12-1-2014

Characteristics of Unintentional Prescription Drug Poisoning Admissions Clark County, Nevada 2009-2013

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CHARACTERISTICS OF UNINTENTIONAL PRESCRIPTION DRUG POISONING ADMISSIONS CLARK COUNTY, NEVADA 2009-2013

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2000

A thesis submitted in partial fulfillment
of the requirements for the

Master of Public Health

School of Community Health Sciences
Division of Health Sciences
The Graduate College

University of Nevada, Las Vegas
December 2014

UNLV | GRADUATE COLLEGE

We recommend the thesis prepared under our supervision by

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entitled

Characteristics of Unintentional Prescription Drug Poisoning Admissions, Clark County, Nevada, 2009-2013

is approved in partial fulfillment of the requirements for the degree of

Master of Public Health - Public Health

School of Community Health Sciences

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December 2014

ABSTRACT

Prescription drug abuse has been the fastest growing drug problem in the United States in recent years, and is the second most commonly abused category of illegal and illicit drugs, after marijuana (SAMHSA, 2013; Carnevale, 2011). Reducing the morbidity and mortality associated with prescription drug abuse in challenging because multiple factors contribute to the problem. Prescribing behaviors and the lack of education among providers and pharmacists along with inadequate counseling and monitoring of patients prescribed pain medication are important factors (Machikanti, 2007; Okie, 2010). Patients' misuse or abuse, diversion or the sharing or sell of pills, and doctor shopping are also contribute to the problem (Okie, 2010). Where they exist, prescription drug monitoring programs are underfunded and ineffective, and there are no established national prescription monitoring programs (Manchikanti, 2007) or substance abuse treatment guidelines for prescription pain relievers. Additionally, nonmedical use, including diversion, is deviant behavior driven by a range of physical, mental and social health problems. Gilson and Kreis suggest that the problem can be effectively mitigated by the development of novel opioid formulations that reduce non medical use, improvements in prescription drug monitoring programs and a better, more accurate understanding of the problem (Gilson and Kreis, 2009). Implementing strategies that target populations at greatest risk requires collaboration among local, state, federal, tribal health entities along with community partners. Further defining populations at greatest risk is critical for development and implementation of effective interventions (JAMA, 2012).

This study aims to contribute to the understanding of the problem by describing the characteristics of persons who experienced an unintentional drug poisoning admission

Clark County, Nevada between 2009 and 2013. This research will help to better define the population that might benefit from targeted risk reduction education and monitoring to prevent continued drug seeking and use behaviors that may lead to continued morbidity and eventual mortality.

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CHAPTER 1
INTRODUCTION and PURPOSE

Drug overdose deaths have become the leading cause of injury death in the United States (CDC, 2014). This is, in large part, thought to be a consequence of more aggressive treatment of acute and chronic pain during the 1990s and the concurrent emergence and explosion of prescription drug abuse over the past two decades. In 2007, the U.S. witnessed approximately 27,000 unintentional drug overdose deaths, equating to one every 19 minutes (CDC, 2012). In 2012, approximately nine of every ten poisonings were caused by drugs and, of these, opioid analgesic pain relievers were involved in more fatal poisonings than any other drug, including cocaine and heroin (CDC-NCHS, 2012). According to the Centers for Disease Control and Prevention (CDC), forty-six people die every day from prescription painkillers (CDC, 2011). The trend in mortality mirrors both the increase in the medical use of pain analgesics and the trend in substance abuse among Americans. Hydrocodone is the most frequently prescribed drug in the U.S.; 120 million prescriptions were issued from 2005-2006 (Manchikanti and Singh, 2008).

Prescription drug abuse has been the fastest growing drug problem in the United States in recent years, and is the second most commonly abused category of illegal and illicit drugs, after marijuana (SAHMSA, 2013; Carnevale, 2011). Between 1992 and 2003, a period that witnessed a 14% population increase, the number of people abusing controlled prescription drugs rose 81%, significantly more than the increase in the number of people abusing marijuana (2 times more), cocaine (5 times more) and heroin (60 times more) (Manchikanti, 2007). By 2008, although Americans only comprised

4.6% of the world population, the nation was consuming 80% of the global opioid supply, 99% of the world's hydrocodone, and two-thirds of illegal drugs globally (Manchikanti and Singh, 2008). Many studies have demonstrated that both the use of prescription drugs such as opioid analgesics and benzodiazepines, and overdoses involving them have increased dramatically in the United States since the 1990s. CDC reports that 113 people die and nearly 7,000 are treated in emergency rooms each day as a result of drug overdose of which approximately 9 of 10 are attributed to prescription drugs (CDC, 2014).

The epidemic of prescription drug abuse has great health, social and economic costs. In addition to the concern for increased mortality related to prescription drug abuse, people who abuse these drugs are at increased risk of unintentional injury, crime-related injury and suicide (CDC, 2011).

Reducing the morbidity and mortality associated with prescription drug abuse in challenging because multiple factors contribute to the problem. Prescribing behaviors and the lack of education among providers and pharmacists along with inadequate counseling and monitoring of patients prescribed pain medication are important factors (Machikanti, 2007; Okie, 2010). Patients' misuse or abuse, diversion or the sharing or sell of pills, and doctor shopping are also contribute to the problem (Okie, 2010). Where they exist, prescription drug monitoring programs are underfunded and ineffective, and there are no established national prescription monitoring programs (Manchikanti, 2007) or substance abuse treatment guidelines for prescription pain relievers. Additionally, nonmedical use, including diversion, is deviant behavior driven by a range of physical, mental and social health problems. Gilson and Kreis suggest that

the problem can be effectively mitigated by the development of novel opioid formulations that reduce non medical use, improvements in prescription drug monitoring programs and a better, more accurate understanding of the problem (Gilson and Kreis, 2009). Implementing strategies that target populations at greatest risk requires collaboration among local, state, federal, tribal health entities along with community partners. Further defining populations at greatest risk is critical for development and implementation of effective interventions (JAMA, 2012).

This study aims to contribute to the understanding of the problem by describing the characteristics of persons who experienced an unintentional drug poisoning admission Clark County, Nevada between 2009 and 2013. This research will help to better define the population that might benefit from targeted risk reduction education and monitoring to prevent continued drug seeking and use behaviors that may lead to continued morbidity and eventual mortality.

CHAPTER 2
BACKGROUND AND SIGNIFICANCE

Drugs of Concern

Pharmaceutical drug abuse is primarily associated with opioid pain analgesics, sedatives and depressants. Accounting for 74% (16,917) of the 22,810 prescription drug related (DR) deaths in the U.S. in 2011 (CDC web), opioid pain analgesics are the predominant drugs of concern. Medications in this class include hydrocodone (ie. Vicodin), oxycodone (ie. Oxycontin, Percoset), morphine (eg. Kadian) and codeine (NIH, 2011). The Drug Enforcement Administration (DEA) categorizes drugs based on the drug's accepted medical use and its potential for abuse and dependency (DEA website). Categories range from Schedule I, drugs with no medical use to Schedule V drugs, drugs with limited quantities of certain narcotics and low potential for abuse. Non-combination opiates – morphine, codeine, hydromorphone and oxycodone - fall into the DEA's Schedule II category, drugs categorized by high abuse potential and severe dependence liability.

When taken as prescribed, the Schedule II pain medications are effective in reducing the perception of pain; however, because the drugs can produce other symptoms such as drowsiness, mental confusion and, in some, a euphoric response, the drugs are often used for non-medical reasons. People who abuse OxyContin may snort or inject it. The illicit use of these drugs is increasing at epidemic proportions (Manchikanti, Whitfield and Pallone, 2005). Nonmedical use increases risk for serious medical complications, including overdose (NIH website, 2011).

In addition to the opioid pain relievers, benzodiazepines, commonly known as sedatives, are contributory and often used concomitantly with opioid pain medications. According to CDC, benzodiazepines are frequently found among people treated in EDs for misusing or abusing drugs and they are often detected in combination with opioids in people who died of drug overdose (CDC, 2012).

Medical Use

Prescription drugs such as narcotic analgesics, anxiolytics, antidepressants, stimulants and sedative-hypnotics play an important role in the management of chronic pain and other conditions. Historically, long-term opioid pain therapy was avoided for two reasons: 1) the fear that chronic use would lead to a high risk of addiction and 2) the belief that opioids are not effective in the treatment of chronic, neuropathic pain (Ballantyne, 2012). Throughout the 1980s and 90s, concern around the under treatment of pain and the collective belief in both the efficacy of use in the treatment of acute and cancer pain allowed for the consideration of treatment of other forms of pain that were thought to be risky because of the fears of addiction (Manchikanti and Singh, 2008). Despite some fears, physicians began to apply their experience in palliative care to the treatment of chronic non-cancer pain, creating a paradigm shift that led to the promotion and permissive use of opioids for the treatment of chronic pain in the U.S. (Ballantyne, 2012).

One in five Americans is prescribed an opioid medication each year (CCOME presentation; data from Stobbe, 2009). Addiction and diversion (the use of prescription drugs for recreational purposes) of prescription pain medications are critical public health issues in the United States today, but, for many, these medications effectively

treat pain and improve quality of life (Okie, 2007). Due to the growing knowledge of adverse consequences related to the medical use of opioids, physicians in the United States are increasingly faced with the dilemma of prescribing medications that have the potential for abuse and diversion along with the possible under-treatment of pain in their patients (Manchikanti, 2005). Patients using these drugs often have a combination of painful conditions, substance abuse, and other forms of mental illness (Paulozzi, Weisler and Patkar, 2011). These medications are used in the treatment of cancer and non-cancer pain. In a study about opioid use in the treatment of long-term non-cancer pain, Boudreau et al., found that the most common diagnoses at index visit (first RX in 6 months) were back pain, extremity pain, and osteoarthritis (Boudreau et al., 2009).

Retail sales of opioid medications increased dramatically from 1997-2005 (Manchikanti, 2007). Since 1990, medical use increased by a factor of 10. This increase was in part influenced by the approval and aggressive marketing of Oxycontin, an extended release form of oxycodone (Okie, 2007). Retail sales of opioid medications increased a total of 127% between 1997 and 2006 when the total amount of commonly utilized opioids (methadone, oxycodone, fentanyl base, hydromorphone, hydrocodone, morphine, meperidine and codeine) increased from 50.7 million grams in 1997 to 115.3 grams in 2006. The increase was most significant for methadone (1177%) and oxycodone (732%) (Manchikanti and Singh, 2008). During the same time period, milligram per person use in the US increased from 73.59 mg to 329.23 grams, a 347% increase (the mg/person increase was 1129% and 899% for methadone and oxycodone, respectively), evidence that the quantity and dose is increasing. By 2010, over 200 million opioid prescriptions were recorded, enough to medicate every American adult

around-the-clock for a month (Dobbs and Byers, n.d.; CDC, 2012). In comparison, the number of prescriptions for stimulants increased from 4 million in 1991 to 45 million in 2010. Aggressive marketing by pharmaceutical companies and the social perception that the drugs are acceptable may be additional factors driving these increases (Dobbs and Byers, NIH, 2011).

