents a set of questions about drug use for many different categories of drugs, including NMPRs (as well as a separate section for OxyContin, a type of NMPR), heroin, alcohol, marijuana, and cocaine, among others. One set of questions, included in each drug use section, asks about past 12 month use of each respective drug. Respondents are asked to choose the easiest way to describe the total number of days they used each substance in the past 12 months with the options: days per week, days per month, or days per year. The NSDUH uses the responses to these variables to calculate a new dichotomous variable for whether the person used the drug within the past 12 months (Yes/No). These variables were used to identify NMPR, non-medical OxyContin, heroin, heavy alcohol, marijuana, and cocaine use in the analyses.

The responses to the past 12 month use of NMPRs and OxyContin were used to stratify the sample. For the three stratification groups the following combinations of responses were used to determine which group to assign each respondent:

	Past 12 month NMPR use	Past 12 month OxyContin use
NMPR-O	-	YES
NMPR-N	YES	NO
NMPR-X	NO	NO

The two primary dependent variables of interest for each of the stratified analyses were a) heroin use in the past 12 months and b) recent heroin initiation. The first paragraph of this section describes how all past 12 month drug use variables were created. A variable identifying

recent heroin initiation was created from a recoded variable in the NSDUH that identifies what the year of first use of heroin is, if that year is the same as the survey, the year prior to the year of the survey, or two years prior to the year of the survey. This variable was derived from responses during the interviews to questions "Did you first use heroin in [CURRENT YEAR - 1] or [CURRENT YEAR]?" and "Did you first use heroin in [CURRENT YEAR - 2] or [CURRENT YEAR - 1]?" Recent heroin initiation was defined as having first used heroin in the same year of the survey or the year immediately prior to the survey.

The initial goal was to create a variable that showed if the respondent initiated heroin in the past 12 months. Although the public use files of the NSDUH do provide a variable for month of first heroin use, they do not provide a variable for the month the survey was completed. Given these facts, if recent heroin use was defined as having first used heroin in the same year of the survey, not all of those initiating heroin in the past 12 months would be captured. The decision was made to define the variable for recent heroin initiation as those who initiated in the year of the survey or the year immediately prior to the survey. The authors believe this decision is justified given that the aims of the study are not to provide prevalence estimates but simply look at associations and compare percentage distributions of stratified groups across survey years. Additionally, prior research has indicated that, at least in recent years, heroin initiation is frequently preceded by NMPR use, while it is very uncommon for NMPR initiation to be preceded by heroin initiation.[29] Therefore, it is likely that a substantial majority of NMPR users that recently initiated heroin according to the definition used in this study were NMPR users before heroin initiation.

The primary independent variable of interest was year of survey completion, as the aim of the study was to investigate heroin use and recent initiation in the stratified groups across time

to see if a positive relationship appeared and if there was a difference in the strength of these relationships depending on NMPR and non-medical OxyContin use status. Year was treated as a categorical variable in the analyses, with 2005 functioning as the reference year. The decision to do so was made so that odds ratios could be calculated for each year comparison. This allowed for identification of specific year differences in odds of heroin use or recent initiation, rather than just identifying if there was a positive association between increase in year and odds of using heroin in the past 12 months/ recently initiating heroin use, which would have been the case if year had been treated as continuous.

Variables identifying past 12 month heavy alcohol, marijuana, and cocaine use were included as independent variables. These were calculated using the method described in the first paragraph of this section. Additionally, a variable for whether the respondent had ever injected any drug was included as an independent variable.

Demographic and population characteristics included as control variables in the analyses were: age, race/ethnicity, income, sex, marital status, and health insurance status. Health insurance was included due to recent legislation expanding health insurance coverage in the United States through the Affordable Care Act (ACA) which may influence access to and use of prescription drugs and heroin differently across years and therefore should be accounted for. A categorized variable was used for age because the NSDUH does not provide the raw age of respondents in the public use files. It was also beneficial to use categorization of age to identify shifts in age groups across time among each stratified group.

Analysis

Descriptive statistics were calculated for each year across each variable in the study. The analyses were stratified by NMPR group (i.e. NMPR-O, NMPR-N, and NMPR-X). Chi-square tests were used to compare each variable across time. For each variable, each year was compared to the year immediately preceding it, i.e. 2014 vs. 2013, and to the first year (reference year) in the study, i.e. 2014 vs. 2005. Weighted percentage distributions and standard errors were reported.

Unadjusted analyses were conducted for the two outcomes: a) recent heroin initiation and b) past 12 month heroin use, and each independent variable. These analyses were stratified by NMPR group. Odds ratios and associated 95% confidence interval were reported. Finally, logistic regression was used to estimate adjusted odds ratios and 95% confidence intervals.

All analyses were conducted using SAS 9.4. In order to adjust for the multi-stage complex survey design of the NSDUH, survey commands were used (PROC SURVEYFREQ and PROC SURVEYLOGISTIC) to allow strata, cluster and weight variables to be included in the analysis, providing appropriately weighted estimates. Additionally, the DOMAIN statement was used to identify and account for the stratified subpopulations of interest within the NSDUH (i.e. NMPR-O, NMPR-N, and NMPR-X). The DOMAIN statement is the appropriate command to use in these instances as it allows for separate analyses for each domain to be performed and at the same time accounts for the random variability that is introduced by each domain's sample size.

RESULTS

Descriptive statistics for each NMPR group by year for the each variable in the study are provided in **Table 3**, with percentages and associated standard errors (SEs) reported.

Clear trends in recent heroin initiation do not appear for any of the stratified populations. However, among the NMPR-N group there was a significant increase in the percentage reporting recent heroin initiation from 2008 (0.2%, SE = 0.1) to 2009 (0.8%, SE = 0.2) that remained similar in subsequent years. Similarly, another significant increase in this group occurred from 2013 (0.9%, SE = 0.3) to 2014 (2.2%, SE = 0.5).

The percentage of non-medical OxyContin (NMPR-O group) users reporting past 12 month heroin use was significantly higher in 2011 (17.1%, SE = 2.9) compared to 2005 (10.0%, SE = 1.7). Subsequent years stayed relatively similar when compared to 2005, except a non-significant decrease in reported past 12 month heroin use between 2013 (18.1%, SE = 2.7) and 2014 (15.6%, SE = 2.8), which resulted in the 2014 to 2005 comparison to no longer be significant at the $\alpha = 0.05$ level. In contrast, both the 2013 to 2014 and the 2005 to 2014 comparisons showed significant increases for both the other NMPR groups. Of respondents in the NMPR-N group for 2005, 1.1% (SE = 0.3) reported using heroin in the past 12 months, while those percentages were 2.7% (SE = 0.4) and 4.9% (SE = 0.7) in 2013 and 2014, respectively. In the NMPR-X group, values for 2005 (0.059% SE = 0.012) and 2013 (0.055% SE = 0.01) were similar, however, 2014 showed a significant increase (0.135%, SE = 0.023) in those reporting heroin use in the past 12 months. Overall, heroin use was much more common among the NMPR-O group (range: 3.2% – 7.8%) compared to both the NMPR-N (range: 0.2% - 2.2%) and NMPR-X (range: 0.01% - 0.04%) groups for all years.

Past 12 month heavy alcohol use appeared to drop among the NMPR-O group from 2005 (41.0%, SE = 3.4) to 2006 (31.4%, SE = 3.1) and remained at similar or lower values in subsequent years. Later years appeared to show modest but mostly significant decreases in heavy alcohol consumption relative to 2005 (22.9%, SE = 1.2), with 2011 and all subsequent years having estimates below 20%. Also of note, heavy alcohol use was more common among the NMPR-O group (range: 24.3% - 41.0%) in comparison to the NMPR-N group (range: 18.0% - 24.3%) and the NMPR-X group (range: 5.6% - 6.2%) for all years.

Past 12 month marijuana use showed a clear pattern of increase since 2009 among the NMPR-X group, with 2005 estimates of 8.5% (SE = 0.2), 2009 estimates of 9.3% (SE = 0.2), and 2014 estimates of 11.9% (SE = 0.2). While past 12 month marijuana use was substantially more common in the NMPR-O (range: 68.4% to 79.7%) and NMPR-N (range: 44.2% to 50.3%) groups, no clear trends from year to year were found.

Although ever having injected a drug was more common reported among NMPR-O users (range: 15.0% to 27.2%) for all years than both the NMPR-N (range: 4.8% to 8.2%) and the NMPR-X (range: 1.1% to 1.3%) groups, the only significant year comparison was a drop seen when comparing 2013 (25.4%, SE = 3.5) to 2014 (15.0%, SE = 3.2).

Racial and ethnic diversity appeared to increase over time for all groups, with all 2005 to 2014 comparisons being significant. The proportion of those reporting to be white, non-Hispanic dropped from 90.6% (SE = 1.4) to 77.5% (SE = 3.0) in the NMPR-O group, 71.4% (SE = 1.3) to 61.6% (SE = 1.2) in the NMPR-N group, and 68.8% (SE=0.6) to 64.2% (SE=0.5) in the NMPR-X group, from 2005 to 2014, respectively. Similarly, all groups appeared to show some trend of increases in age, with those reporting to be 50+ going from 4.8% (SE = 3.8) to 12.7% (SE = 4.3) in the NMPR-O group, 11.7% (SE = 1.6) to 20.3% (SE = 1.8) in the NMPR-N group, and 36.1%

(SE = 0.6) to 41.2% (SE = 0.4) in the NMPR-X group, when comparing 2005 to 2014, respectively.

No clear trends appear for the NMPR-O group, nor the NMPR-N group, in terms of sex, income, health insurance, and marital status. The NMPR-X group appears to show a pattern of increased income, with more individuals reporting being in the 75,000+ income category in 2014 (34.9%, SE = 0.5) than in 2005 (28.5%, SE = 0.5); although, these values do not represent real income as they do not take into account inflation and therefore this pattern would be expected. Additionally, patterns in health insurance and marital status appeared in the NMPR-X groups, with having health insurance becoming more common (86.2%, SE = 0.3 in 2005 vs. 88.2%, SE = 0.2 in 2014) and being married becoming less common (51.6%, SE = 0.4 in 2005 vs. 47.8%, SE = 0.4 in 2014), over time.

Table 4 provides unadjusted odds ratios (ORs) and 95% confidence intervals (CIs) for recent heroin initiation and past 12 month heroin use by each independent variable, stratified by NMPR group.

Beginning with the recent heroin initiation analyses, when comparing odds of recent heroin initiation for different years, only unadjusted ORs for 2013 (OR = 2.58; 95% CI = 1.06, 6.29) and 2014 (OR = 6.69; 95% CI = 3.08, 14.56) for the NMPR-N group were found to be significant, with survey respondents in 2013 and 2014 having greater odds of reporting recent heroin initiation than in the reference year of 2005.

Past 12 month heavy use of alcohol, use of marijuana, and use of cocaine were consistently associated with greater odds of recent heroin initiation for all NMPR groups, except for heavy alcohol use in the NMPR-O group. The ORs were the largest for NMPR-X group across all three substances, with ORs of 4.95 (95% CI = 3.03, 8.07), 39.51 (95% CI = 22.73,

68.67), and 70.22 (95% CI = 47.25, 104.36), for past 12 month heavy alcohol use, marijuana use, and cocaine use, respectively. Odds ratios for the NMPR-N group were 1.63 (95% CI = 1.09, 2.44), 10.75 (95% CI = 6.14, 18.82), and 6.37 (95% CI = 4.25, 9.56), for the same variables, respectively; while the ORs for the NMPR-O group were smaller but significant for marijuana and cocaine use were 2.68 (95% CI = 1.57, 4.58) and 4.93 (95% CI = 3.51, 6.93), respectively, and not significant for heavy alcohol use.

