The number of overdose deaths from prescription and non-prescription opioid analgesics has more than quadrupled since 1999. Between 2000 and 2015, more than 500,000 people died from drug overdoses; 91 Americans die every day from an opioid overdose. In 2015 alone, there were 52,404 drug-overdose deaths, an increase of more than 11 percent in a single year. The Kaiser Family Foundation found that 25 percent of Americans know a close friend or family member who has abused prescription opioids, and 56 percent have some personal connection to the issue.

Given the similarity in molecular structure and effect on the brain between prescription opioids and heroin, it should come as no surprise that an increase in heroin addiction and heroin-related deaths has mirrored that of prescription opioids. The recent increase in opioid overdose deaths—whether from prescription opioids or illicit opioids such as heroin—has reached the point where the situation is referred to as a “public health crisis” in the U.S. The crisis is poised to lead to an increase in injection drug use (IDU) and its health-related consequences, including acute Hepatitis C and HIV infection.

This article provides an overview of the epidemiology of drug-overdose deaths and opioid prescribing and the intersection between these trends. It also summarizes some of the theories behind increased prescribing and provides an overview of the benefits and risks of prescription opioid therapy, including HIV and Hepatitis C.

Part 1: Changing Trends

According to the Centers for Disease Control & Prevention (CDC), during 2014, 10.3 million persons reported using prescription opioids non-medically, and in 2015, 52,404 drug-overdose deaths occurred in the U.S. Opioids were involved in 33,091 (63 percent) of these deaths. More people died from drug overdoses in the U.S. in 2015 than during any previous year on record; there were one and a half times more drug-overdose deaths in the U.S. than deaths from motor vehicle crashes. In June 2016, The New York Times reported that the (overall) death rate in the U.S. rose in 2015 for the first time in a decade, in part driven by more people dying from drug overdoses (see Figure 1).
NJ Advance Media has reported that in New Jersey the heroin-overdose death rate alone now eclipses not only car accidents, but also homicide, suicide and AIDS as a cause of death in the state. In Camden and Atlantic counties, heroin kills more people each year than the flu and pneumonia combined. Much of the most recent increase is blamed on the use of illicitly manufactured fentanyl, a synthetic opioid; in New Jersey, fentanyl was responsible for more than 400 deaths in 2015, in comparison to 46 just two years earlier. To make matters worse, the use of heroin and fentanyl are expected to continue to drive the increase in overdose deaths in 2016 and beyond.

The number of deaths is the proverbial “tip of the iceberg” hiding the fact that nationally, about 1.4 million emergency department visits in 2011 were due to prescription drug use or abuse (including 420,000 due to prescription opioids and 501,000 to anxiety, sleep and other related medications). That number was 144,600 in 2004 and 305,900 in 2008.

The following are trends linked to heroin-related drug-overdose deaths in the U.S.:

- From 2000 to 2013, the rate of drug-overdose deaths involving prescription opioids was higher than the rate for deaths involving heroin. Although the rate of deaths involving prescription opioids has leveled off in recent years (mostly since 2006), from 2000 through 2013 the rate for heroin-overdose deaths nearly quadrupled. In terms of geographic spread, the increase in drug-overdose deaths is nationwide, affecting every region of the country.

- The number of deaths involving heroin was nearly four times higher for men (6,525 deaths) than women (1,732 deaths) in 2013. However, women were twice as likely to be using heroin in 2011 – 2013 than in 2002 – 2004.

- In 2000, (non-Hispanic) black persons aged 45 – 64 had the highest rate of death involving heroin (2.0/100,000). In 2013, (non-Hispanic) white persons aged 18 – 44 had the highest rate (7.0/100,000). Although heroin-related death rates have increased for both race and ethnic groups, the largest increases were among white persons. Similarly, although heroin-related deaths have increased in all age groups, those ages 25 – 44 had the highest rate of deaths involving heroin (see Figure 2).

Figure 1. Rates of Drug-Overdose Deaths and Drug-Overdose Deaths Involving Opioids, U.S., 2000–2014

Drug misuse: When an individual takes a drug for a purpose other than that for which it was prescribed or when one takes a drug that was not prescribed to him or her. Misuse includes taking a drug in a manner or at a dose other than that which was recommended.

Drug abuse: Misuse is considered abuse if a drug is taken to get pleasant or euphoric feelings, particularly if taken at higher doses than prescribed.

Addiction: Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors. Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one’s behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.