A study conducted by Boudreau et al. of patients prescribed COT for non-cancer pain, revealed that not only is long-term therapy increasingly prevalent, but the concurrent use of opioids and sedative-hypnotics (i.e. valium) is unexpectedly common (Boudreau et al, 2009). Risk of fatal or nonfatal opioid overdose may be higher among those prescribed the medication when compared to those who obtain medicine through diversion. A study demonstrated the risk of overdose among persons not being treated with opioids to be 0.04% per year and 0.22% among those being treated (Ballantyne, 2012).

Non-medical Use

While many people take pain analgesics under medical management for the treatment of acute or chronic pain, non-medical use, the use of the medication in a manner not prescribed by a doctor or the use for non-medical purposes, is also a concern. Non-medical use of prescription pain relievers is likely an important driving factor of the epidemic of prescription drug overdose.

Nonmedical use of a prescription drug is defined as taking a higher-than-recommended dose, taking a drug prescribed for another person, drug facilitated assault, or documented misuse or abuse (DAWN, CDC 2010). The highest rate of nonmedical use of pain relievers has been observed in the 18 to 25 year age group. In a study

conducted in 2005 by Manchikanti et al., males were more likely than females to have used a prescription type pain reliever non-medically in the past year (5.2 vs. 4.4%, respectively), however among youths aged 12 to 17, females were more likely than males to have used pain medication non-medically in the past year (7.9 vs 6.8%, respectively) (Manchikanti, 2007).

Diversion

Diversion is defined as the unlawful transfer of a drug from a legal to an illicit distribution network. A qualitative study conducted from 2008-2009 in Florida identified diversion as one of six problem areas contributing to the increase in prescription drug abuse in the state. This study showed that pain clinics played a prominent role in the diversion of narcotic analgesics, sedatives and anti-anxiety medications (Rigg, March, and Inciardi, 2010). According to Frank Falco of the American Society of Interventional Pain Physicians (ASIPP) 80% of Americans aged 12 to 20 have used a controlled substance that was prescribed for someone else (Holmes, 2012). Sources of prescription drugs for illicit use include pill mills, fraud, internet sales, and doctor shopping; however, overwhelmingly friends and family that had been prescribed the medicine from a prescriber are the source of prescription drugs (McLeod, 2012). According to a U.S. Department of Health and Human Services (HHS) survey, 70% of abusers obtained prescription drugs illegally from friend or relative either for free, by purchasing them or by stealing them (McLeod, 2012), highlighting the need for programs and education about safe disposal of left-over drugs. The diversion of some opioids to abusers may be a growing problem, given that the frequency of medical

examiner reports of oxycodone and fentanyl in the Drug Abuse Warning Network (DAWN) system are increasing even faster than sales of those drugs (Paulozzi, 2006).

Epidemiology

Trends in Substance Abuse

Prescription drugs are highly associated with current (past month), chronic and lifetime drug abuse. According to the Substance Abuse and Mental Health Services Administration's (SAMHSA) 2013 National Survey on Drug Use and Health (NSDUH), 9.4 percent of the U.S. population aged 12 and older were current illicit drug users. Illicit drugs include marijuana, cocaine, heroin as well as prescription-type psychotherapeutics or prescription pain relievers, tranquilizers, sedatives and stimulants used for non-medical purposes. In addition, the survey showed that 2.8 million people age 12 and older used an illicit drug for the first time in 2013; of these, prescription drugs were the second most common type of drug used on initiation after marijuana at 1.5 million new users, a slight decrease from the number observed between 2002 and 2012 (SAHMSA, 2014). Eighty percent of Americans between the ages of 12 and 20 have used a controlled substance not prescribed for them (Holmes, 2012). Every year since 2002, 2.5 to 2.8 million Americans have abused prescription drugs for the first time, outpacing all drugs except marijuana (Carnevale, 2012; CCOMCE 2013; SAMHSA, NSDUH 2008).

Trends in Mortality

Trends in overdose mortality highlight this pressing public health problem. Although deaths related to opioid analgesics could not be studied until a new coding scheme was implemented in 1999, evidence as early as 1995, when opioid prescribing

was just beginning to increase, demonstrate an increase in the drug overdose death rate (Ballantyne, 2012). New codes enhanced surveillance data as they allowed for more specific data about drugs involved in poisonings to be analyzed. The rate of overdose mortality increased sharply in the United States in the decade between 1999 and 2007, when the rate of unintentional overdose death in the United States increased by 124%. This increase is thought to be largely because of increases in prescription opioid overdoses (Bohnert, 2011). Rates of overdose deaths involving prescription drugs increased rapidly in the United States during 1999-2006 (CDC, 2010). In 2007, CDC reported that approximately 27,000 unintentional drug overdoses occurred in the United States, equating to one death every 19 minutes (CDC, 2012). In 2009, more than 15,500 people died in the U.S., four times the number in 1999 (McLeod, 2012). Indeed, deaths by poisonings (90% of them cause by drug overdoses) surpassed motor vehicle crashes several years ago as the most common cause of accidental death in many states in the U.S. (Okie, 2011).

Morbidity

Around the same time overdose deaths were observed to rise sharply, emergency visits from opioid overdoses multiplied (Ballantyne, 2012). Findings from a study conducted in 2010 by CDC and SAMHSA demonstrate a substantial increase in drug related (DR) morbidity as well. In a review of drug related hospital emergency department data from 2004-2008, researchers observed an estimated 111% increase in ED visits for nonmedical use of opioid analgesics during the study period and an 89% increase in visits associated with nonmedical use of benzodiazepines (SAMHSA, 2010). For every unintentional DR overdose death, nine persons are admitted for substance

abuse treatment, 35 visit emergency departments, 161 report drug abuse or dependence, and 461 report nonmedical uses of opioid analgesics (CDC, 2012). Visits to emergency departments for opioid abuse more than doubled between 2004 and 2008, substance abuse treatment program admissions increased by 400% between 1998 and 2008. Among these admissions, prescription painkillers were the second most prevalent type of abused drug after marijuana (Okie, 2010).

Risk Groups

The National Center for Health Statistics (NCHS) reported that between 2000 and 2010, the death rate per 100,000 population increased for males and females, all race/ethnicity groups and all ages (CDC-NCHS, 2012). Overall, rates of opioid misuse and overdose deaths are highest among men, persons aged 20-64 years, American Indians/Alaskan Natives and non-Hispanic whites, persons with mental illness and poor and rural populations (JAMA, 2012).

Females were observed to have a higher rate of increase (130%) than males (80%); however the age-adjusted death rate among males (15.0) was 1.5 times higher than females (9.6). Among all drug poisoning deaths, age adjusted death rates were highest among American Indians/Alaskan Natives (16.8), followed by non-Hispanic whites (15.7), non-Hispanic blacks (8.0), Hispanics/Latinos (5.6) and Asian/Pacific Islanders (1.9) (CDC-NCHS, 2012). With regard to age, NCHS reports that since 2004, the drug poisoning death rate has been highest among 45-54 year olds; however, between 2009 and 2010, the largest age-specific increase was among adults age 55-64 years (CDC-NCHS, 2012). Poisonings among this age group are most concerning because this is the fastest growing segment of the population in the United States.

Persons who a have mental illness are overrepresented among those who are prescribed opioids and those who overdose on them (CDC, 2012). Psychotropic drugs such as benzodiazepines are used in the management of persons with diagnosed mental health disorders. Benzodiazepine-based tranquilizers contributed to 48.8% of prescription overdose deaths in West Virginia in 2006. Of decedents whose deaths involved benzodiazepines, 46.3% did not have a previous prescription for the drug (Toblin et al., 2010). These data indicate that prescription of benzodiazepines to treat mental illness may be a significant risk factor contributing to the rising incidence of drug-related poisonings.

Region

The overall age-adjusted drug poisoning death rate in 2010 was 12.3 deaths per 100,000 population. Rates varied widely by state with the lowest rate observed 3.4 in North Dakota to the highest in West Virginia (28.9). Per capita opioid sales and death rates vary widely among the 50 states. Studies have found a strong correlation between drug-poisoning mortality and opioid consumption; per capita sales are most strongly linked with methadone- and oxycodone- related mortality (Okie, 2010). Nevada was among the five states with the highest death rates at 20.7 per 100, 000 population. Initially, the increase in fatal prescription drug overdoses was observed in rural areas and rural states. Rural areas also observed the sharpest increase in admissions for substance abuse treatment for narcotic pain medication addiction (Paulozzi, 2006). By 2002, opioid analgesics were involved in more deaths than illicit drugs traditionally known to be problematic in urban areas like heroin and cocaine (Paulozzi, 2006). Admissions data analyzed from DAWN showed a similar trend - with opioid related

admissions increasing 101.4%, and heroin and cocaine related visits increasing 32.2% and 23.7% respectively (Paulozzi, 2006).

Drug Type

Reviews of mortality data reveal that in many cases of fatal poisoning, multiple substances are present (North Carolina Center for Health Statistics, 2007). The most frequent combination is an opioid pain analgesic along with a benzodiazepine. Alcohol is also often involved. Recent studies have shown that methadone may be an emerging problem. Methadone is an opioid generally used in the treatment of substance abuse related to heroin; however, data show its use in pain management and its role in drug-related (DR) mortality is becoming more prevalent. In a study conducted by Paulozzi et al., (2009), of mortality data in West Virginia from 2006, overdose deaths related to methadone were observed to be more prevalent in younger age group (> 25% were in the 18-25 year range) and less likely to have ever been prescribed. In 2007, researchers in North Carolina noted that methadone contributed to over 1/3 of fatal poisonings observed that year.