Additionally, ever having injected a drug was also a positive predictor of recent heroin initiation among all NMPR groups. Again, the NMPR-X group showed the largest ORs (OR = 46.57; 95% CI = 30.39, 71.36), though the ORs for the NMPR-N (OR = 9.41; 95% CI = 6.26, 14.12) and NMPR-O (OR = 2.52, 95% CI = 1.76, 3.61) groups were still substantial.

Black non-Hispanic race/ethnicity was associated with decreased odds of recent heroin initiation in the NMPR-O (OR = 0.15, 95% CI = 0.03, 0.64) and NMPR-X (OR = 0.11; 95% CI = 0.04, 0.34) groups, while male gender was a positive predictor in the NMPR-N (OR = 1.47; 95% CI = 1.00, 2.17) and NMPR-X groups (OR = 2.33; 95% CI = 1.48, 3.66).

All income categories: 25,000-49,999 (OR = 0.47; 95% CI = 0.28, 0.79), 50,000-74,999 (OR = 0.34; 95% CI = 0.19, 0.62), and 75,000+ (OR = 0.19; 95% CI = 0.11, 0.34), were associated with decreased odds of heroin initiation in the NMPR-X group when compared to the <25,000 reference category, while only the 75,000+ category (OR = 0.47; 95% CI = 0.25, 0.87) was associated with decreased odds in the NMPR-N group, and no associations were found in the NMPR-O group.

Several of the age categories were significant in each of the stratified groups, with the general pattern being for those that are significant to show decreased odds of recent heroin initiation relative to the reference category of ages 18-25. The significant ORs with the greatest

magnitude for the NMPR-O and NMPR-X groups were the comparisons between the 50+ group to the reference category, with ORs of 0.04 (95% CI = 0.01, 0.30) and 0.14 (95% CI = 0.03, 0.60), respectively; while the comparison with the greatest magnitude in the NMPR-N group was the comparison of the 35-49 age group to the reference category (OR = 0.34; 95% CI = 0.17, 0.66)

Health insurance was only found to have a significant odds ratio in the NMPR-X group, with those having health insurance having decreased odds of recent heroin initiation (OR = 0.37; 95% CI = 0.24, 0.59). Finally, those that were married were found to have decreased odds of recent heroin initiation in all groups, with ORs of 0.18 (95% CI = 0.08, 0.39), 0.18 (95% CI = 0.09, 0.35), and 0.03 (95% CI = 0.01, 0.08), for the NMPR-O, NMPR-N, and NMPR-X groups, respectively.

Table 4 also provides the results for the unadjusted analyses for past 12 month heroin use as a dependent variable. For the NMPR-O group, respondents from 2011, 2012, and 2013 had greater odd of past 12 month heroin use, with ORs of 1.86 (95% CI = 1.04, 3.32), 2.04 (95% CI = 1.12, 3.69), and 1.99 (95% CI = 1.24, 3.17), respectively, when compared to the 2005 reference group. Among the NMPR-N group, respondents from 2009 (OR = 1.96; 95% CI = 1.01, 3.80), 2013 (OR = 2.41; 95% CI = 1.37, 4.25) and 2014 (OR = 4.54; 95% CI =2.62, 7.86) when compared to the reference year. In the NMPR-X group, unexpectedly, 2007 was associated with decreased odds of past 12 month heroin use (OR = 0.46; 95% CI = 0.23, 0.91). Additionally, 2014 was associated with greater odds of past 12 month heroin use (OR = 2.30; 95% CI = 1.37, 3.85), among this group.

Past 12 month heavy alcohol use, marijuana use, cocaine use, and ever having injected any drugs showed similar results in the past 12 month heroin use analysis as the recent heroin

initiation analysis, with all consistently associated with greater odds of use, except heavy alcohol use in the NMPR-O group.

Interestingly, black non-Hispanic race/ethnicity was associated with greater odds (OR = 2.00; 95% CI = 1.40, 2.85) of heroin use in the past 12 months among the NMPR-X group when compared to the white non-Hispanic reference group, which is in contrast to the decreased odds found among the same group in the recent heroin initiation analysis. Additionally, the all other race ethnicity category was found to have decreased odds of past 12 month heroin use (OR = 0.50; 95% CI = 0.28, 0.90), when compared to the reference, in the NMPR-N group. No other associations for race/ethnicity were significant.

Most higher income groups were associated with decreased odds of past 12 month heroin use when compared to the less than $25,000 reference for all NMPR groups, while male sex was consistently associated with higher odds in each of the NMPR groups. The age category 12-17 was consistently associated with decreased odds in all NMPR groups when compared to the 18-25 age category, which is consistent with the recent heroin initiation findings. Interestingly, the 26-34 age group was associated with greater odds of past 12 month heroin use in the NMPR-N group (OR = 1.40; 95% CI = 1.03, 1.90). Finally, both having health insurance and being married showed significantly lower odds of past 12 month heroin use among all NMPR groups.

Table 5 provides results from logistic regression modeling for each stratified groups of the two outcomes of interest, recent heroin initiation and past 12 month heroin use. Adjusted odds ratios and 95% confidence intervals are reported.

The relationship between year and each of the outcomes becomes more apparent after adjustment for covariates in both the NMPR-O and NMPR-N groups. In the NMPR-N group, 2009 (OR = 2.63; 95% CI = 1.06, 6.52), 2011 (OR = 2.75; 95% CI = 1.14, 6.67), 2013 (OR =

2.72; 95% CI = 1.11, 6.66), and 2014 (OR = 2.29; 95% CI = 1.07, 4.92) were all associated with greater odds of recent heroin initiation, while 2013 was associated with the same in the NMPR-O group (OR = 2.29; 95% CI = 1.07, 4.92). No associations were found between year and recent heroin initiation in the NMPR-O group.

After adjustment for covariates, there was a more obvious pattern in the odds ratios between year and past 12 month heroin use in both the NMPR-O and NMPR-X groups, although contrary to the authors' prediction, the pattern appeared to be similar in magnitude for the two groups. In the NMPR-O group 2010 (OR = 2.06; 95% CI = 1.16, 3.68), 2011 (OR = 2.86; 95% CI = 1.52, 5.39), 2012 (OR = 2.23; 95% CI = 1.26, 3.96), 2013 (OR = 2.52; 95% CI = 1.40, 4.52), and 2014 (OR = 3.03; 95% CI = 1.65, 5.57), were associated with increased odds of past 12 month heroin use. Similarly, 2009 (OR = 2.42; 95% CI = 1.26, 4.65), 2010 (OR = 2.21; 95% CI = 1.30, 3.74), 2011 (OR = 2.62; 95% CI = 1.35, 5.06), 2012 (OR = 1.98; 95% CI = 1.03, 3.78), 2013 (OR = 2.60; 95% CI = 1.56, 4.32), and 2014 (OR = 5.80; 95% CI = 3.19, 10.52), were associated with increased odds in the NMPR-N group. Relationships between years and past 12 month heroin use did not significantly change after adjustment for the NMPR-X group.

In contrast to some of the unadjusted results, heavy alcohol was associated with decreased odds of both recent heroin initiation (OR = 0.64; 95% CI = 0.46, 0.89) and past 12 month heroin use (OR = 0.64; 95% CI = 0.46, 0.88) in the NMPR-O group, and past 12 month heroin use in the NMPR-N (OR = 0.69; 95% CI = 0.47, 0.99) and NMPR-X (OR = 0.63; 95% CI = 0.40, 0.99) groups. Past 12 month marijuana use, cocaine use, and ever having injected a drug remained similar to the unadjusted results, showing consistently increased odds of recent heroin initiation and past 12 month heroin use, however many of the ORs were smaller in the adjusted analyses.

Consistent with the unadjusted findings, black non-Hispanic race/ethnicity was associated with decreased odds (OR = 0.09; 0.03, 0.30) of recent heroin initiation and increased odds (OR = 2.11; 95% CI = 1.39, 3.21) of past 12 month heroin use in the NMPR-X group. In the NMPR-N group, black non-Hispanic and Hispanic race/ethnicity were associated with increased odds of past 12 month heroin use, with ORs of 2.10 (95% CI = 1.26, 3.50) and 1.58 (95% CI = 1.00, 2.48), respectively.

None of the income categories were significant for either outcome in the NMPR-O and NMPR-N groups. However, all of the income categories, 25,000-49,999 (OR = 0.65; 95% CI = 0.46, 0.93), 50,000-74,999 (OR = 0.53; 95% CI = 0.35, 0.81), and 75,000+ (OR = 0.46; 95% CI = 0.30, 0.70), were associated with decreased odds of past 12 month heroin use in the NMPR-X group. Additionally, the 75,000+ group was associated with decreased odds of recent heroin initiation in the NMPR-X group as well (OR = 0.41; 95% CI = 0.22, 0.76).

The majority of the significant associations found in the unadjusted analyses for sex, age, and health insurance no longer remained in the logistic regression analyses. However, being married was still found to be consistently associated with decreased odds of recent heroin initiation and past 12 month heroin use in all groups in the adjusted analyses.

DISCUSSION

The study indicated that past 12 month heroin use has increased in the both NMPR using subgroups in recent years. Additionally, heroin use was more common among the OxyContin users (NMPR-O) than the non-OxyContin using NMPR users (NMPR-N). However, contrary to the authors' expectations, the strength of the relationship between year and heroin use was no more prominent in the NMPR-O group than the NMPR-N group, indicating growth in heroin use

may be similar in the two groups. Additionally, there was no obvious trend in past 12 month heroin use in the non-NMPR using population (NMPR-X). Finally, only the NMPR-N subgroup showed a pattern of increased recent heroin initiation in later years of the study.

The pattern of increased past 12 month heroin use across time is consistent with current literature investigating heroin use trends.[61,68] One study of heroin use in the United States showed a growth of average annual rates of past year heroin use from 1.6 per 1,000 between 2002 and 2004 to 2.6 per 1,000 between 2011 and 2013.[61] It is also important to note that the growth in heroin use appeared to be primarily concentrated in NMPR users, supporting the notion presented by other literature that NMPR use frequently predates heroin use.[26,29–31,68,69,74,75]

One potential explanation for the increase in heroin use among NMPR users across time is that certain types of NMPR users may be being driven out of the NMPR using population at different rates. The recent growth of PDMPs and introduction of abuse-deterrent reformulations may be creating an environment in which certain users find it more difficult than others to obtain NMPRs and some may be more or less likely to continue using NMPRs. This is supported by literature associating the introduction of PDMPs with slowed growth in the supply of prescription drugs, and decreased NMPR treatment rates, prescription rates, and poison enter calls.[28,34,39–44] Additionally, introduction of abuse-deterrent formulations have been associated with reductions in NMPR misuse, availability, and decreased reported associated fatalities.[19–22] These factors combined with increasing access to and decreasing cost of heroin may also create a "perfect storm" of sorts to that leads to increased heroin use, particularly among NMPR users.