Factors associated with increased risk for misuse include history of substance use disorder, younger age, major depression and use of psychotropic medications. Higher doses of prescription opioids are associated with increased risk.12

Naloxone and Opioid-Related Epidemiology

Consistent with the Overdose Prevention Act, in April 2014, New Jersey implemented a pilot project to allow police and emergency medical technicians (EMTs) to provide naloxone for overdoses. This required collaboration between the New Jersey Department of Law and Public Safety, New Jersey Division of Consumer Affairs (DCA), the New Jersey Department of Health (DOH), county prosecutors and local police. The Board of Medical Examiners’ (BME) Certificate of Waiver provided the regulatory ability for physicians to prescribe naloxone to be used by police and emergency medical technicians. The DOH developed a waiver to allow EMTs to give naloxone.

The DCA provided training to the police on how to identify the symptoms of a drug overdose, how to administer the intranasal naloxone spray and where to refer drug-abusing individuals for care. Naloxone administration by police and EMTs is available in all 21 counties in New Jersey. According to personal communication with Douglas Collier, MA, Drug Initiative Coordinator at the NJ DCA, as of September 2015, more than 28,000 certified EMTs had been trained to administer naloxone. In 2015 alone, 6,548 naloxone kits were deployed by law enforcement personnel and emergency medical services. Interestingly, the use of naloxone was considered responsible for the small, albeit temporary, reduction in the number and rate of drug-overdose deaths in New Jersey experienced in 2014. The drop was small (3.4 percent: from 1,294 in 2013 to 1,253 in 2014) and not due to declines in opioid drug abuse, but, rather, deaths due to overdoses. By 2015, increases in deaths from the opioid drug fentanyl erased all gains from reversals due to the use of naloxone.13

Heroin: Cheaper and More Abundant

At a CDC telebriefing on July 7, 2015, Dr. Thomas Frieden explained that in addition to the fact that an increasing number of people are “primed for heroin addiction” because of an addiction or exposure to prescription opioids, the shift to heroin has been facilitated by an increase in supply and decrease in cost.14 High purity may reflect a glut of heroin on the market. According to local enforcement officials, heroin costs only $4 to $6 a bag on the street; in comparison, prescription drugs can cost a user between five and six times that amount.7

Most of New Jersey’s heroin originates from South America and comes into the state through the seaports in Newark, Elizabeth and Philadelphia, and through international airports and along interstate highways.15 Illegal drugs purchased near to port of entry are purer as the drug has been handled by fewer buyers and sellers (each of whom tends to cut the drug to increase profit). New Jersey has
some of the purest heroin in the U.S., according to September 2014 Drug Enforcement Administration (DEA) laboratory testing. In September 2014, the DEA issued an advisory warning that the purest levels averaged 58 percent, an increase of 12 percent from 2011.15

Although New Jersey’s heroin is relatively pure, bags are increasingly being laced with other substances, such as the synthetic opioid analogues fentanyl, as noted previously, or the pesticide Carbaryl.16 A surge in overdose deaths from heroin laced with fentanyl prompted the DEA to issue a nationwide alert in March of 2015.

The Increased Availability of Prescription Opioids

A National Institute on Drug Abuse report cites a number of factors that may have contributed to the availability of prescription medications in general and prescription opioids in particular and the consequent prescription drug abuse problem.17 These factors include the following:

• Drastic increases in the number of prescriptions written and dispensed
• Greater social acceptability for using medications for different purposes
• Aggressive marketing by pharmaceutical companies

The total number of opioid analgesics prescribed in the U.S. has skyrocketed in the past 25 years (see Figure 3) from approximately 76 million in 1991 to nearly 207 million in 2013. However, in 2015, that number dropped by 17 million nationally, giving some optimism that opioid prescribing is finally falling.18 From 1991 to 2013, opioid prescribing rates increased more for family practice, general practice and internal medicine compared with other specialties.19 The number of annual opioid prescriptions written in the U.S. is now roughly equal to the number of adults in the population.19 However, opioid prescriptions are not exclusive-ly written for adults: There was a significant increase in opioid prescriptions for pediatric populations from 2001 to 2010; a large proportion of adolescents are commonly pre-
scribed opioid pain medications for conditions such as headaches and sports injuries.12

Theories Behind Increased Prescribing

Other factors have contributed to the increase in prescription opioid use and abuse in recent years. Glenn Treisman, MD, PhD, Director of AIDS Psychiatry Services, Johns Hopkins University School of Medicine, discussed two contributing factors: the Pain as the 5th Vital Sign campaign and increased emphasis on patient satisfaction.20 The field of pain medicine is very new, having developed only in the past two to three decades. Prior to this time, treatments for pain were limited, and standardized tools for pain assessment were non-existent. It is now well-recognized that, historically, pain was both significantly under-treated and under-recognized. On this foundation, the medical community sought to improve the care of patients by ensuring their pain was recognized and treated.21 However, a number of recent studies have questioned whether pain management had been improved by redefining it as the 5th vital sign.22