Long term Use and Dose

Pain, sometimes described as the "fifth sense" (Boudreau et al., 2009), has recieved much closer attention in the recent past as an indicator of health and wellbeing. Chronic non-cancer pain is a contributing factor in the growing problem of prescription overdose. Opioid analgesics were approved for widespread use in the treatment and control of chronic pain in the 1990s. There is some evidence that higher prescribed doses increase the risk of drug overdose among individuals treated with opioids for chronic non-cancer pain. Specifically, the risk of drug-related adverse events is higher

among individuals prescribed opioids at doses equal to 50 mg/d or more of morphine (Bohnert, 2001). Boudreau found that long term users tend to use opioid analgesic with sedative hypnotic medication (Boudreau et al., 2009). According to CDC the two most at-risk groups are 1) long term medial users (reportedly 9 million) and 2) non-medical users of opioids who report past month use (reportedly 5 million).

The Cost of Prescription Drug Abuse

In addition to the epidemiological cost of prescription drug use and abuse, there are significant associated economic costs. Total economic costs include workplace, healthcare and criminal justice expenditures. In 2001 the total economic burden was estimated to be $8.6 billion. Per capita annual direct health care costs from 1998 to2002 were nearly $16, 000 for abusers of prescription and nonprescription opioids and $1,800 for nonusers with at least one prescription insurance claim (Strassels, 2009). A 2011 study estimated the total non-medical cost to be $53.4 billion - comprised of $42 billion due to loss of productivity, $8.2 billion to criminal justice costs, $2.2 billion to drug abuse treatment and $944 million to medical complications (McLeod, 2012). Many health and social problems are related to this epidemic. For example, New York is experiencing a record number of overdoses, suicides, new addictions, and armed pharmacy robberies, some of which have resulted in casualties (Hannon, et al. New York)

Prescription Drug Poisoning in Nevada

Trends in Substance Abuse

According to data from NSDUH, Nevada has observed one of the highest rates of drug use and abuse in the United States. In 2007-2008, approximately 9% of Nevada

residents reported illicit drug use during the past-month. Nevada was among the top ten states for high rates in several drug-use categories. Among these categories were past-year non-medical use of pain relievers among persons age 12 and older and among young adults 18-25. Nevada was also among the top ten states for past-month illicit drug use among persons age 12 years and older (ONDCP, 2011). Additionally, Nevadans report a higher rate of using illicit drugs other than marijuana in the past month. Stimulants are the most commonly cited drugs among primary drug treatment admissions in Nevada.

Mortality Trends

In 2012, Nevada had the 4th highest drug overdose mortality rate (20.7 per 100,000 population) in the nation. An analysis of prescription drug overdose deaths in Clark County between 2000 and 2011 revealed the age adjusted death rate was 70% higher in Clark County than the national average (Feng & Middaugh, 2013). In 2007, 515 deaths were attributed to drug use. In the same time period 407 persons died from motor vehicle accidents and 414 due to firearms.

In an analysis conducted by the Southern Nevada Health District (2013) of mortality data from 2000 to 2011, they found that the mortality rate of fatal poisonings nearly doubled during that time period, accounting for 38% of all injury deaths. Of these, 80% were attributed to prescription drugs. Between 2009 and 2011, poisoning surpassed firearms as the leading cause of injury death in Clark County, accounting for 38% of all injury deaths (Feng & Middaugh, 2013). More than eight of every ten DR deaths in Clark County involved opioids or other narcotics; two-thirds involved opioid analgesics. The highest rate of DR mortality was among 45-54 year olds. Males had the

majority of the overall number of DR deaths, but rates increased significantly for both males and females, with females comprising 56% of the DR deaths involving synthetic narcotics (excluding methadone). Benzodiazepines were involved in 24% of DR deaths; combination drug use, where an opioid or other narcotic was present with a benzodiazepine, was identified in 22% of all deaths. Use of an opioid with another depressant like alcohol was documented in 9% of deaths.

Findings from the Clark County Office of the Coroner and Medical Examiner show a similar trend. Among the 14,995 deaths investigated by CCOCME, in 2012, 331 of 522 accidental deaths were attributed to prescription drugs. Additionally, CCOCME reported that in 2012, the number of drug related deaths due to prescription medication (72.5%) was 3 times greater than the rate of illicit street drug related deaths (Clark County observed a 30% decrease in OD deaths related to street drugs during this time period). Additional trends observed by CCOCME during this time were polydrug use (average of 4 different substances/compounds), predominance of oxycodone/oxymorphone, methadone, and morphine, and a 700% increase of accidental prescription drug and alcohol related deaths in the past 10 years in individuals over 60 years old (CCOCME, 2014).

To date, no study has been done to describe the morbidity of prescription drug overdose cases diagnosed at hospitals within Clark County, Nevada.

CHAPTER 3
STUDY DESIGN

Study Design

This study was a population based retrospective case series analysis of hospital discharges related to prescription drug poisonings (DP) associated with opiates and related narcotics, antidepressants, sedatives and tranquilizers for hospitals in Clark County, Nevada between 2009 and 2013.

Discharge data were obtained from the Center for Health Information Analysis (CHIA), a research center at the University of Nevada, Las Vegas within the School of Community Health Sciences. CHIA receives hospital discharge data, ambulatory surgical center and public transparency in health data on a monthly or quarterly basis. Reporting is mandated by state law (AB146). The mission of the Center for Health Information Analysis (CHIA) is to act as a central health data hub for Nevada, in an effort to improve data quality and increase available knowledge via public transparency works. To this end, they collect emergency room and hospital discharge data. CHIA data are compliant with the Health Insurance Portability and Accountability Act (HIPAA). All researchers using CHIA data for this study have an approved Limited Data Set Use Agreement (LDSUA) as required. For the purpose of this study, both hospital inpatient and outpatient data were used.

Research Questions

1. What was the trend in prescription drug poisoning admissions in Clark County, Nevada between 2009 and 2013?
   H1: The rate of drug related hospitalizations increased between 2009 and 2013 among all demographic groups.

Method: Count and rate calculations were generated for each age, gender, race using population estimates from the American Community Survey.

2. What were the characteristics of prescription drug poisoning cases in Clark County between 2009 and 2013?

   H1: Males will represent the majority of the overall DP cases.
   H2: Among persons age 20 – 35, the number of females will be higher.
   H3: Non-Hispanic whites have the highest incidence of prescription drug related admissions.

   Method: Descriptive statistics were utilized to describe characteristics of drug poisoning admissions. Frequencies and rates were calculated for each selected demographic characteristic.

3. What were the most common drugs related to overdose admissions in Clark County, Nevada?

   H1: Opioids are the most common contributory drug type associated with prescription drug poisoning admissions.
   H2: Most DP admissions will involve multiple drugs (including alcohol).

   Method: Frequencies were calculated for drug poisoning type indicated in the primary diagnosis and for each commonly identified drug combination including any drug and alcohol.

4. What are the characteristics of repeat overdose case?

   H1: Repeat cases will be more likely to be young, female.
   H2: The greatest number of repeat cases will be persons older than 60 years.

   Method: Descriptive statistics were utilized to describe characteristics of drug poisoning admissions. Frequencies and rates were calculated for each selected demographic characteristic.

5. What characteristics predict that alcohol will be involved in a drug poisoning?

   H1: Male gender will increase odds when compared to females.
   H2: Persons age 35-44 and 45-64 will have higher odds of alcohol involvement.
   H3: Single status will increase the odds when compared to other marital status categories persons.
   H4: Medicaid and uninsured payer source will increase odds when compared to private insurance.

Method: Binary logistic regression was used to test relationship between demographic characteristics of gender, age, marital status and payer source against a reference a group to identify predictors of alcohol involvement in drug poisonings.

6. What characteristics predict that multiple contributory drugs will be involved in a drug poisoning?

   H1: Female gender will increase odds of a drug poisoning involving multiple drugs.

   H2: Public payer source will increase odds of a DP involving multiple drugs.

   H3: Age and marital status will have no effect on the odds of DP involving multiple drugs.

   Method: Binary logistic regression was used to test relationship between demographic characteristics of gender, age, marital status and payer source against a reference a group to identify predictors of combination/multiple drug use in drug poisoning admissions.

7. What characteristics predict a person will have repeat poisoning admissions?

   H1: Female gender will predict a multiple admission.

   H2: Age 45-64 will predict a multiple admission.

   H3: Public payer type will increase odds of a multiple admission.

   Method: Binary logistic regression was used to test relationship between demographic characteristics of gender, age, marital status and payer source against a reference a group to identify predictors of multiple DP admissions in a given year.

Case Selection

Drug Poisoning Case

We identified all hospital admissions (inpatient and emergency department) related to unintentional prescription drug poisonings that occurred in Clark County, Nevada between 2009 and 2013. Cases were found by querying hospital discharge data from the Center for Health Information Analysis for the appropriate International Statistical Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes. Cases were

included if the admission listed a primary diagnosis of drug poisoning by one of four major drug categories of interest as follows:

- Poisoning by methadone
- Poisoning by opiates and related narcotics
- Poisoning by antidepressants, sedative-hypnotics, tranquilizers
- Poisoning by benzodiazepine-based tranquilizers

and an Supplementary Classification of External Causes of Injury and Poisoning external cause of injury code (E-code) suggesting the poisoning was accidental (Table 1).

The principal diagnosis generally represents the primary reason for the health care contact. For hospitalizations, the principal or primary diagnosis is the condition established at the end of the hospitalization to be chiefly responsible for occasioning the admission of the patient to the hospital for care. In the case of ED visits, the principal or primary diagnosis code is the diagnosis established to be chiefly responsible for occasioning the ED visit. Unintentional poisonings are poisonings in which individuals exposed to the substance did not attempt to cause harm to themselves or others. The range of codes specific to unintentional poisonings are E850-E858 (Unintentional Poisoning by Drugs, Medicinal Substances, and Biologicals) and E860-E864 and E866-E869. Unintentional drug poisonings are classified according to E-codes 850-858. (Harmon, 2010) Poisoning determined to be intentional or those where intent is undetermined are coded accordingly.

Table 1. Diagnosis and External Cause of Injury Codes Related to Unintentional Prescription Drug Poisoning by Select Drug Type

Drug Category	Diagnosis Codes (ICD-9)	Corresponding E-codes
Opiates and related narcotics	965.00, 965.03-09	E850 (.1-.2)
Methadone	965.02	E850.1
Antidepressants, sedative-hypnotics (includes barbituates, tranquilizers, other psychotropic agents)	966, 967, 969, 970	(E851-E853, E854 (.0 - .2, .8), E855.0)
Benzodiazepines	969.4	E853.2

Codes for opium (965.00) and heroin (965.01) were excluded from this analysis. Drug poisonings involving illicit drugs, non-opioid painkillers, and certain stimulants were not included. Also excluded were poisonings that listed excessive alcohol consumption as primary cause of injury even where E-codes indicating unintentional drug poisoning were present.