To illustrate this point further, think of NMPR users in terms of frequency of NMPR use: frequent and infrequent, based on some number of days of use in the past 12 months. It could be that infrequent NMPR users are more likely to stop NMPR use when faced with increased

difficulty obtaining NMPRs than frequent users. Previous literature has shown that NMPR users that use NMPRs more frequently (greater number of total days used) are also more likely to use heroin in the past 12 months.[31] If frequent NMPR users have greater odds of heroin use and infrequent NMPR users are becoming more likely to stop NMPR use in recent years, this would result in a greater concentration of frequent NMPR users in the NMPR using population and would result in greater frequency of past 12 month heroin use being reported as well. Additional research comparing heroin use over time across NMPR users stratified by frequency of NMPR use may provide insight into whether or not this explanation may be valid.

The lack of noticeable differences in association between year and heroin use in NMPR-O users compared to NMPR-N users may indicate that the growing heroin epidemic is impacting NMPR users similarly regardless of type of NMPR used and may be less associated with individual policies than the change in the overall environment, policy and attitude in the U.S. toward prescription opioids. However, there may also be flaws in the design of the study that mask differences in particular types of NMPR users.

There have been several other types of abuse-deterrent formulations introduced recently in the market, including extended-release (ER) OxyContin, Embeda, ER Hysingla, ER Zohydro, and ER Targiniq, that target substances other than oxycodone to prevent misuse.[48,50–52] Interestingly, heroin use was much more common among OxyContin users than other NMPR users. It would be interesting to further stratify the NMPR-N group into groups of users based on some additional factors such as abuse potential of most frequently used NMPR, whether or not there is an abuse-deterrent version of the NMPR most commonly used, or some other factor that may influence increased heroin use. However, there would be significant difficulties in using the NSDUH to this effect. The OxyContin using subgroup was easily divided because the NSDUH

has an entire section devoted to the drug, treating it essentially as its own drug category. For other NMPRs, respondents are only asked which ones they have used in the specified time. Questions on frequency of use are only asked for NMPRs as a whole for these drugs and therefore subdividing this group further would prove challenging and misclassification would be a major concern. For these reasons the study did not pursue the above described additional stratification.

The majority of non-opioid substances were shown to be positive predictors of heroin use in most cases. However, heavy alcohol use was associated with decreased odds of heroin use in all NMPR groups and decreased odds of recent heroin initiation in the NMPR-O group. A previous study showed an inverse relationship between alcohol use and heroin consumption among a groups of addicts presenting for treatment that were subsequently followed over time.[81] One explanation could be that NMPR that supplement their addiction with alcohol are less likely to find the need for heroin use and vice versa. Essentially, the two may function in a similar role in supplementing NMPR use, with users being more likely to use one or the other rather than both. Additionally, it could be that the types of NMPR users that use alcohol are inherently different than those NMPR users willing to use heroin. Heroin is typically considered a "harder" substance to abuse than NMPRs or alcohol, in addition to the fact that the latter can be obtained legally, while heroin cannot.

The lack of significant change in heroin use among non-NMPR users indicates that the NMPR epidemic and heroin epidemic are closely tied. It cannot be said from this study what the causes or influencing factors are, but it is abundantly clear that there is an overall opioid epidemic currently in the U.S. and policy development should take into consideration all opioid abuse and develop strategies for deterring illicit use of these substances together.

Limitations

The cross-sectional design of the survey used in the study prevents temporal conclusions from being made. This is a limitation in that the study is attempting to look at time trends of heroin use among NMPR subgroups and panel data would be superior in investigating these trends. However, the NSDUH is designed to be a nationally representative survey and therefore comparing use of heroin in the population from year to year does at least give insight as to whether or not heroin use is becoming more common among the populations of interest, even if we cannot say who is entering and exiting the population.

It must be noted that there are no state-level variables provided in the NSDUH public use files. PDMP policies vary significantly across states in terms of implementation and requirements. Additionally, state-level factors also likely influence drug use behavior. The study cannot account for any state-level variation. Also, both heroin use outcomes are rare in many of the stratified groups. This is especially an issue for recent heroin initiation in the NMPR-O group because it has a much smaller overall sample size than the other stratified groups. The sample size for the NMPR-O group may not be large enough to give an accurate depiction of recent heroin initiation in this group and therefore estimates should be interpreted with caution.

Finally, the study cannot directly associate the results with prescription opioid policies; there are many other factors that could be influencing the composition and drug use behavior of the opioid using population. It could be that access to heroin has happened to increase at the same time of these policies or that the market for heroin grew as restrictions on prescription opioids increased and drug dealers ceased this opportunity to make profit. The study cannot determine how these factors influenced users of prescription opioids and heroin in various

populations, however, the findings do suggest that they may have some kind of impact and further investigation into the subject may prove worthwhile.

Conclusion

Future analyses should further stratify prescription opioid type used in the NMPR-N group based on potency, abuse potential, and research indicating which prescription opioids are being abused most often and route of intake. Additionally, further analyses of different groupings of user types such as heavy, moderate, and lights, may also be beneficial and provide insight into the characteristics of those using prescription opioids frequently. Finally, further research exploring the history and growth of the heroin and prescription opioid epidemics may further explain how these two epidemics grew simultaneously and how they have and do influence each other. Research of this type would give insight into the impact different drug markets have on each other and how those engaging in these markets respond to changes in supply and demand.

CHAPTER V: PUBLIC HEALTH AND POLICY IMPLICATIONS

The three papers presented in Chapters II, III, and IV provide evidence to support the notion that opioid policy and opioid use have changed in many ways over the past decade and these two factors may be associated with each other. Recent prescription opioid targeting policies been shown to be associated with several improved non-medical prescription opioid use related outcomes. These include slowed growth in prescription drug supply; decreased treatment rates, prescription rates and poison center calls; decreases in both non-oral and oral misuse of the targeted prescription opioid; and decreases in reported fatalities.[19–22,28,34,39–45] However, previous studies and the results of the analyses indicate that some of these policies may be associated with the rise in heroin use.[26,29–31]

Policies and interventions related to prescription opioids have heavily focused on reducing access to prescription opioids. The majority of heroin associated policies have focused on other factors such as reducing the risk of spreading disease through needle exchange programs and reducing the risk of death when an overdose occurs through improving access to naloxone, a substance that can reverse the effects of an opioid overdose.[82–90] Although, these policies do provide many benefits in terms of mitigating and preventing negative health outcomes associated with non-medical opioid use, one major problem is the non-medical prescription opioid epidemic and the heroin epidemic have largely been looked at separately by policy makers. It may be more beneficial for policy development to look at these two epidemics as one, i.e. a single opioid epidemic.

The policies targeting heroin, such as needle exchanges and increased naloxone access, likely benefit both heroin and non-medical prescription opioid users in that they can prevent

disease spread in all needle using opioid users and naloxone can reverse an overdose of prescription opioids in the same way it can reverse the effects in heroin users. However, the prescription opioid targeted policies such as prescription drug monitoring programs (PDMPs) and abuse-deterrent formulations, do not factor in heroin access, which may lead to increased heroin use among non-medical prescription opioid users. Development of policies that target heroin access in conjunction with these policies may lead to better health outcomes over the past decade; however, policies decreasing access to heroin are likely to prove much more difficult to develop given that the heroin market is an entirely illicit one. It is also important to note that medication assisted treatments, such as access methadone and buprenorphine, also benefit both types of non-medical opioid users similarly.[91–96]

There have been at least some policies developed to reduce access to and use of heroin, primarily ones focusing on increased criminal punishment for heroin trafficking.[97] Additional policies that target heroin access in other ways, though, are likely needed given that the illicit heroin market has grown in recent years even with severe trafficking laws in place. Cultivation of the plant *Papaver somniferum*, a.k.a. the opium poppy, which is used to make heroin, is not common in the U.S.[98,99] The majority of the heroin used in the United State comes from other countries, primarily Mexico and Columbia.[98,99] This implies that in order to reduce access to heroin in the United States, international cooperation and coordination between countries from which heroin is coming into the U.S. may be necessary to reduce the heroin epidemic. Improved methods for detection of imports containing heroin and individuals entering the U.S. carrying heroin from these countries may also prove beneficial, although may not be realistic given potential costs of such policies.

At least one study has been published arguing against the notion that the increase in prescription opioid policy is associated with the rise in heroin use, primarily arguing that the heroin epidemic began before many of these policies were enacted.[100] However, the fact that the epidemic may have begun before many of the non-medical prescription opioid use policies were enacted does not mean that there is no association between the two. There may be an interactive effect in that the increased access to and decrease price of heroin in addition to the development of these policies resulted in the heroin together resulted in the heroin epidemic being larger than it would have been had one of the factors been absent. Given how recent many of these policies were developed, it may be many years before research can adequately answer whether or not this was the case.

Finally, there are several concerning recent developments in the opioid epidemic that will certainly need to be addressed quickly. New and more dangerous substances are being introduced to the illicit opioid market; examples include fentanyl and "krokodil".[101,102] Fentanyl is a highly potent opioid, 30-50 times more so than heroin, and there has been a recent surge in overdoses associated with heroin laced fentanyl.[101] Additionally, "krokodil", the street name for a home-made injectable substance that is a cheap alternative to heroin has begun to be introduced into the heroin market.[102] The homemade process used to make krokodil has been shown to include agents that result in ulcerations, gangrene, and necrosis, and leading to limb amputation and death.[102,103] Although, krokodil has been shown not to have significantly penetrated the U.S. illicit opioid market, the health consequences associated with it are severe and it is a potential risk that should be monitored.[104] These recent introductions show that the illicit opioid market is an evolving one and can adapt to targeted policy. Public health officials and policy developers will have to be vigilant and adaptive in order to combat this ever evolving epidemic.

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TABLES

Table 1. Demographic characteristics of past 12 month non-medical pain reliever users

	2005-2006 N = 8,620		2007-2008 N = 8,551		2009-2010 N = 8,415		2011-2012 N = 7,633		2013-2014 N = 5,871	
	%	SE	%	SE	%	SE	%	SE	%	SE
Residence										
Metro	-	-	83.9	0.7	84.5	0.7	85.8	0.8	74.8	0.9
Non-Metro	-	-	16.1	0.7	15.5	0.7	14.2	0.8	15.2	0.9
Race/Ethnicity										
White Non-Hispanic	73.2	1.0	73.9	0.8	72.0	0.9	67.6	1.0	65.1	1.0
Black Non-Hispanic	8.8	0.6	9.6	0.6	8.9	0.5	11.0	0.8	11.9	0.7
Hispanic	13.5	0.8	11.5	0.7	13.6	0.8	16.3	0.8	16.7	0.8
All Other	4.5	0.4	5.0	0.5	5.6	0.7	5.1	0.4	6.3	0.5
Highest Education										
Less than H.S.	17.7	0.8	15.9	0.7	15.5	0.7	16.1	0.7	15.8	0.8
H.S.	27.8	0.8	29.0	0.9	27.8	0.9	28.3	1.0	26.9	1.0
College	39.8	0.9	41.9	1.2	44.0	1.1	43.5	0.8	46.4	1.1
12-17 years old	14.8	0.4	13.2	0.4	12.8	0.4	12.1	0.4	10.8	0.4
Income										
<20,000	24.9	0.7	22.6	0.7	24.5	0.9	24.7	0.9	25.6	0.9
20,000-49,999	35.6	0.9	35.0	1.2	34.9	1.1	36.0	1.0	33.1	1.1
50,000-74,999	16.2	0.7	17.1	0.8	14.6	0.7	15.3	0.7	16.0	0.8
75,000+	23.3	0.9	25.3	0.9	26.0	1.1	24.0	1.0	25.3	0.9
Sex										
Male	55.2	1.0	55.4	0.9	56.8	0.9	54.5	1.3	53.5	1.1
Female	44.8	1.0	44.7	0.9	43.2	0.9	45.5	1.3	46.5	1.1
Age										
12-17	14.8	0.4	13.2	0.4	12.8	0.4	12.1	0.4	10.8	0.4
18-25	33.7	0.9	32.8	0.8	31.2	0.9	28.7	0.9	26.9	0.8
26-34	19.7	0.7	19.3	0.9	21.9	0.9	23.1	1.0	23.2	1.0
35-49	22.1	0.9	23.6	0.9	21.0	1.0	21.5	1.1	21.4	0.9
50+	9.8	1.0	11.1	1.1	13.2	1.0	14.5	1.1	17.6	1.2
Health Insurance										
Yes	76.0	0.8	75.1	0.7	74.7	0.8	75.2	1.0	77.6	1.0
No	24.0	0.8	24.9	0.7	25.3	0.8	24.8	1.0	22.4	1.0
Marital Status										
Married	27.6	1.3	29.0	1.0	26.3	1.3	28.1	1.1	28.3	1.2
Not Married	72.4	1.3	71.0	1.0	73.7	1.3	71.9	1.1	71.7	1.2