The Pain as the 5th Vital Sign campaign that the Veterans Health Administration launched in 1999 and the Joint Commission pain awareness campaign launched in 1996 have been linked to the trend to prescribe more opioids.23 Interestingly, in an April 2016 statement on its website, the Joint Commission set forth to clarify standards for pain assessment and treatment and to deny any role that its standards may have had in the increase in opioid prescriptions.24

Another issue that has added to the prescription drug abuse debate is the increasing emphasis on patient satisfaction—a poorly described measurement that has nonetheless become a common metric when discussing healthcare quality. Physicians report that trying to improve patient satisfaction often results in pressure to do things that may not be in the best interest of healthcare. This was underscored by a study that showed improved patient satisfaction correlated with increased mortality. The conclusion of this report reads: “In a nationally representative sample, higher patient satisfaction was associated with less emergency department use but with greater inpatient use, higher overall health care and prescription drug expenditures, and increased mortality.”25

Other authors have suggested that the following may have also contributed to the over-prescribing commonly seen in medical practice today: standard physician training that emphasizes cure, inadequate undergraduate and graduate training in pain management, and heightened public and media awareness of undertreated pain. It should also be noted that some patients, especially those with mental health or substance abuse disorders, exploit physici-ans’ sensitivity towards pain and demand opioids for pain relief.26

How Prescription Opioids Get to the Misuser/Abuser

With more prescriptions in circulation, there are more pills—including more pills that can get into the wrong hands. Although 17.3 percent of those who abuse prescription opioids get them through physicians’ prescriptions, more than 66 percent obtain them (for free or for purchase) from friends or relatives, 4.8 percent are stolen from relatives or friends and only 4.4 percent are bought from drug dealers.27 The Center for Substance Abuse Research concluded the following:

The increase in deaths and sales are highly correlated (r=0.99), supporting previous research showing a strong, statistically significant correlation between states with the highest drug overdose mortality rates and states with the highest overall per capita sales of prescription opioids. These findings suggest that the increased sales of prescription opioids over the past decade may have inadvertently contributed to increases in prescription opioid overdose deaths.28

Prescription opioids are pharmacologically similar to and act on the same brain systems affected by heroin and morphine.29

The pathway from non-medical use of prescription opioids to heroin was described only in 2003 based on evidence from Ohio.30 That study was supported by multiple studies with similar findings that followed over the next 10 years. One study of young urban people who injected heroin in New York and Los Angeles in 2008 and 2009 showed that 86 percent had used prescription opioids non-medically before using heroin.31 This was not the pattern 40 or 50 years ago. Among persons who began their opioid use in the 1960s, more than 80 percent reported that their first opioid was heroin; conversely, in the 2000s, 75 percent of users initiated opioid use with prescription opioids.29

In New York City between April 2012 and March 2016, Mateu-Gelabert32 found that among participants who injected in the past 12 months:
The mean age at prescription opioid initiation was 16.5 years
The mean age of prescription opioid use on a regular basis (three or more times/week) was 18.2 years
The mean age at heroin initiation was 19.1 years
The mean age of heroin use on a regular basis was 19.9 years
The mean age at first heroin injection was 20.3 years
This progression from prescription opioid initiation to heroin initiation over a period of less than three years is supported by the research of other authors. According to Compton and colleagues, non-medical users of prescription opioids often start with oral non-medical use of opioids. As tolerance to opioids develops, and it becomes costlier to maintain abuse patterns, users move to more efficient routes of administration, such as inhaling, smoking or injecting. They tend to initiate heroin use—often through contact with drug users, sexual partners or drug dealers—because it is more available, stronger and easier to smoke, snort or inject.

Benefits and Risks of Prescription Opioid Therapy
Opioid efficacy in acute and cancer pain is well established. An in-depth discussion of the efficacy of opioids for non-cancer chronic pain (defined as pain that persists past the normal time of healing and lasts for three months or longer) is beyond the scope of this paper, but a summary of current evidence suggests that only 30–50 percent of carefully screened patients with non-cancer chronic pain report a decrease in pain with opioids.

Studies that compared the analgesic effect of opioids with other drugs found opioids are not superior to non-steroidal anti-inflammatory drugs (NSAIDs), tricyclic or anticonvulsant drugs with respect to pain and disability. A meta-analysis that pooled data from trials with weak and strong opioids also found no difference in pain outcomes with the use of opioids or NSAIDs, but when data for strong opioids were analyzed separately, strong opioid was more effective than 1000 mg/day of naproxen.