The case selection methodology closely follows the recommendations suggested by the Safe States Injury Surveillance Workgroup's Consensus Recommendations for National and State Poisoning Surveillance (Safe States, 2012).

Repeat Case

CHIA uses a probabilistic data linking method to generate a unique patient identifier (PUID) to identify multiple hospital encounters over a 15 month period. The PUID was used to identify repeat cases in order to compare characteristics of repeat cases to single incident cases in each of the five years for which the study was conducted. A repeat case was counted if there were 2 or more admissions for the same

person within a calendar year in the respective inpatient or emergency department data set. Cases could not be tracked across inpatient and ED data due to limitations of the data tracking system.

Statistical Analysis

Statistical methods were primarily descriptive. Demographic characteristics of age, gender, race/ethnicity, marital status and payer type were analyzed. Age and sex standardized incidence rates were calculated using county-level population estimates from the American Community Survey for the corresponding study year. The overall and gender-specific rates were calculated as a weighted number of discharges per 100,000 population in each age grouping. Ages were grouped as follows: 18-24, 25-34, 35-44, 45-64, and 65 and older. Additionally, race/ethnic group specific rates were calculated per 100,000 population. Counts and frequencies were then tabulated to determine the characteristics of persons that who had a drug poisoning encounter. The distribution of each characteristic was calculated. Comparisons were made between groups of different demographic categories.

Zip code of residence was used to examine the burden of drug poisonings of residents compared to visitors. As a proxy for socio economic status, payer source was used.

Contributory drugs were identified by using the specific ICD-9 code listed as a primary diagnosis plus any listed E-codes. Counts and percentages were calculated to demonstrate the frequency of each drug category in drug poisoning admissions using the primary diagnosis code.

Logistic regression and chi square analysis were utilized to calculate odds ratios for repeat cases, drug plus alcohol use and multiple drug use based on descriptive characteristics. Odds ratios identified descriptive characteristics that were associated with increased risk or that were protective.

Statistical significance was defined as a p value of $< .05$. Groups with rates significantly above or below the overall rate were identified.

Software

Statistical Package for the Social Sciences (SPSS) Version 22.0 was used to conduct all analyses.

Human Subjects Consideration

This study was a granted an exemption from the UNLV Institutional Review Board.

CHAPTER 4
RESULTS

Trends in Pharmaceutical Drug Poisoning Clark County 2009-2013

The number of admissions for a prescription drug poisoning involving methadone, opiates or other related narcotics, antidepressants and benzodiazepines are shown in Table 2. Between 2009 and 2013 there were 7414 admissions to Clark County hospitals with a primary diagnosis of an unintentional poisoning due to a prescription drug. Of these, 2742 were inpatient admissions and 4672 were emergency department visits. Inpatient admissions increased between 2009 and 2013. Emergency department visits remained relatively stable throughout the five- year study period. The overall number of inpatient and emergency department discharges with diagnostic codes indicating unintentional drug overdose increased from 1368 in 2009 to 1450 in 2013, with peak incidence in 2011 (n=1609). The epidemic curve is displayed in Figure 1.

Table 2. Number of Admissions for Prescription Drug Poisoning by Year and by Admission Type

	Admission Type		
	IP	ED	Total by Year
Discharge Year			
2009	471	897	1368
2010	469	999	1468
2011	602	1007	1609
2012	611	908	1519
2013	589	861	1450
Total by Admission Type	2742	4672	7414

IP=inpatient admission ED=emergency department admission

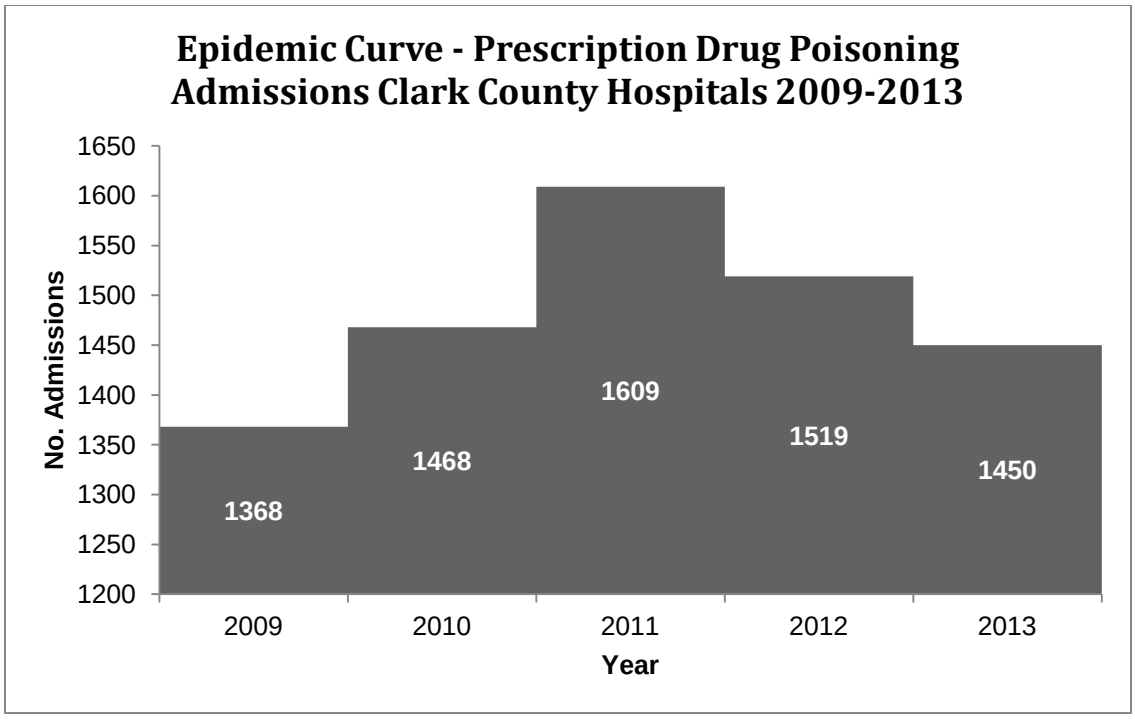

Figure 1. Epidemic Curve – Drug Poisoning Admissions Involving Select Prescription Drugs – Methadone, Opioids, Antidepressants, Benzodiazepines – at Clark County, Nevada Hospitals 2009-2013

Characteristics of Admissions for Unintentional Pharmaceutical Drug Poisonings

Characteristics of persons admitted for an unintentional pharmaceutical drug poisoning are described in Table 3. The demographic characteristics were similar in all five study years and between inpatient and emergency department admissions (See Tables 4-6).

Gender

In each year of the study women represented slightly over half of all admissions. The average overall admissions rate for the five year study period among females was 85.23 per 100, 000 compared to 65.37 per 100, 00 males (Figure 2 & 3).

Age

The greatest percentage of admissions occurred among persons 35 to 64 years old. Rates among younger age groups (18-24 and 25-34) were higher in 2009 and 2010 as shown in Figure 4. Admission rates increased among persons age 65 and older. The

difference in admissions between males and females was most substantial in the 45-64 year old age group. The distribution of admissions by age and gender for each year is displayed in Figure 2.

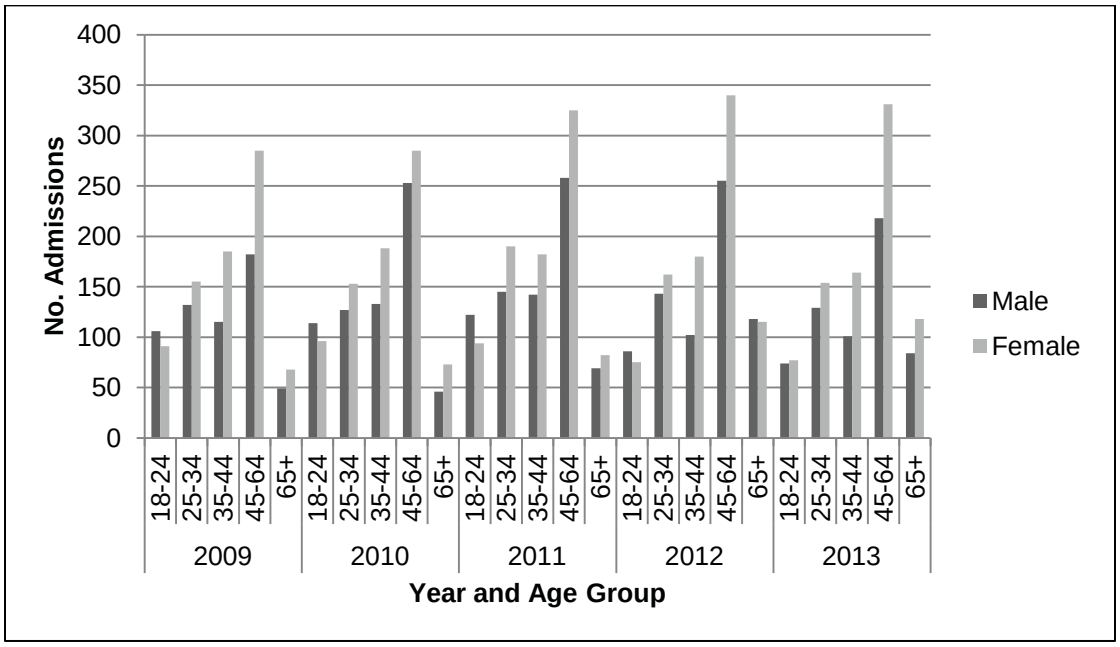

Figure 2. Annual Distribution of Prescription Drug Poisoning Admissions by Age and Gender, Clark County, Nevada 2009-2013

Race

Non-Hispanic whites accounted for the largest percentage (five year average >75.12%; range 71.1 to 77.7%) of all drug poisoning admissions among inpatient and emergency department discharges for all years analyzed. The most significant rate increase was observed among Native American/Alaskan Native subgroup where rates increased sharply between 2012 and 2013 from 13 to 120 Per 100,000 population (Figure 5). It is important to note that this result may be a result of the small sample size of Native Americans in our population.

Marital Status

Single persons accounted for 45% of inpatient admission and most of the admissions during the study period.

Payer Source

Uninsured was the most frequent (38.5%, n=2856) payer type associated with drug poisoning admissions. Uninsured was a categorical group comprise of self-pay, charity and indigent payer sources. Medicare and Medicaid were also common and combined these public payer types comprised 34.5% of all admissions combined. Private insurance payers accounted for 23.3% and of admissions. Veterans Administration insurance was the payer source in only 1.6% of DP admissions.