= $p<0.05$ for comparison to 2005-2006 year group category

= $p<0.05$ for comparison to previous year group category

Table 2. Drug use among past 12 month non-medical pain reliever users

	2005-2006 N = 8,620		2007-2008 N = 8,551		2009-2010 N = 8,415		2011-2012 N = 7,633		2013-2014 N = 5,871	
	%	SE	%	SE	%	SE	%	SE	%	SE
NMPR Use Last 12 Months										
1-29 Days	66.0	1.0	64.4	0.9	62.7	1.2	62.1	1.0	59.2	1.1
30-89 Days	18.8	0.8	19.2	0.7	18.9	1.0	19.7	0.7	20.9	0.9
90+ Days	15.2	0.8	16.2	0.7	18.5	0.9	18.1	0.8	19.8	0.9
OxyContin Use Last 12 M										
None	89.5	0.6	88.3	0.6	85.5	0.7	86.6	0.8	87.7	0.7
1-29 Days	7.5	0.5	7.8	0.4	9.7	0.5	8.3	0.7	7.9	0.5
30-89 Days	1.6	0.2	2.0	0.3	2.3	0.2	2.1	0.3	1.9	0.3
90+ Days	1.3	0.2	1.9	0.3	2.5	0.3	3.0	0.3	2.5	0.3
Heroin Use Last 12 M										
None	97.5	0.3	97.4	0.3	96.3	0.4	96	0.4	94.6	0.4
1-29 Days	1.2	0.2	1.2	0.2	1.7	0.2	1.7	0.2	2.4	0.3
30-89 Days	0.2	0.1	0.4	0.1	0.9	0.2	0.6	0.1	0.7	0.1
90+ Days	1.1	0.3	0.9	0.1	1.1	0.2	1.7	0.2	2.2	0.3
Alcohol Use Last 12 M										
None	13.3	0.8	13.2	0.6	13.3	0.8	14.5	0.9	16.2	0.8
1-29 Days	22.6	0.8	21.9	0.7	22.6	0.8	24.6	0.9	22.3	0.8
30-89 Days	21.4	0.8	21.8	0.8	21.4	0.8	21.5	0.8	22.6	0.9
90+ Days	42.7	0.9	43.1	0.9	42.7	0.9	39.4	1.1	39.0	1.0
Cocaine Use Last 12 M										
None	79.8	0.6	81.2	0.7	84.0	0.6	84.9	0.5	84	0.8
1-29 Days	12.6	0.6	13.3	0.6	11.4	0.5	10.3	0.4	11.1	0.6
30-89 Days	3.6	0.3	2.6	0.3	2.4	0.3	2.5	0.3	2.7	0.3
90+ Days	4.0	0.4	2.9	0.3	2.2	0.3	2.3	0.3	2.2	0.3
Crack Use Last 12 M										
None	95.0	0.4	95.9	0.3	96.3	0.4	96.9	0.4	97.3	0.3
1-29 Days	3.0	0.3	2.4	0.2	2.0	0.3	1.8	0.2	1.2	0.2
30-89 Days	1.2	0.2	0.7	0.1	0.6	0.2	0.5	0.2	0.5	0.1
90+ Days	0.8	0.2	1.1	0.2	1.0	0.2	0.8	0.2	1.0	0.2

= $p<0.05$ for comparison to 2005-2006 year group category

= $p<0.05$ for comparison to previous year group category, i.e. 2013-2014 vs. 2011-2012

Table 2 Continued. Drug use among past 12 month non-medical pain reliever users

	2005-2006 N = 8,620		2007-2008 N = 8,551		2009-2010 N = 8,415		2011-2012 N = 7,633		2013-2014 N = 5,871	
	%	SE	%	SE	%	SE	%	SE	%	SE
Stimulant Use Last 12 M										
None	87.8	0.5	88.8	0.5	88.5	0.5	89.3	0.6	87.7	0.7
1-29 Days	7.1	0.4	6.3	0.4	6.3	0.4	6.1	0.5	6.2	0.4
30-89 Days	2.1	0.3	2.3	0.3	2.8	0.3	2.1	0.3	2.9	0.5
90+ Days	3.0	0.4	2.6	0.3	2.5	0.3	2.5	0.3	3.2	0.3
Marijuana Use Last 12 M										
None	51.6	0.9	51.7	1.0	48.8	1.0	48.8	1.2	49.3	1.1
1-29 Days	16.7	0.7	16.1	0.7	15.7	0.6	15.1	0.7	14.6	0.8
30-89 Days	7.7	0.5	7.6	0.4	8.0	0.6	7.8	0.5	7.6	0.6
90+ Days	24.0	0.6	24.5	0.7	27.4	0.9	28.3	1.1	28.5	0.9
Sedative Use Last 12 M										
None	96.4	0.4	96.9	0.3	96.0	0.4	97.8	0.3	96.9	0.4
1-29 Days	2.2	0.2	1.8	0.2	2.1	0.3	1.3	0.2	1.8	0.3
30-89 Days	0.7	0.2	0.4	0.1	1.1	0.2	0.4	0.1	0.6	0.1
90+ Days	0.7	0.2	0.9	0.2	0.7	0.2	0.5	0.1	0.7	0.2
Tranquilizer Use Last 12 M										
None	72.8	0.7	74.3	0.7	72.6	0.9	71.4	0.9	73.8	1.0
1-29 Days	17.4	0.7	16.6	0.6	17.0	0.8	17.9	0.8	16.1	0.8
30-89 Days	5.4	0.4	5.0	0.4	5.6	0.4	6.1	0.4	5.2	0.4
90+ Days	4.4	0.3	4.1	0.4	4.8	0.4	4.6	0.4	5.1	0.6
Hallucinate Use Last 12 M										
None	84.5	0.6	84.6	0.5	84.0	0.5	85.0	0.5	85.9	0.7
1-29 Days	12.7	0.5	12.9	0.5	13.6	0.5	12.4	0.5	12.3	0.6
30-89 Days	1.9	0.2	1.8	0.2	1.7	0.2	1.8	0.2	1.2	0.2
90+ Days	0.9	0.1	0.7	0.1	0.7	0.1	0.7	0.2	0.6	0.1
Inhalant Use Last 12 M										
None	93.6	0.4	93.6	0.4	93.8	0.4	94.7	0.5	95.9	0.3
1-29 Days	5.0	0.3	4.8	0.3	4.8	0.4	3.8	0.4	3.4	0.3
30-89 Days	0.7	0.1	0.9	0.1	0.7	0.1	1.0	0.3	0.5	0.1
90+ Days	0.6	0.1	0.6	0.1	0.8	0.3	0.5	0.1	0.2	0.1
Injection Drug Use Ever										
Yes	6.9	0.5	7.6	0.6	8.3	0.6	8.8	0.7	9.4	0.6
No	93.1	0.5	92.4	0.6	91.7	0.6	91.2	0.7	90.5	0.6

= $p<0.05$ for comparison to 2005-2006 year group category

= $p<0.05$ for comparison to previous year group category, i.e. 2013-2014 vs. 2011-2012

Table 3. Sample Characteristics by Non-Medical Pain Reliever (NMPR) Use and Year

	2005 N = 55,905		2006 N = 55,279		2007 N = 55,435		2008 N = 55,110		2009 N = 55,234		2010 N = 57,313		2011 N = 58,397		2012 N = 55,268		2013 N = 55,160		2014 N = 55,271	
Sample Size																				
NMPR OxyContin Users (N)	*593*		*551*		*616*		*634*		*747*		*742*		*643*		*538*		*429*		*368*	
Non-OxyContin NMPR Users (N)	*3,746*		*3,730*		*3,663*		*3,638*		*3,595*		*3,331*		*3,317*		*3,135*		*2,745*		*2,329*	
NMPR Non-Users (N)	*51,566*		*50,998*		*51,156*		*50,838*		*50,892*		*53,240*		*54,437*		*51,595*		*51,986*		*52,574*	
Variable	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
Recent Heroin Initiation																				
Non-Medical OxyContin Users (NMPR-O)	4.7	1.1	3.2	0.7	4.1	1.4	3.5	0.8	4.2	0.8	5.2	1.1	5.2	1.1	5.7	1.2	7.8	2.2	3.9	1.0
Non-OxyContin NMPR Users (NMPR-N)	0.3	0.1	0.5	0.1	0.5	0.1	0.2	0.1	0.8	0.2	0.9	0.5	0.8	0.2	0.6	0.1	0.9	0.3	2.2	0.5
No NMPR Use (NMPR-X)	0.02	0.01	0.02	0.01	0.01	0.00	0.03	0.01	0.02	0.01	0.01	0.00	0.02	0.01	0.01	0.00	0.02	0.00	0.04	0.01
Heroin Use in Past 12 Months																				
NMPR-O	10.0	1.7	11.4	3.2	11.2	2.5	11.3	2.1	13.8	1.9	13.4	2.1	17.1	2.9	18.4	3.2	18.1	2.7	15.6	2.8
NMPR-N	1.1	0.3	2.0	0.6	1.3	0.3	1.6	0.4	2.2	0.5	1.8	0.4	1.9	0.4	1.9	0.4	2.7	0.4	4.9	0.7
NMPR-X	0.06	0.01	0.08	0.02	0.03	0.01	0.06	0.02	0.08	0.02	0.08	0.02	0.08	0.02	0.07	0.02	0.06	0.01	0.14	0.02
Heavy Alcohol Use Past 12 Months																				
NMPR-O	41.0	3.4	31.4	3.1	32.4	3.1	30.5	3.0	33.1	2.7	31.3	2.8	31.5	3.2	24.3	3.5	24.8	3.0	26.9	3.9
NMPR-N	22.9	1.2	22.6	0.9	21.7	1.1	24.3	1.3	22.2	1.2	22.4	1.3	19.5	1.3	19.0	1.1	19.4	1.7	18.0	1.0
NMPR-X	5.6	0.2	6.0	0.2	5.9	0.2	6.2	0.2	6.0	0.2	5.8	0.2	5.5	0.2	5.8	0.2	5.7	0.2	5.6	0.2
Marijuana Use Past 12 Months																				
NMPR-O	74.4	3.6	75.1	2.8	73.3	3.9	76.4	3.1	79.7	2.5	75.1	2.6	76.8	3.4	74.2	3.9	68.4	4.2	69.9	3.3
NMPR-N	45.5	1.5	45.2	1.4	45.6	1.4	44.2	1.4	48.2	1.8	45.5	1.5	49.2	1.5	45.9	1.8	50.3	1.7	46.8	1.5
NMPR-X	8.5	0.2	8.3	0.2	8.1	0.2	8.4	0.2	9.3	0.2	9.7	0.2	9.6	0.2	10.3	0.2	10.8	0.2	11.9	0.2