There is a lack of studies showing that prescription opioids improve physical activity, function, sleep, mood or quality of life; there is no evidence that opioids decrease depression, anxiety or physical disability or that they increase return-to-work rates among patients with chronic pain. Uncontrolled prospective studies with follow-up intervals of 6–24 months show that the majority of patients who initially respond to prescription opioids abandon treatment either due to declining efficacy or side effects. The majority of patients with non-cancer chronic pain remain dissatisfied with their treatment, contributing to dose escalation and consequent increase in related adverse effects. In addition, it is well-known that opioid therapy is associated with multiple side effects, and 80 percent of patients experience more than one side effect.

Long-Term Public Health Risks of Opioid Abuse
When any substance is injected using non-sterile injecting equipment there is a risk of infection and disease, particularly if the injecting equipment was previously used. Findings from several authors suggest that many youth (defined by Mateu-Gelabert as ages 18 – 32) perceived prescription opioids as “relatively benign compared to illegal drugs,” i.e., less addictive and safer. Those who injected prescription opioids reported having very little knowledge of HIV and Hepatitis C risk—the blood borne infections most commonly transmitted by needle-syringe-equipment sharing among IDUs—despite “engaging in sporadic instances of syringe-sharing.”

HIV and Hepatitis C
New Jersey’s HIV epidemic was, from the 1980s, fueled by IDU. The percentage of HIV cases attributable to IDU started dropping by 1998, by which time the IDU community started to become saturated with harm-reduction messages. The downward trend continued with the establishment of pilot syringe access programs and later the legalization of the sale of syringes without prescriptions. So far, New Jersey has not seen a significant increase in the percentage and number of HIV cases attributable to IDU. Between 2012 and 2013, the percentage of HIV cases attributable to IDU went from 3 percent to 4 percent and has stayed at 4 percent since.

However, given a resurgence of IDU related to the prescription opioid abuse epidemic, concern still exists about an increase in IDU-related HIV and viral Hepatitis (B, C) infections. This concern is more than theoretical: An HIV outbreak in Indiana took place in a small town of 4,200 in Scott County in early 2015. The incidence of HIV infection went from 5 cases per year to 175 confirmed cases in the first seven months of 2015. The majority of new cases were residents of the same community and were linked to syringe-sharing partners injecting opioid oxymorphone. Coinfection with Hepatitis C was diagnosed in 114 (84.4 percent).

According to the official New Jersey State Hepatitis C statistics, the number of acute Hepatitis C cases has gone from one case in 2004 and 16 in 2005, to 130 in 2015. According to personal communication with Ellen Rudowski, Surveillance Coordinator of New Jersey Department of Health, CDS, the New Jersey Hepatitis C Surveillance data show that although New Jersey has not yet seen a consequent increase in HIV incidence due to increased IDU, a minimum of 70 percent of acute Hepatitis C virus infection cases since 2011 have been linked to IDU. In April 2016, Kathleen O’Brien reported in NJ.com that two out of every five young suburban heroin users in New Jersey are likely to be infected with Hepatitis C. Additionally, they are more likely to have a more aggressive strain of the virus (Hepatitis C3), which is more likely to produce liver cancer, fibrosis or cirrhosis. The study warned of the future public health costs of treating chronic Hepatitis C in today’s IDU population.
Neonatal abstinence syndrome
Abuse of opioids, whether prescription pain relievers or illegal street drugs, by pregnant women can result in neonatal abstinence syndrome (NAS). NAS has increased by almost 300 percent in the U.S. between 2000 and 2009. This increase is driven by both the high rate of opioid prescriptions given to pregnant women as well as by the use of street drugs. In a study published in 2014, 14.4 percent of insured pregnant women were prescribed an opioid at some point during their pregnancy. The safety of opioids to manage pain in pregnancy remains ill-defined. Another study published in 2014 reported that five percent of pregnant women used illicit drugs, including primarily opioids, hallucinogens and central nervous system depressants and stimulants in the preceding 30 days.

Conclusion
The abuse of opioids, whether prescription or illicit, is, as Nora D. Volkow, MD, says, “a serious global problem that affects the health, social and economic welfare of all societies.” This is a public health issue, the resolution to which will require a multifaceted, multiagency, collaborative effort at both clinical and public health levels to support prevention, care and treatment efforts.

The total number of opioids prescribed in the U.S. has skyrocketed in the past 25 years, from approximately 76 million in 1991 to nearly 207 million in 2013 (see Figure 3). This over-prescribing has led to an epidemic of misuse, abuse and addiction to both prescription and non-prescription opioids and, as a consequence, increasing rates of overdose deaths. Over the past decade, heroin use has increased in all age, gender and ethnic/racial groups, but the largest increases were among women, (non-Hispanic) whites and other groups that have historically had lower rates of heroin use (see Figure 2). The misuse and abuse of opioids has been followed by an increase in Hepatitis C infection, NAS and, in some parts of the country, HIV infection.

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