Residence

Over 90% of all admissions were persons with residences within Clark County. Zip codes with high incidence of inpatient admission were 89101, 89108 and 89121. Among ED admissions, zip codes with incidences over 100 included 89101, 89108, 89103, 89117, 89014, 89015, 89103, 89104, 89110, 89119, 89121, 89122, and 89123.

Table 3. Characteristics of Drug Poisoning Admissions, Clark County Hospitals, 2009-2013

	2009				2010				2011				2012				2013			
	IP		ED		IP		ED		IP		ED		IP		ED		IP		ED	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Characteristic																				
Total	471	100.00	897	100.00	469	100	999	100.00	602	100	1007	100	611	100.00	908	100.00	589	100.00	861	100.00
Gender																				
Male	213	45.22	371	41.36	231	49.25	442	44.24	286	47.51	450	44.687	262	42.88	385	42.40	263	44.65	343	39.84
Female	258	54.78	526	58.64	238	50.75	557	55.76	316	52.49	557	55.313	349	57.12	523	57.60	326	55.35	518	60.16
Age																				
18-24	43	9.13	154	17.17	39	8.316	171	17.12	63	10.47	153	15.194	33	5.40	28	3.08	31	5.26	120	13.94
25-34	84	17.83	203	22.63	65	13.86	215	21.52	80	13.29	255	25.323	83	13.58	222	24.45	84	14.26	199	23.11
35-44	105	22.29	195	21.74	91	19.40	230	23.02	124	20.6	200	19.861	97	15.88	185	20.37	88	14.94	177	20.56
45-64	172	36.52	295	32.89	207	44.14	331	33.13	245	40.70	338	33.565	292	47.79	303	33.37	264	44.82	285	33.10
65+	67	14.23	50	5.57	67	14.29	52	5.21	90	14.95	61	6.0576	106	17.35	70	7.71	122	20.71	80	9.29
Race/Ethnicity																				
Hispanic	48	10.19	97	10.81	45	9.595	110	11.01	48	7.973	113	11.221	53	8.67	128	14.10	38	6.45	85	9.87
NH White	366	77.71	619	69.01	357	76.12	723	72.37	455	75.58	702	69.712	459	75.12	615	67.73	419	71.14	574	66.67
NH Black	32	6.79	112	12.49	41	8.74	111	11.11	56	9.30	124	12.314	48	7.86	99	10.90	61	10.36	102	11.85
Native American	3	0.64	5	0.56	2	0.43	0	0.00	1	0.167	1	0.0993	1	0.16	3	0.33	12	2.04	20	2.32
Asian	9	1.91	29	3.23	12	2.56	18	1.80	12	1.99	26	2.5819	15	2.45	32	3.52	15	2.55	22	2.56
Marital Status																				
Single	228	48.41	513	57.19	217	46.27	545	54.55	299	49.67	546	54.22	249	40.75	478	52.64	233	39.56	434	50.41
Married/Life Partner	157	33.33	244	27.20	144	30.70	306	30.63	177	29.40	324	32.175	236	38.63	275	30.29	233	39.56	267	31.01
Divorced	44	9.34	87	9.70	63	13.43	97	9.71	75	12.46	95	9.434	65	10.64	94	10.35	65	11.04	92	10.69
Legally Separated	6	1.27	21	2.34	6	1.27	15	1.50	5	0.83	9	0.8937	11	1.80	26	2.86	12	2.04	22	2.56
Widow	21	4.46	14	1.56	23	4.90	24	2.40	35	5.81	29	2.8798	43	7.04	30	3.30	34	5.77	34	3.95
Payer Type																				
Private	96	20.38	247	27.54	79	16.84	252	25.23	127	21.10	256	25.422	112	18.33	250	27.53	110	18.68	199	23.11
Medicaid	88	18.68	76	8.47	89	18.98	106	10.61	105	17.44	128	12.711	97	15.88	110	12.11	100	16.98	108	12.54
Medicare	114	24.20	110	12.26	128	27.29	142	14.21	171	28.41	148	14.697	202	33.06	171	18.83	217	36.84	169	19.63
VA/Champus	5	1.06	18	2.01	3	0.64	21	2.10	3	0.498	19	1.8868	12	1.96	9	0.99	15	2.55	16	1.86
Uninsured	165	35.03	405	45.15	161	34.3	470	47.05	185	30.73	438	43.496	179	29.30	359	39.54	144	24.45	350	40.65

Table 4. Rate of Overall Admissions for Unintentional Prescription Drug Poisoning by Select Characteristics, Clark County, NV Hospitals 2009-2013

Characteristic	2009		2010		2011		2012		2013	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Total	1368	71.89	1468	75.12	1609	82.33	1519	75.92	1450	71.50
Gender										
Male	584	60.36	673	68.34	736	45.39	647	64.34	606	59.57
Female	784	83.82	795	82.00	873	56.91	872	87.62	844	83.51
Age										
18-24	197	120.38	210	116.80	216	84.42	161	87.47	151	81.83
25-34	287	95.37	280	95.00	335	86.70	305	102.78	283	94.70
35-44	300	106.68	321	111.57	324	69.81	282	97.74	265	91.85
45-64	467	103.14	538	111.64	583	69.14	595	119.96	549	108.58
65+	117	57.48	119	53.68	151	26.42	176	71.62	202	77.65
Race/Ethnicity										
Hispanic	145	26.02	155	27.14	161	19.34	181	30.36	123	20.23
White	985	68.11	1080	77.59	1157	50.47	1074	78.95	993	74.07
Black	144	68.48	152	66.53	180	53.01	147	59.75	163	65.02
Native American	8	29.11	2	25.61	2	3.57	4	13.00	32	120.74
Asian (includes Hawaiian/PI)	38	19.90	30	16.61	38	10.85	47	18.98	37	14.21

Rate per 100,000 population. Rates calculated based on population estimates from American Community Survey for each corresponding year.

Table 5. Rates of Inpatient Admissions for Unintentional Prescription Drug Poisoning by Select Characteristics Clark County, Nevada 2009-2013

	2009		2010		2011		2012		2013	
Characteristic	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Total	471	24.75	469	24.00	602	30.56	611	30.54	589	29.05
Gender										
Male	213	22.01	231	23.46	286	28.85	262	26.02	263	25.85
Female	258	27.58	238	24.55	316	32.29	349	35.07	326	32.26
Age										
18-24	43	26.28	39	21.69	63	34.76	33	17.93	31	16.8
25-34	84	27.91	65	22.05	80	27.20	83	27.97	84	28.11
35-44	105	37.34	91	31.63	124	43.28	97	33.62	88	30.5
45-64	172	37.99	207	42.95	245	50.12	292	58.87	264	52.22
65+	67	32.91	67	30.22	90	38.98	106	43.14	122	46.89
Race/Ethnicity										
Hispanic	48	8.61	45	7.88	48	8.21	53	8.89	38	6.25
White	366	25.31	357	25.65	455	32.71	459	33.74	419	31.25
Black	32	15.22	41	17.94	56	23.94	48	19.51	61	24.33
Native American	3	10.91	2	25.61	1	3.57	1	3.25	12	45.28
Asian (includes Hawaiian/PI)	9	4.71	12	6.64	12	5.00	15	6.06	15	5.76

Rate per 100,000 population; Rates calculated based on population estimates from American Community Survey for each corresponding year.

Table 6. Rates of Emergency Department Admissions for Unintentional Prescription Drug Poisoning Select Characteristics Clark County, Nevada 2009-2013

	2009		2010		2011		2012		2013	
Characteristic	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Total	897	47.14	999	51.11	1007	51.12	908	45.38	861	42.46
Gender										
Male	371	38.35	442	44.88	450	45.39	385	38.29	343	33.72
Female	526	56.24	557	57.45	557	56.91	523	52.55	518	51.26
Age										
18-24	154	94.01	171	95.11	153	84.42	128	69.54	120	65.03
25-34	203	67.55	215	72.95	255	86.7	222	74.81	199	66.59
35-44	195	69.34	230	79.94	200	69.81	185	64.12	177	61.35
45-64	295	65.15	331	68.69	338	69.14	303	61.09	285	56.37
65+	50	24.56	52	23.46	61	26.42	70	28.49	80	30.75
Race/Ethnicity										
Hispanic	97	17.41	110	19.26	113	19.34	128	21.47	85	13.98
White	619	42.8	723	51.94	702	50.47	615	45.21	574	42.81
Black	112	53.26	111	48.58	124	53.01	99	40.24	102	40.69
Native American	5	18.2	0	0	1	3.57	3	9.75	20	75.46
Asian (includes Hawaiian/PI)	29	15.19	18	9.97	26	10.85	32	12.92	22	8.45

Rate per 100,000 population; Rates calculated based on population estimates from American Community Survey for each corresponding year.