Significantly different from 2005 at the α=0.05 level

Significantly different from previous year at the α=0.05 level

Table 3 Continued. Sample Characteristics by Non-Medical Pain Reliever (NMPR) Use and Year

Variable	2005		2006		2007		2008		2009		2010		2011		2012		2013		2014	
	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
Cocaine Use Past 12 Months																				
NMPR-O	45.4	3.4	44.4	3.1	47.2	3.9	43.4	3.7	37.2	3.0	37.8	3.1	32.8	2.6	35.9	3.4	29.4	3.4	32.8	3.5
NMPR-N	17.2	1.0	17.7	1.1	15.2	1.1	15.7	1.0	13.6	0.9	11.0	0.9	10.7	0.9	13.3	0.9	14.7	1.3	13.1	1.0
NMPR-X	1.3	0.1	1.5	0.1	1.5	0.1	1.3	0.1	1.2	0.1	1.1	0.1	0.9	0.1	1.1	0.1	1.0	0.1	1.2	0.1
Injection Drug Use Ever																				
NMPR-O	20.3	2.4	17.8	3.6	20.2	3.8	25.1	4.1	22.7	3.2	17.9	2.5	20.4	2.6	27.2	4.5	25.4	3.5	15.0	3.2
NMPR-N	5.6	0.8	5.4	0.7	6.3	1.0	4.8	0.7	6.6	1.0	6.0	0.9	5.9	0.8	7.1	1.0	8.2	1.0	7.6	0.8
NMPR-X	1.2	0.1	1.3	0.1	1.2	0.1	1.3	0.1	1.1	0.1	1.1	0.1	1.1	0.1	1.1	0.1	1.3	0.1	1.3	0.1
Race/Ethnicity																				
NMPR-O																				
White Non-Hispanic	90.6	1.4	89.1	3.0	84.0	3.4	89.0	1.6	85.2	1.7	83.4	2.2	81.6	2.5	80.3	3.0	84.1	3.6	77.5	3.0
Black Non-Hispanic	0.7	0.2	2.2	1.2	6.8	3.1	3.4	1.4	3.6	1.0	4.6	1.2	6.1	1.5	4.4	1.6	3.4	1.7	5.9	1.7
Hispanic	5.4	1.4	7.2	2.9	4.7	1.3	4.4	1.1	8.2	1.4	6.0	1.4	8.7	1.9	10.0	2.1	9.5	2.7	10.1	2.0
All Other	3.3	0.8	1.6	0.6	4.6	1.6	3.3	0.7	3.0	0.8	5.4	1.5	3.6	0.8	5.5	1.2	3.0	0.7	6.5	1.6
NMPR-N																				
White Non-Hispanic	71.4	1.3	71.2	1.6	71.9	1.6	72.4	1.0	72.4	1.3	67.3	1.4	67.6	1.6	63.7	1.7	64.0	1.7	61.6	1.2
Black Non-Hispanic	10.2	0.9	9.1	0.9	10.0	0.9	10.5	0.8	9.5	0.9	9.9	1.0	10.0	0.8	13.6	1.3	11.0	1.1	15.0	1.0
Hispanic	13.9	1.2	14.8	1.1	13.2	1.1	11.7	0.9	12.8	1.0	16.7	1.3	17.2	1.4	17.5	1.4	17.9	1.5	17.4	1.0
All Other	4.6	0.7	4.9	0.6	4.9	0.6	5.4	0.7	5.3	0.8	6.2	1.2	5.3	0.7	5.2	0.7	7.1	0.9	6.0	0.8
NMPR-X																				
White Non-Hispanic	68.8	0.6	68.2	0.6	67.9	0.5	67.5	0.5	67.1	0.5	66.9	0.4	65.5	0.5	65.2	0.5	64.7	0.5	64.2	0.5
Black Non-Hispanic	11.9	0.3	12.0	0.3	11.9	0.4	11.9	0.3	12.1	0.3	12.1	0.3	11.9	0.3	11.8	0.4	12.0	0.4	11.9	0.3
Hispanic	13.2	0.4	16.6	0.4	13.9	0.4	14.2	0.3	14.4	0.4	14.5	0.3	15.3	0.4	15.4	0.4	15.7	0.3	16.0	0.4
All Other	6.1	0.3	6.2	0.3	6.2	0.2	6.4	0.2	6.4	0.3	6.6	0.3	7.4	0.3	7.6	0.3	7.6	0.3	8.0	0.3

Significantly different from 2005 at the α=0.05 level

Significantly different from previous year at the α=0.05 level

Table 3 Continued. Sample Characteristics by Non-Medical Pain Reliever (NMPR) Use and Year

Variable	2005		2006		2007		2008		2009		2010		2011		2012		2013		2014	
	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
Sex (% Male)																				
NMPR-O	59.0	3.8	55.5	4.2	58.2	3.9	60.6	3.1	61.4	3.1	56.8	3.1	61.1	2.8	62.0	2.8	65.6	3.3	56.5	3.3
NMPR-N	52.8	1.5	57.1	1.4	55.4	1.1	54.2	1.5	55.2	1.3	57.8	1.7	52.9	1.8	53.9	2.0	51.1	1.9	53.7	1.3
NMPR-X	48.2	0.5	48.1	0.4	48.1	0.4	48.2	0.5	48.2	0.4	48.2	0.5	48.1	0.4	48.1	0.4	48.2	0.4	48.2	0.3
Age																				
NMPR-O																				
12-17	15.4	1.7	16.2	1.8	15.6	1.6	15.0	1.6	13.9	1.5	12.9	1.4	13.9	1.6	11.6	1.5	9.9	1.2	14.0	1.6
18-25	45.4	3.1	45.1	3.5	40.4	3.7	40.4	3.3	45.9	2.9	39.9	2.8	37.7	2.9	37.2	2.9	33.0	3.8	32.2	3.3
26-34	19.1	2.9	14.4	2.3	19.3	3.5	22.9	3.4	19.6	2.9	24.4	3.3	25.0	2.9	23.0	3.4	26.6	3.7	23.8	3.3
35+	15.3	3.0	16.6	3.3	15.2	3.1	18.2	4.3	11.9	2.6	16.7	2.7	16.1	2.8	14.0	2.9	17.0	3.1	17.3	3.0
50+	4.8	3.8	7.7	3.7	9.4	3.9	3.5	1.6	8.8	2.7	6.0	2.5	7.3	3.1	14.2	4.4	13.5	4.4	12.7	4.3
NMPR-N																				
12-17	14.8	0.7	14.5	0.5	13.0	0.6	12.8	0.6	13.2	0.7	12.1	0.6	13.8	0.7	10.4	0.6	10.1	0.6	11.3	0.6
18-25	33.2	1.0	31.5	1.2	31.5	1.1	32.1	1.2	29.9	1.1	28.5	1.1	28.7	1.2	26.2	1.3	27.3	1.2	24.9	1.1
26-34	19.4	1.1	20.6	1.2	18.7	1.2	19.5	1.1	21.0	1.1	22.7	1.6	23.7	1.4	22.4	1.6	23.9	1.9	21.9	1.2
35-49	20.9	1.4	24.5	1.2	24.8	1.4	24.1	1.4	22.2	1.4	22.1	1.4	21.2	1.8	23.7	1.4	22.5	1.6	21.6	1.2
50+	11.7	1.6	8.9	1.2	12.0	1.6	11.5	1.5	13.7	1.6	14.7	1.6	12.6	1.8	17.3	1.9	16.3	2.0	20.3	1.8
NMPR-X																				
12-17	10.2	0.2	10.1	0.1	10.0	0.1	9.8	0.1	9.6	0.1	9.5	0.1	9.5	0.1	9.5	0.1	9.5	0.1	9.3	0.1
18-25	12.3	0.2	12.3	0.2	12.2	0.2	12.2	0.2	12.4	0.2	12.6	0.2	12.6	0.2	12.6	0.2	12.6	0.2	12.7	0.2
26-34	14.1	0.2	14.0	0.2	14.0	0.3	14.0	0.3	14.0	0.3	14.0	0.3	13.7	0.3	13.8	0.3	13.8	0.3	14.0	0.2
35-49	27.3	0.4	26.5	0.4	26.5	0.4	26.0	0.3	25.7	0.4	24.9	0.3	24.0	0.3	23.5	0.4	23.2	0.4	22.8	0.3
50+	36.1	0.6	37.2	0.5	37.3	0.6	38.1	0.5	38.4	0.5	39.1	0.5	40.3	0.5	40.7	0.5	40.9	0.5	41.2	0.4

Significantly different from 2005 at the α=0.05 level

Significantly different from previous year at the α=0.05 level

Table 3 Continued. Sample Characteristics by Non-Medical Pain Reliever (NMPR) Use and Year