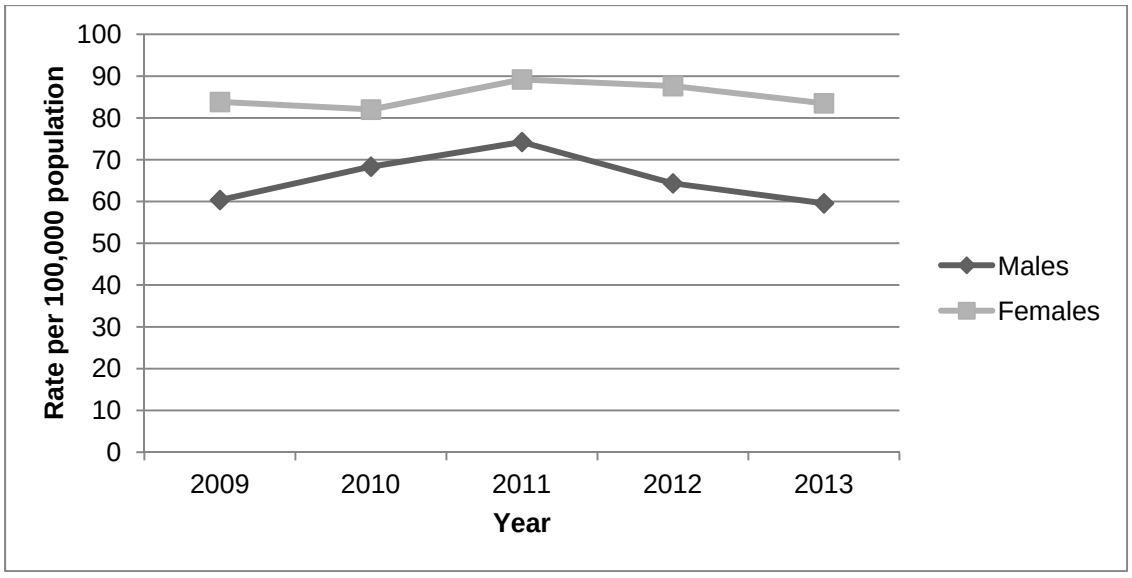

Figure 3. Unintentional Prescription Drug Poisoning Admission Rates by Gender – Total Admissions 2009-2013

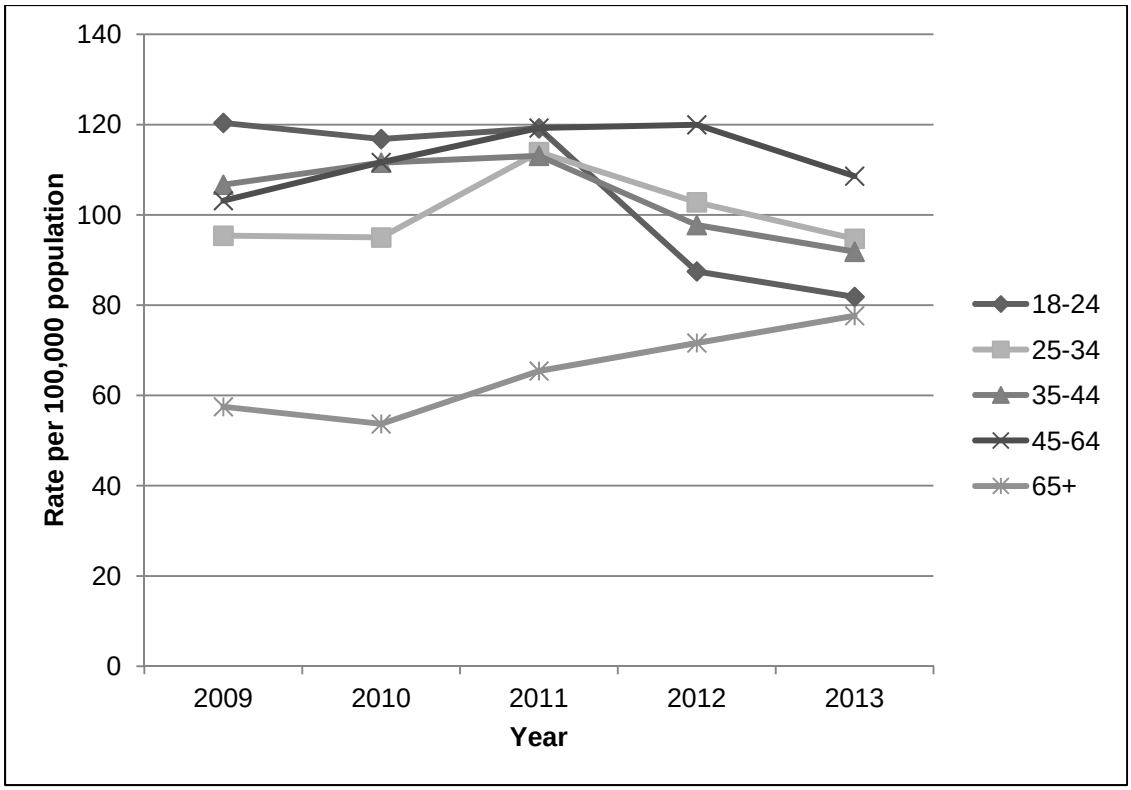

Figure 4. Unintentional Prescription Drug Poisoning Admission Rates by Age – Total Admissions 2009-2013

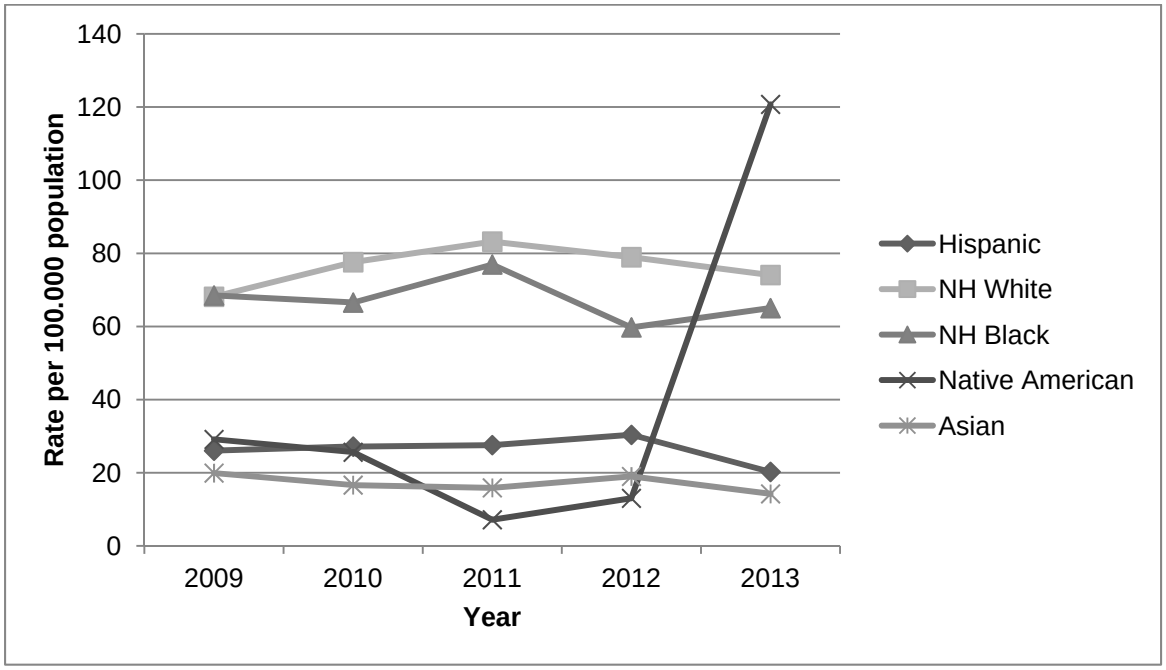

Figure 5. Unintentional Prescription Drug Poisoning Admission Rates by Race/Ethnicity – Total Admissions 2009-2013

Drug Type

Benzodiazepines and opioids (including related narcotics) were the most prevalent drug categories listed as the primary diagnosis in prescription drug poisoning admissions during the study period (Table 7 & Table 8, Figure 6 & Figure 7). Benzodiazepines were involved in 49% of all admissions and listed as the primary diagnosis category in 45% admissions. When compared to males, females had 38% greater odds (OR=1.38, 95% CI 1.25 to 1.51, p<.0001) of having benzodiazepine listed as the primary contributory drug. Opioids and other related narcotics were the second most common drug type listed as a primary diagnosis in 29% of all admissions. More females had benzodiazepines and other sedatives as the primary contributory drug, while males represented most of the cases with methadone as the primary contributory drug. Contributory drug patters were similar among all age groups. DP incidence by

methadone was very low in the 65 and older group and benzodiazepines poisonings were very high in the 45-64 age group.

Table 7. Number of Unintentional Prescription Drug Poisoning Admissions by Drug Category listed as Primary Diagnosis by Year

	Methadone		**Opioids**		**Antidepressant**		**Benzodiazepine**		
Year	IP	ED	IP	ED	IP	ED	IP	ED	Total Admissions by Year
2009	27	28	138	238	113	192	193	439	1368
2010	27	31	131	287	87	187	224	494	1468
2011	32	27	181	294	139	231	250	455	1609
2012	30	18	186	286	153	195	242	409	1519
2013	21	17	174	237	184	187	210	420	1450
Total	137	121	810	1342	676	992	1119	2217	7414
Total Admissions by Drug type	258 (3%)		2152 (29%)		1668 (22.5%)		3336 (45%)		7414 (100%)

Table 8. Contributory Drug by Primary Diagnosis and Gender – Unintentional Prescription Drug Poisoning Admissions – Total Admissions, Clark County, NV 2009-2013

		Methadone	**Opioids**	**Antidepressant**	**Benzodiazepine**	**Total**
Female	N	111	1185	825	2020	4141
	% between genders	43.0%	55.1%	51.4%	60.6%	56.3%
	% in gender	2.7%	28.6%	19.9%	48.8%	100%
Male	N	147	967	779	1316	3209
	% between genders	57.0%	44.9%	48.6%	39.4%	43.7%
	% in gender	4.6%	30.1%	10.6%	41.0%	100%
Total	N	258	2152	1604	3336	7350
	% of Total	3.5%	29.3%	21.8%	45.4%	100.0%

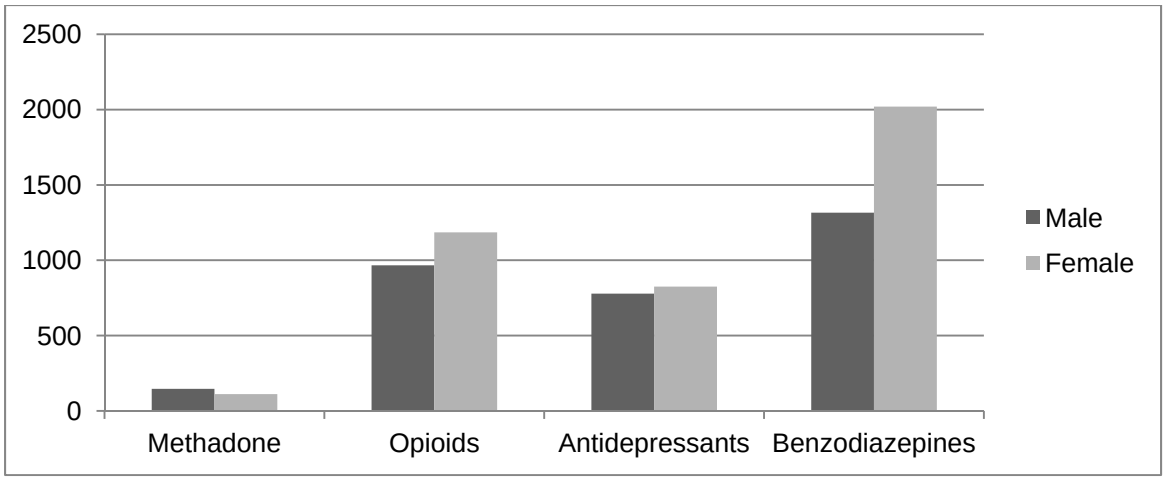

Figure 6. Distribution of Primary Contributory Drug Type in Unintentional Prescription Drug Poisoning Admissions by Gender – Total Admissions 2009-2013