Variable	2005		2006		2007		2008		2009		2010		2011		2012		2013		2014	
	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
Income																				
NMPR-O																				
<25,000	26.4	3.0	28.5	3.4	22.0	2.5	21.9	2.0	30.4	3.6	24.5	2.7	19.3	2.1	27.5	2.9	27.5	3.7	25.3	2.7
25,000-49,999	33.9	3.2	31.7	3.1	32.1	3.6	36.6	3.6	33.6	3.6	37.9	2.6	36.6	3.0	37.7	3.8	27.1	3.8	33.2	2.8
50,000-75,000	15.4	2.2	13.7	2.3	18.0	2.9	12.6	2.2	12.6	1.9	10.5	1.7	18.3	2.8	11.1	1.7	18.1	3.9	15.1	3.3
75,000+	24.3	3.5	26.1	3.4	27.9	3.1	28.8	3.6	23.4	2.4	27.1	3.0	25.8	2.9	23.7	4.0	27.3	3.1	26.4	3.5
NMPR-N																				
<25,000	24.9	1.1	24.2	1.0	24.2	1.2	21.2	1.0	24.0	1.2	24.0	1.5	26.1	1.4	23.8	1.4	25.4	1.3	25.5	1.3
25,000-49,999	37.8	1.3	34.2	1.4	36.2	1.5	34.0	1.7	33.9	1.5	35.5	1.6	37.7	1.7	34.3	1.4	34.1	1.9	33.0	1.4
50,000-75,000	14.7	1.1	17.9	1.0	15.8	1.0	18.8	1.2	14.2	1.1	16.1	1.1	16.1	1.3	14.8	1.0	15.3	1.3	16.5	1.0
75,000+	22.5	1.5	23.6	1.3	23.7	1.2	26.1	1.5	27.9	1.7	24.3	1.2	20.1	1.4	27.1	1.5	25.2	1.6	25.0	1.2
NMPR-X																				
<25,000	18.7	0.4	18.8	0.4	17.8	0.4	16.6	0.3	17.1	0.4	18.3	0.4	18.9	0.4	18.6	0.3	18.0	0.4	17.8	0.3
25,000-49,999	34.4	0.5	34.5	0.4	32.7	0.5	32.3	0.4	32.5	0.4	33.2	0.5	32.2	0.3	32.5	0.5	31.2	0.4	30.7	0.4
50,000-75,000	18.4	0.3	17.6	0.2	18.4	0.4	18.5	0.3	17.4	0.3	17.0	0.3	17.1	0.3	16.7	0.3	17.2	0.4	16.5	0.3
75,000+	28.5	0.5	29.1	0.4	31.1	0.7	32.6	0.5	33.0	0.6	31.5	0.6	31.9	0.5	32.2	0.5	33.6	0.6	34.9	0.5
Married																				
NMPR-O	15.1	3.1	11.6	3.0	19.7	4.8	21.7	4.4	9.6	1.9	14.6	2.5	18.3	3.0	24.3	4.5	19.4	4.2	19.3	3.5
NMPR-N	29.0	1.7	29.5	1.7	29.6	1.5	30.6	1.8	29.7	1.8	27.6	1.8	26.8	1.5	31.2	2.0	30.0	1.9	29.2	1.7
NMPR-X	51.6	0.4	50.9	0.4	50.9	0.4	50.6	0.4	50.4	0.5	48.7	0.5	48.8	0.5	48.5	0.5	48.0	0.4	47.8	0.4
Health Insurance																				
NMPR-O	68.8	3.2	66.5	3.9	76.8	2.5	64.8	4.2	63.1	3.6	71.2	2.8	72.8	3.1	72.0	3.4	72.9	4.2	77.1	3.3
NMPR-N	78.1	1.3	75.9	1.1	74.5	1.2	76.8	1.3	75.9	1.1	75.9	1.5	74.7	1.6	76.4	1.5	75.4	1.7	79.7	1.2
NMPR-X	86.2	0.3	85.8	0.2	85.7	0.4	85.9	0.3	85.2	0.3	84.3	0.3	84.8	0.3	85.0	0.3	85.3	0.3	88.2	0.2

Significantly different from 2005 at the α=0.05 level

Significantly different from previous year at the α=0.05 level

Table 4. Unadjusted ORs and 95% CIs for Heroin Initiation in Past 12 Months and Heroin Use in Past 12 Months Independent Variables Stratified by Non-Medical Pain Reliever (NMPR) User Type

Variable	Recent Heroin Initiation									Heroin Use in Last 12 Months								
	Non-Medical OxyContin Users			Non-OxyContin NMPR Users			No NMPR Use			Non-Medical OxyContin Users			Non-OxyContin NMPR Users			No NMPR Use		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Year																		
2005	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
2006	0.67	0.33	1.37	1.53	0.64	3.66	1.00	0.45	2.27	1.16	0.54	2.52	1.82	0.76	4.34	1.30	0.71	2.37
2007	0.87	0.40	1.90	1.57	0.65	3.79	0.45	0.18	1.14	1.14	0.62	2.09	1.18	0.57	2.46	0.46	0.23	0.91
2008	0.74	0.37	1.47	0.58	0.24	1.42	1.36	0.52	3.55	1.14	0.65	2.01	1.44	0.70	2.96	1.08	0.57	2.05
2009	0.88	0.47	1.68	2.23	0.93	5.33	1.05	0.40	2.71	1.44	0.90	2.33	1.96	1.01	3.80	1.29	0.69	2.42
2010	1.12	0.65	1.95	2.56	0.71	9.30	0.49	0.19	1.25	1.40	0.87	2.23	1.64	0.91	2.96	1.29	0.66	2.50
2011	1.12	0.54	2.32	2.30	0.97	5.43	0.94	0.35	2.55	1.86	1.04	3.32	1.71	0.89	3.31	1.32	0.70	2.48
2012	1.22	0.62	2.40	1.70	0.72	4.01	0.48	0.19	1.21	2.04	1.12	3.69	1.70	0.94	3.06	1.23	0.70	2.18
2013	1.73	0.82	3.63	2.58	1.06	6.29	0.74	0.34	1.63	1.99	1.24	3.17	2.41	1.37	4.25	0.92	0.56	1.54
2014	0.82	0.40	1.69	6.69	3.08	14.56	1.59	0.70	3.59	1.67	0.96	2.91	4.54	2.62	7.86	2.30	1.37	3.85
Heavy Alcohol Use Past 12 M																		
Yes	0.96	0.72	1.30	1.63	1.09	2.44	4.95	3.03	8.07	0.92	0.70	1.21	1.62	1.17	2.24	3.48	2.50	4.84
No	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Marijuana Use Past 12 Months																		
Yes	2.68	1.57	4.58	10.75	6.14	18.82	39.51	22.73	68.67	2.45	1.80	3.34	3.89	2.68	5.66	14.72	10.69	20.27
No	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Cocaine Use Past 12 Months																		
Yes	4.93	3.51	6.93	6.37	4.25	9.56	70.22	47.25	104.36	5.15	3.81	6.96	10.37	7.42	14.50	89.13	67.10	118.40
No	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Injection Drug Use Ever																		
Yes	2.52	1.76	3.61	9.41	6.26	14.12	46.57	30.39	71.36	10.85	8.07	14.59	28.59	21.50	38.03	87.02	65.61	115.43
No	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-

Significant Odds Ratio at the α=0.05 level

Table 4 Continued. Unadjusted ORs and 95% CIs for Heroin Initiation in Past 12 Months and Heroin Use in Past 12 Months Independent Variables Stratified by Non-Medical Pain Reliever (NMPR) User Type

Variable	Recent Heroin Initiation									Heroin Use in Last 12 Months								
	Non-Medical OxyContin Users			Non-OxyContin NMPR Users			No NMPR Use			Non-Medical OxyContin Users			Non-OxyContin NMPR Users			No NMPR Use		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Race/Ethnicity																		
White Non-Hispanic	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Black Non-Hispanic	0.15	0.03	0.64	0.47	0.17	1.31	0.11	0.04	0.34	0.58	0.23	1.48	1.02	0.64	1.62	2.00	1.40	2.85
Hispanic	0.65	0.37	1.15	0.57	0.32	1.00	1.04	0.58	1.84	1.16	0.63	2.12	0.98	0.61	1.56	1.48	0.96	2.27
All Other	0.98	0.48	2.01	0.67	0.31	1.45	0.62	0.27	1.45	0.63	0.35	1.15	0.50	0.28	0.90	0.80	0.43	1.51
Sex																		
Male	1.19	0.86	1.63	1.47	1.00	2.17	2.33	1.48	3.66	1.91	1.53	2.38	1.94	1.44	2.61	1.82	1.32	2.50
Female	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Age																		
12-17	0.66	0.48	0.90	0.62	0.41	0.93	0.60	0.46	0.78	0.37	0.27	0.50	0.40	0.28	0.58	0.32	0.23	0.43
18-25	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
26-34	0.80	0.52	1.23	0.63	0.38	1.05	0.65	0.46	0.90	1.29	0.95	1.74	1.40	1.03	1.90	0.96	0.68	1.34
35-49	0.23	0.09	0.56	0.34	0.17	0.66	0.24	0.14	0.41	0.76	0.50	1.16	0.77	0.54	1.10	0.54	0.39	0.74
50+	0.04	0.01	0.30	0.25	0.05	1.18	0.14	0.03	0.60	0.76	0.32	1.79	0.83	0.42	1.63	0.20	0.12	0.33
Income																		
<25,000	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
25,000-49,999	0.90	0.62	1.31	0.74	0.44	1.25	0.47	0.28	0.79	0.70	0.50	0.98	0.79	0.54	1.15	0.36	0.26	0.50
50,000-74,999	0.76	0.46	1.27	0.69	0.38	1.27	0.34	0.19	0.62	0.61	0.36	1.04	0.49	0.35	0.68	0.21	0.15	0.31
75,000+	1.20	0.77	1.86	0.47	0.25	0.87	0.19	0.11	0.34	0.71	0.48	1.04	0.45	0.31	0.66	0.15	0.10	0.22
Marital Status																		
Married	0.18	0.08	0.39	0.18	0.09	0.35	0.03	0.01	0.08	0.43	0.27	0.67	0.29	0.19	0.45	0.16	0.10	0.25
Not Married	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Health Insurance																		
Yes	1.02	0.68	1.52	0.67	0.45	1.00	0.37	0.24	0.59	0.58	0.42	0.82	0.51	0.38	0.68	0.27	0.20	0.36
No	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-

Significant Odds Ratio at the α=0.05 level

Table 5. Adjusted ORs and 95% CIs for Heroin Initiation in Past 12 Months and Heroin Use in Past 12 Months Independent Variables Stratified by Non-Medical Pain Reliever (NMPR) User Type

Variable	Recent Heroin Initiation									Heroin Use in Past 12 Months								
	Non-Medical OxyContin Users			Non-OxyContin NMPR Users			No NMPR Use			Non-Medical OxyContin Users			Non-OxyContin NMPR Users			No NMPR Use		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Year																		
2005	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
2006	0.72	0.34	1.53	1.51	0.61	3.77	1.03	0.43	2.48	1.24	0.59	2.59	1.74	0.72	4.22	1.30	0.62	2.72
2007	0.95	0.45	2.01	1.70	0.69	4.18	0.45	0.18	1.14	1.31	0.66	2.58	1.35	0.66	2.79	0.41	0.19	0.91
2008	0.77	0.39	1.52	0.66	0.26	1.66	1.92	0.72	5.12	1.24	0.71	2.19	2.04	0.93	4.49	1.57	0.74	3.34
2009	1.02	0.54	1.92	2.63	1.06	6.52	1.24	0.44	3.46	1.59	0.87	2.90	2.42	1.26	4.65	1.75	0.86	3.58
2010	1.34	0.78	2.31	3.31	0.97	11.34	0.60	0.21	1.66	2.06	1.16	3.68	2.21	1.30	3.74	1.84	0.81	4.16
2011	1.43	0.65	3.17	2.75	1.14	6.67	1.23	0.44	3.46	2.86	1.52	5.39	2.62	1.35	5.06	2.05	0.98	4.27
2012	1.42	0.71	2.87	2.03	0.84	4.91	0.56	0.22	1.39	2.23	1.26	3.96	1.98	1.03	3.78	1.77	0.91	3.47
2013	2.29	1.07	4.92	2.72	1.11	6.66	0.78	0.35	1.73	2.52	1.40	4.52	2.60	1.56	4.32	1.17	0.64	2.13
2014	1.06	0.50	2.25	7.48	3.42	16.38	1.66	0.70	3.92	3.03	1.65	5.57	5.80	3.19	10.52	3.09	1.60	5.95
Heavy Alcohol Use Past 12 M																		
Yes	0.64	0.46	0.89	0.78	0.50	1.22	0.77	0.41	1.45	0.64	0.46	0.88	0.69	0.47	0.99	0.63	0.40	0.99
No	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Marijuana Use Past 12 Months																		
Yes	1.45	0.81	2.59	4.78	2.60	8.80	9.28	4.43	19.46	2.18	1.36	3.49	1.59	1.01	2.49	2.75	1.59	4.76
No	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Cocaine Use Past 12 Months																		
Yes	3.82	2.59	5.62	3.12	2.08	4.67	7.69	4.05	14.49	4.99	3.57	7.14	6.76	4.59	10.00	16.67	9.90	27.78
No	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Injection Drug Use Ever																		
Yes	2.65	1.75	4.01	6.73	3.83	11.83	17.04	9.36	31.00	12.39	9.08	16.91	23.85	17.63	32.24	35.70	23.77	53.62
No	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-

Significant Odds Ratio at the α=0.05 level

Table 5 Continued. Adjusted ORs and 95% CIs for Heroin Initiation in Past 12 Months and Heroin Use in Past 12 Months Independent Variables Stratified by Non-Medical Pain Reliever (NMPR) User Type

Variable	Recent Heroin Initiation									Heroin Use in Past 12 Months								
	Non-Medical OxyContin Users			Non-OxyContin NMPR Users			No NMPR Use			Non-Medical OxyContin Users			Non-OxyContin NMPR Users			No NMPR Use		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Race/Ethnicity																		
White Non-Hispanic	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Black Non-Hispanic	0.26	0.06	1.12	0.70	0.25	1.95	0.09	0.03	0.30	1.19	0.49	2.89	2.10	1.26	3.50	2.11	1.39	3.21
Hispanic	0.56	0.32	0.98	0.69	0.39	1.22	0.85	0.44	1.65	1.00	0.56	1.80	1.58	1.00	2.48	1.46	0.91	2.35
All Other	1.03	0.52	2.05	0.85	0.37	1.93	0.66	0.27	1.61	0.68	0.32	1.43	0.67	0.31	1.47	0.97	0.51	1.84
Sex																		
Male	1.07	0.77	1.50	1.13	0.74	1.73	1.61	0.99	2.60	1.65	1.24	2.20	1.43	1.03	1.97	1.21	0.81	1.79
Female	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Age																		
12-17	0.88	0.64	1.21	1.09	0.70	1.71	1.32	0.84	2.10	0.60	0.43	0.84	0.72	0.48	1.07	0.83	0.58	1.19
18-25	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
26-34	0.84	0.53	1.34	0.63	0.35	1.14	0.43	0.16	1.14	1.01	0.69	1.46	1.26	0.86	1.85	1.03	0.69	1.56
35-49	0.32	0.12	0.82	0.49	0.23	1.07	0.50	0.22	1.13	0.68	0.40	1.14	0.69	0.43	1.10	0.77	0.49	1.22
50+	0.06	0.01	0.46	0.38	0.06	2.25	0.10	0.02	0.54	0.64	0.30	1.36	0.76	0.36	1.60	0.42	0.20	0.88
Income																		
<25,000	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
25,000-49,999	1.08	0.71	1.65	0.92	0.52	1.64	0.78	0.46	1.32	0.92	0.62	1.36	0.95	0.60	1.49	0.65	0.46	0.93
50,000-74,999	0.88	0.52	1.48	1.04	0.51	2.11	0.71	0.38	1.31	1.02	0.62	1.69	0.84	0.53	1.32	0.53	0.35	0.81
75,000+	1.47	0.94	2.29	0.70	0.35	1.37	0.41	0.22	0.76	1.28	0.83	1.99	0.94	0.58	1.52	0.46	0.30	0.70
Marital Status																		
Married	0.32	0.13	0.77	0.43	0.19	0.97	0.13	0.05	0.36	0.48	0.28	0.85	0.46	0.28	0.77	0.42	0.24	0.75
Not Married	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-
Health Insurance																		
Yes	1.27	0.84	1.90	0.93	0.61	1.40	0.93	0.54	1.59	0.90	0.64	1.26	0.84	0.58	1.22	0.70	0.50	0.99
No	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-	REF	-	-

Significant Odds Ratio at the α=0.05 level

FIGURES

Figure 1: Percentage of past 12 month non-medical prescription opioid users reporting race/ethinicty as category other than 'white non-Hispanic'

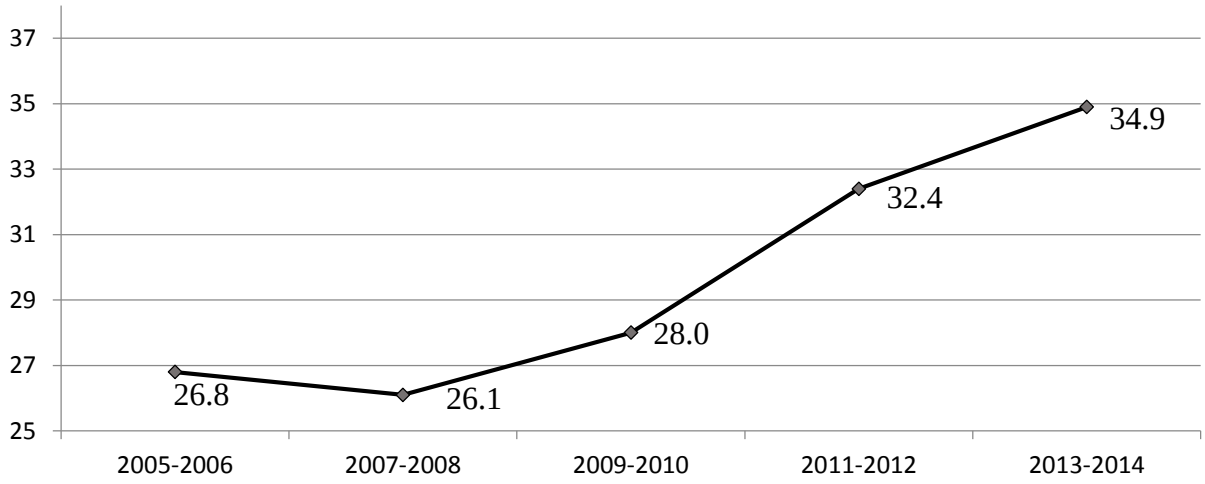


Figure 2: Percentage of past 12 month non-medical prescription opioid users by age category

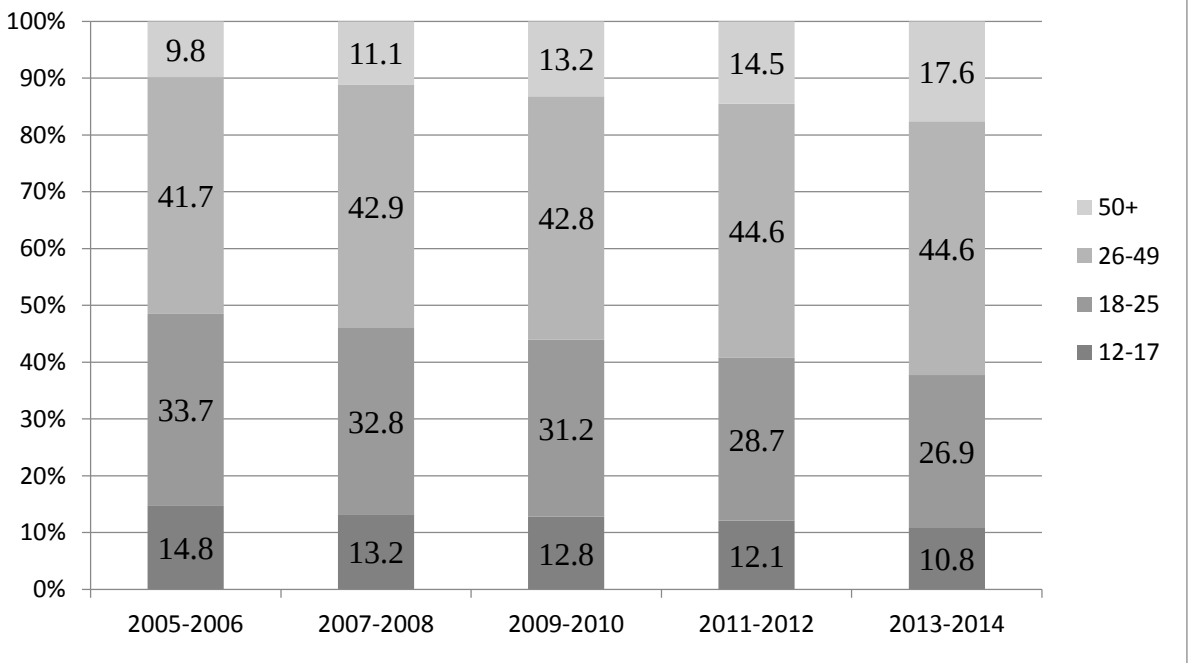


Figure 3: Frequency of non-medical prescription opioid use among past 12 month non-medical prescription opioid users

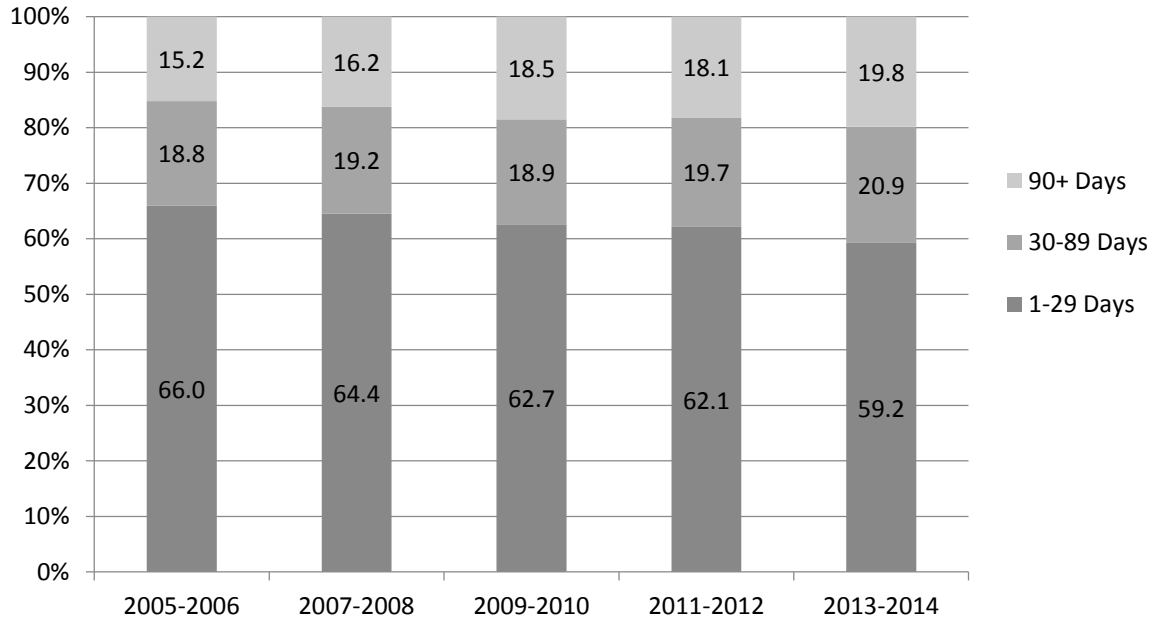


Figure 4: Percentage of past 12 month non-medical prescription opioid users using OxyContin in the past 12 months