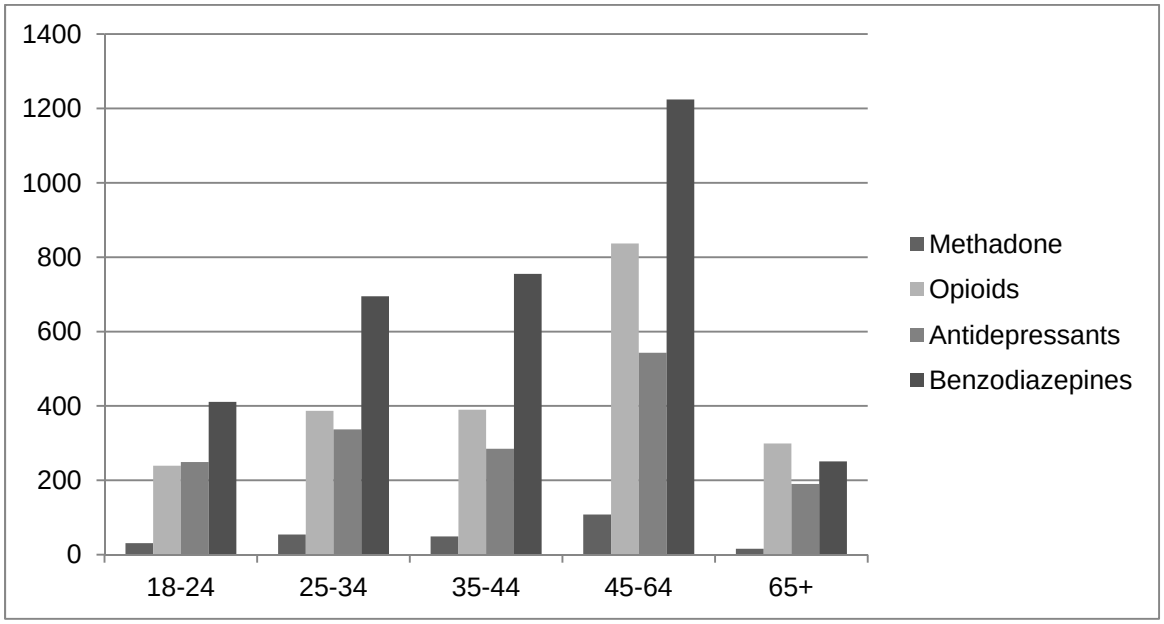

Figure 7. Distribution of Primary Contributory Drug Type in Unintentional Prescription Drug Poisoning Admissions by Age – Total Admissions 2009-2013

Seventy-eight percent (78%) of all drug poisoning admissions involved a single drug type. Benzodiazepines, antidepressants and opioids were the most common type of drugs involved in drug poisoning admissions. Multiple drugs were listed in 25% of all inpatient admissions versus 20% of emergency department (ED) admissions and in 22%

of all admissions overall (Table 9). The most common drug combination found among poisoning admissions indicating multiple drug use was an antidepressant and a benzodiazepine. The distribution of primary contributory drug type among all age groups, marital status, race and payer source mirrored the overall distribution.

Alcohol Involvement

Alcohol was involved in less than 1% of all admissions, but was twice as prevalent among inpatient admissions when compared to ED admissions (Table 9). The majority of ED admissions were related to a drug poisoning by a single category of drugs (n=3075, 66%) with no alcohol. Only 26 ED poisoning admissions had associated alcohol as indicated by related E-codes. Of these 17 were poisonings due to multi-drug use and alcohol. In the 65 and older age group, no poisonings were associated with alcohol use.

Table 9. Frequency of Contributory Drugs involved in Unintentional Prescription Drug Poisoning Admissions, Clark County Hospitals, 2009-2013

	Inpatient % (N)	ED % (N)	Total %(N)
Single Drug	**75 (2059)**	**79.2 (3699)**	**77.6 (5758)**
Multiple Drugs*	**25 (683)**	**20.8 (973)**	**22 (1656)**
Admissions by Primary Diagnosis Category			
Methadone	5.0 (137)	2.6 (121)	3.5 (268)
Opiate or other narcotic	29.5 (810)	28.7 (1342)	29.0 (2152)
Antidepressant	24.7 (676)	21.2 (992)	22.5 (1668)
Benzodiazepine	40.8 (1119)	47.5 (2217)	45.0 (3336)
Admissions involving Alcohol	1.6 (44)	.56 (26)	.94 (70)
Admissions involving Drug Combinations			
Antidepressant and Benzodiazepine	18.5 (508)	17.3 (808)	17.8 (1316)
Antidepressant and Opiates	8.5 (233)	5.4 (252)	6.5 (485)
Opiate and Benzodiazepine	6.7 (185)	4.8 (200)	5.2 (385)
Opiate and Methadone	5.2 (142)	2.6 (121)	3.5 (263)
Methadone and Antidepressant	0.95 (26)	.26 (12)	.5 (38)
Methadone and Benzodiazepine	.8 (22)	.17 (8)	.4 (30)

*Admissions that listed at least 2 diagnoses and/or E-codes

Repeat Cases

We identified 384 repeat cases among all admissions during the study period. Characteristics of repeat cases are displayed in Table 10. Unlike single cases, males comprised the majority of repeat cases (62%). Like single cases, poisoning by benzodiazepines was the most common primary diagnosis among repeat cases; the frequency of poisoning by antidepressants was relatively low when compared to single incident cases. Repeat cases had a higher percentage of opioids as primary diagnosis. Alcohol was more prevalent among repeat cases when compared to single cases (11.5% versus .94%, respectively). Other characteristics were similar between single and repeat cases.

Table 10. Select Characteristics of Repeat Cases, All Admissions for Unintentional Drug Poisoning by Select Prescription Drugs, Clark County Hospitals, 2009-2013

Characteristic	N	%	Characteristic	N	%
Admission Type			**Marital Status**		
Inpatient	153	39.84	Single	225	58.59
Emergency Dept.	231	60.16	Married/Life Partner	86	22.40
Total	384	100.00	Divorced	48	12.50
Admissions by Year			Legally Separated	5	1.30
2009	59	15.36	Widow	11	2.86
2010	80	20.83	**Payer Type**		
2011	104	27.08	Private	78	20.31
2012	75	19.53	Medicaid	59	15.36
2013	66	17.19	Medicare	72	18.75
Gender			VA/Champus	2	0.52
Male	238	61.98	Uninsured	166	43.23
Female	146	38.02			
Age					
18-24	48	12.50			
25-34	83	21.61			
35-44	77	20.05			
45-64	157	40.89			
65+	19	4.95			
Race/Ethnicity					
Hispanic	37	9.64			
NH White	296	77.08			
NH Black	35	9.11			
Native American	2	0.52			
Asian	1	0.26			

Predictors of Select Outcomes

We used binary logistic regression to identify predictors for three outcomes: alcohol and drug use, multiple drug use and repeat/multiple admissions. Regression results for each outcome are shown in Tables 11, 12 and 13, respectively. Significant values are displayed in bolded text. The dependent variable was the dichotomous yes/no for combined alcohol plus drugs, multiple drugs, and repeat/multiple admissions. The independent variables were gender, race, marital status, payer type and age. Because

each of the independent variables was categorical, the reference categories were: male, white, single, private health insurance and 18-24.

Combined Drug and Alcohol Use

Regression results provided evidence that when compared to males, females have 50% lower odds of having alcohol listed as an external cause of injury in drug poisoning admissions. Gender was the only significant predictor of alcohol use among drug poisoning admissions.

Table 11. Predictors of Alcohol Involvement in Unintentional Prescription Drug Poisoning Admission Cases

	B	Sig.	Exp(B)	95% C.I.for EXP(B)	
				Lower	Upper
Gender					
Female*	-.696	**.006**	**.499**	**.303**	**.822**
Race					
Black	.563	.103	1.756	.893	3.455
Asian	-.434	.669	.648	.088	4.758
Native American	.923	.372	2.516	.332	19.056
Hispanic	-.162	.714	.850	.357	2.025
Marital Status					
Married	-.413	.185	.661	.359	1.219
Divorced	-.795	.194	.452	.136	1.499
Legally Separated	-.340	.739	.712	.096	5.281
Widow	.638	.409	1.894	.416	8.623
Payer Type					
Medicaid	-.218	.607	.804	.350	1.846
Medicare	-1.057	.074	.347	.109	1.110
VA	.944	.141	2.570	.732	9.020
Uninsured	.038	.899	1.039	.573	1.886
Age					
25-34	.109	.782	1.116	.514	2.420
35-44	.455	.245	1.577	.732	3.397
45-64	-.020	.960	.980	.447	2.149
65+	-1.280	.260	.278	.030	2.577

Multiple Drug Use

Significant predictors of multiple drug use among all drug poisoning admissions were gender, payer source and age. Among predictor characteristics, female gender was protective, where females had a 20% lower odds of having used multiple drugs. Medicaid, Medicare and uninsured cases had greater odds of multiple drug use (OR 1.66 (p=.000 95% CI 1.41-1.97), 1.68 (p=.000, 95% CI 1.43 – 1.98) and 1.38 (p=.000, 95% CI 1.20 – 1.57). Persons 45-64 (OR=1.37 (p=.000, 95% CI 1.56-1.63) and 65 and older (OR=1.61 (p=.000, 95% CI 1.26 – 2.06) also had greater odds of polysubstance admissions.

Table 12. Predictors of Multiple Drug Use Among Drug Poisoning Admission Cases

				95% C.I.for EXP(B)	
	B	Sig.	Exp(B)	Lower	Upper
Gender					
Female	-.214	**.000**	**.807**	**.732**	**.891**
Race					
Black	.099	.217	1.104	.944	1.292
Asian	-.285	.086	.752	.544	1.041
Native American	.153	.606	1.166	.651	2.088
Hispanic	-.012	.880	.988	.840	1.161
Marital Status					
Married	.071	.237	1.073	.955	1.207
Divorced	-.077	.373	.926	.781	1.097
Legally separated	.061	.744	1.063	.737	1.532
Widow	.352	.009	1.421	1.094	1.847
Payer Type					
Medicaid	.509	**.000**	**1.664**	**1.406**	**1.969**
Medicare	.520	**.000**	**1.681**	**1.426**	**1.982**
VA	.069	.737	1.071	.718	1.599
Uninsured	.319	**.000**	**1.375**	**1.204**	**1.571**
Age					
25-34	.095	.301	1.099	.919	1.315
35-44	.064	.495	1.066	.887	1.281
45-64	.317	**.000**	**1.374**	**1.155**	**1.633**
65+	1	**.000**	**1.614**	**1.264**	**2.062**

Multiple Admissions (Repeat Cases)

Female gender (p=.010, OR=.759 95% CI .615-.937), married marital status (p=.014, .718, 95% CI .551-.936) and black race (p=.002, OR=.525 95% CI .350-.787) race were all protective. Females had 25% less odds of having multiple admissions when compared to males. Married individuals had 30% lower odds of having multiple admissions when compared to single cases. With regards to payer status, admissions that had a payer source of Medicaid and Medicare had greater odds of having a multiple admission (OR=1.48 (p=.030 95 CI 1.04 – 2.10) and 1.68 (p=.003 95% CI 1.12 – 2.36) respectively).

Table 13. Predictors of Multiple Unintentional Prescription Drug Poisoning Admissions by Select Characteristics

	B	Sig.	Exp(B)	95% C.I.for EXP(B)	
				Lower	Upper
Gender					
Female	-.275	**.010**	**.759**	**.615**	**.937**
Race					
Black	-.644	**.002**	**.525**	**.350**	**.787**
Asian	-18.301	.995	.000	0.000	
Native American	-1.165	.251	.312	.043	2.280
Hispanic	-.243	.190	.784	.545	1.128
Marital Status					
Married	-.331	**.014**	**.718**	**.551**	**.936**
Divorced	-.017	.920	.983	.705	1.371
Legally Separated	.037	.921	1.038	.497	2.169
Widow	-.218	.470	.804	.445	1.453
Payer Source					
Medicaid	.390	**.030**	**1.477**	**1.040**	**2.099**
Medicare	.518	**.003**	**1.678**	**1.196**	**2.355**
VA Champus	-1.094	.131	.335	.081	1.385
Self Pay	.027	.859	1.027	.764	1.381
Age					
25-34	.033	.871	1.033	.695	1.537
35-44	-.030	.884	.970	.645	1.458
45-64	.302	.112	1.353	.932	1.964
65+	-.432	.132	.649	.370	1.139

CHAPTER 6
DISCUSSION, CONCLUSION AND RECOMMENDATIONS

This study aimed to examine the occurrence and distribution of prescription drug poisoning admissions to emergency departments and inpatient units at hospitals in Clark County, Nevada between 2009-2013 in order to describe the demographic characteristics and their relationship to specified outcomes. Demographic characteristics were selected based on review of related literature.

Females were overrepresented in the drug poisoning (DP) counts, percentages and rates in every year included in this analysis. This conflicts with some of the reports using national statistics which suggest that although females have experienced sharper increases in DP in recent years, overall, males experience higher rates of drug poisonings. However, other studies have demonstrated a differential risk for women. Cohen et al., found that in comparison to patients hospitalized for poisoning from other substances, those hospitalized for prescription opioids, sedatives, and tranquilizers were more likely to be women, aged >34 years, and to present to a rural or urban nonteaching hospital (Cohen, 2010). The prominent involvement of benzodiazepines in female DPs may contribute to the differential risk for women. Among our study population, women were 38% more likely to have a DP attributed to a benzodiazepine when compared to males. This finding provides insight for targeted prevention opportunities.

Information from this study is consistent with the national pattern of DP among different age groups. Persons aged 35-64 were more frequently represented in our population. This trend may be related to the prevalence of chronic long-term opioid users. Currently, more than 3% of US adults receive long-term opioid therapy for

chronic non-cancer pain and patients that are on long-term regimens tend to take higher doses which puts them at greater risk (Okie, 2010). This may also contribute to the higher incidence among persons 65 and older, a group with more complex medical conditions that may be treated with narcotic pain medication.

In addition, the study showed an increase in the rate among persons 65 and older. It is important to note is that persons in this age group were more frequently admitted to the hospital whereas the other age groups are more frequently seen in the ED only. This is likely because older populations have more complex underlying medical conditions which may complicate the clinical course of a drug poisoning event. Additionally, they were 1.6 times more likely to have multiple drugs in their system upon admission, which may have resulted in a greater hospital admission rate.

With regards to race, Native Americans exhibited the most dramatic increase in DP rates. CDC also reported that age-adjusted death rates in 2010 were highest among this same group (NCHS, 2012). Although numbers of DP admissions are relatively low among Native Americans, these findings suggest a potentially emerging problem in this population that warrants further study.

Although the percentage of DP involving alcohol was small, we were able to determine that males had greater odds of a combined drug and alcohol overdose when compared to females. This finding is consistent with patterns of drinking and alcohol abuse described in the literature that indicate males have higher rates of alcohol consumption (White, 2011). The role of combined alcohol and drug overdose may be grossly underestimated in this study due to the methods we used for inclusion to construct our study population. Cases were included only if their primary diagnosis indicated

poisoning by one of the selected drug categories. Admissions that listed alcohol poisoning as a primary diagnosis were excluded even if they had an E-code indicating combined alcohol and drug use. Including admissions coded as alcohol poisoning also involving a prescription drug as indicated by the listed E-codes may yield a different and important result and should be considered for future studies.

Males also had higher odds of a poisoning involving multiple drugs and having a repeat visit within a year for a DP. These findings suggest that although females have higher rates of DP admissions overall, males may engage in more dangerous drug use behaviors that puts them at risk for multiple hospitalizations and possibly death. The warning label on some Percoset containers, an opioid medication containing oxycodone, states, "Oxycodone may be expected to have additive effects when used in conjunction with alcohol, other opioids or illicit drugs that cause central nervous system depression" (White, 2011).

Some studies have suggested an emerging problem of drug poisonings associated with methadone, an opioid traditionally used in the treatment of heroin abuse. A study conducted by the CDC of prescription overdose deaths in Washington from 2004-2007 of identified Medicaid enrollees, demonstrated increased risk and the relationship between methadone and overdose in this population (MMWR, 2009). Our findings did not support this. Methadone poisonings represented only 3.4% of DPs in the Medicaid population and 3% of the overall admissions in all categories. However, because the national data suggest that methadone is being increasingly used in the treatment of chronic pain, likely because it is relatively cheap, it has been observed to play a prominent role in overdose mortality. Further observation of the trend is recommended.

Although, beyond of the scope of this study, the increase in drug poisonings is thought to be a consequence of nonmedical use of opioids and other prescription drugs. Our study showed that a large percentage of drug poisonings occurred among uninsured persons. Uninsured was defined as self, discounted, negotiated rate and indigent payer sources. This may indicate that this population is acquiring prescription drugs through nonmedical distribution channels or namely, diversion. Studies have shown that most (60%) persons who use prescription drugs non-medically obtain them from a friend or family member to whom they were prescribed (CDC, 2010). One in every five Americans is prescribed a prescription pain medication each day (CCOME, 2012) and enough medication is prescribed to dose every adult American for one month. The increase in prescriptions and sales has led to an increase in accessibility. Our study supports diversion as a probable factor in the DP epidemic in Clark County.

The findings of this study provide information to suggest that interventions should be targeted at several demographic groups. Non-Hispanic whites, men and women aged 35-64 and poorer populations (we used Medicaid and uninsured payer source as a proxy) would benefit from risk reduction programs including education, substance abuse treatment and monitoring. In addition, Native Americans and persons over 65, groups that show a more recent upward trend in DP admissions, should also be targeted to reduce prescription drug poisonings.

Limitations

There are several limitations inherent to this study. It is possible that some of our findings were an artifact of a small sample size or collinear effects. For example, the rate increase observed among Native Americans may be due to the relatively small population

size. The regression model may have been affected by multicollinearity where independent variables like single marital status and public medical insurance may have been highly correlated, as they are both potentially indicators of lower socio-economic status. As such, it may be low SES that is the true predictor of multiple admissions rather than the individual independent variables.

The case selection methodology may have resulted in an underestimate of alcohol involvement in unintentional prescription drug poisoning admissions. Cases were included if they had a primary diagnosis indicating poisoning by methadone, opiates, antidepressants or benzodiazepines. Admissions where alcohol poisoning was listed as the primary diagnosis were excluded even if the admission listed a corresponding E-code. Additionally, the case selection method was dependent on the accurate coding by medical personnel at the reporting hospitals. It is possible that cases were missed due to provider bias in diagnosing and/or coding diagnoses. It is also possible that E-codes were missing from records and as such were excluded from our analysis. Data quality is dependent on coding by specific hospitals, which may differ by hospital or coder.

Another limitation associated with coding of drug poisonings is that the codes are not specific enough to determine which specific drug was contributory in each category. Future studies should examine the possibilities of selecting for codes that indicate the specific drug type involved in the poisoning, ie. Oxycodone.

With regards to selecting for repeat cases we were limited by the strength of the probabilistic method employed by CHIA to track persons over time, namely, repeat cases could only be identified within a calendar year and within a data set (inpatient or ED). We were not able to assess for how poisoning deaths may have impacted the accuracy of

our analysis of repeat cases because data linkages cannot be made between data sets. This may have particularly impacted our analysis of repeat admissions as persons who die do not have the opportunity to be admitted multiple times. Future studies should include disposition at discharge to help control for fatal outcomes.

Conclusions and Recommendations

Changes in the medical use of opioid analgesics and related drugs led to a flooding in the U.S. of pharmaceuticals with high potential for dependency and abuse. The incidence of prescription drug poisoning has risen dramatically and is a significant factor making poisoning the leading cause of injury related mortality in the U.S. Prescription drug poisoning mortality is most strongly associated with opioid analgesics and related drugs often co-prescribed such as benzodiazepines and antidepressants. In Clark County, Nevada, the rate of fatal poisonings involving opioid pain analgesics is above the national rate. Many of these deaths involve sedatives and tranquilizers. This study demonstrated that these same drugs are important contributors to the morbidity associated with prescription drugs, particularly among women.

Unintentional injuries are preventable. In Clark County, Nevada, public health interventions that target non-Hispanic white men and women age 35-64, Native Americans and persons 65 may help prevent prescription drug poisonings from occurring. Studies like this should be replicated and expounded upon to further define the risk population and gain an understanding of the risk factors in order to develop strategies to reduce risk and the associated morbidity and mortality burden.

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