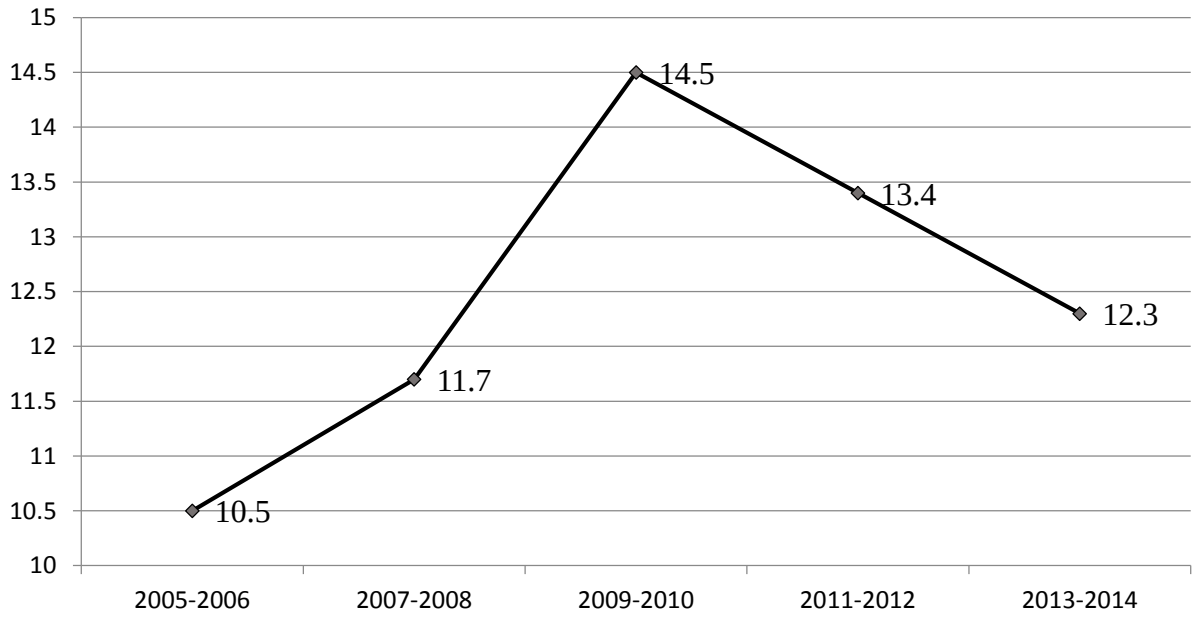


Figure 5: Percentage of past 12 month non-medical prescription opioid users using heroin in past 12 months

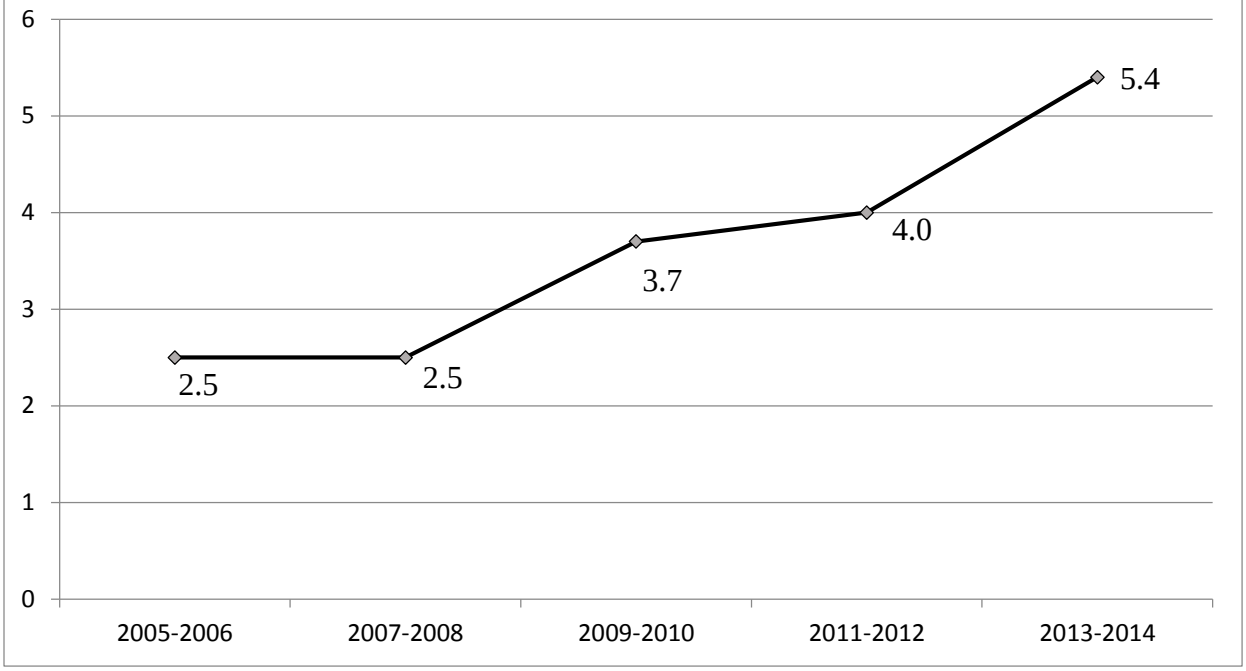


Figure 6: Percentage of past 12 month non-medical prescription opioid users using cocaine in past 12 months

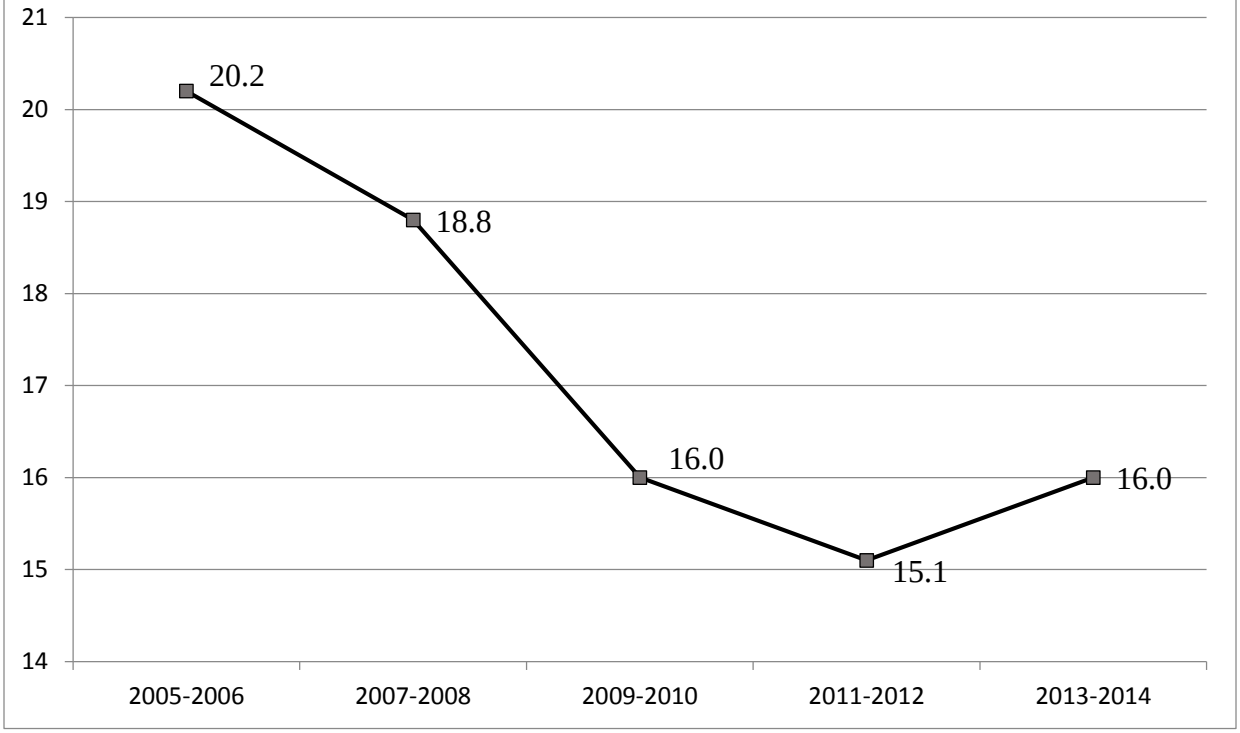
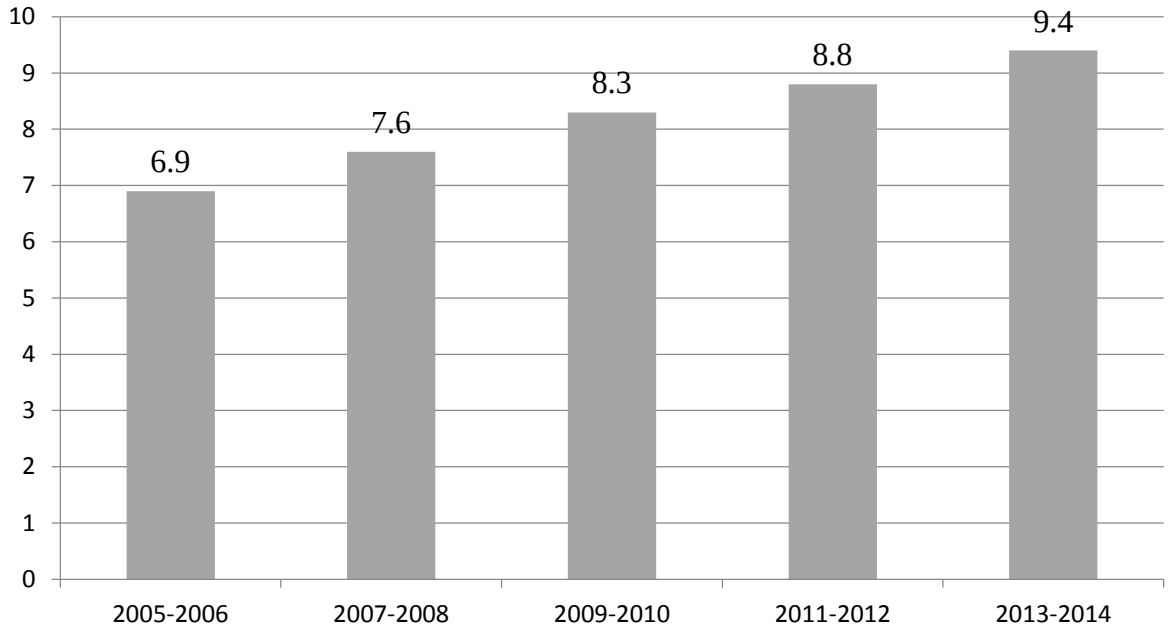


Figure 7: Percentage of past 12 month non-medical prescription opioid users reporting ever injecting drugs



APPENDIX A: ACRONYM GUIDE

ACA	Affordable Care Act
CI	Confidence Interval
DEA	U.S. Drug Enforcement Agency
ER	Extended-Release
ER-OC	Extended-Release OxyContin
ICPSR	Inter-university Consortium for Political and Social Research
KASPER	Kentucky All Schedule Prescription Electronic Reporting System
NASPER	National All Schedule Prescription Electronic Reporting Act of 2005
NMPR	Non-Medical Pain Reliever
NMPR-N	Non-Medical Pain Reliever Users Not Using OxyContin in Past 12 Months
NMPR-O	Non-Medical Pain Reliever Users Using OxyContin in Past 12 Months
NMPR-X	Non-Users of Non-Medical Pain Relievers in Past 12 Months
NSDUH	National Survey on Drug Use and Health
OMB	Office of Management and Budget
OR	Odds Ratio
PDMP	Prescription Drug Monitoring Program
RADARS	Researched, Abuse, Diversion and Addiction-Related Surveillance
SAMHSA	Substance Abuse and Mental Health Services Administration
SE	Standard Error
TEDS	Treatment Episode Data Set