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Psychostimulant-Related Deaths among Former Inmates

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Abstract

Objectives—Psychostimulants are highly addictive and their use is increasing. Little is known about psychostimulant-related deaths. This study identified characteristics, risk factors, and contributing substances reported upon death among former prison inmates who died from a psychostimulant-related death.

Methods—This retrospective cohort study of released inmates from 1999–2003 (N=30,237) linked data from the Washington State Department of Corrections with the National Death Index. We examined characteristics of individuals who died with psychostimulants listed among their causes-of-death. These were categorized into three groups: 1) non-cocaine psychostimulants, 2) cocaine only, and 3) all psychostimulants. Cox proportional hazards regression determined risk factors for death in each group, and the risk of death in the first two weeks after release from prison

Results—Of the 443 inmates who died, 25(6%) had non-cocaine psychostimulants listed among their causes-of-death. Six of these 25 deaths had both non-cocaine psychostimulants and cocaine listed among their causes-of-death. Most of the former inmates who died with non-cocaine psychostimulants were male (n=21, 84%) and non-Hispanic white (88%, n=22). Cocaine only was listed among the causes-of-death for 49 former inmates; most were male (n=35, 71%) and non-Hispanic white (n=27, 55%). Longer length of incarceration was associated with a reduced risk of death from any psychostimulant use (HR=0.76, CI=0.63–0.920 for each additional year of incarceration) and from use of non-cocaine psychostimulants (Hazard Ratio [HR] =0.42, 95% Confidence interval [CI] =0.22 to 0.80). Risk of death was highest during the first 2 weeks post release for cocaine only-related deaths (Incidence mortality ratio [IMR]=1,224.0, CI=583–1,865).

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Conclusions—Former prisoners have a significant risk of death from psychostimulants, especially within the first two weeks post release.

Keywords

methamphetamine; prison; overdose

Introduction

Methamphetamine, cocaine, and other psychostimulants are highly addictive. Their use is increasing across the United States (U.S.) impacting the criminal justice system through psychostimulant-related crimes. Although cocaine is traditionally viewed as the most widely abused psychostimulant, methamphetamine abuse exploded in the Western U.S. in the late 1990s and continues to be a rampant problem (Reding, 2009). In 2007, 1.3 million people aged 12 years or older had used methamphetamine in the past year (SAMHSA-TEDS, 2007). It is inexpensive, easily available, and can be manufactured from pseudoephedrine, an ingredient found in cold decongestants (U.S. Drug Enforcement Administration, 2010). Due to its relatively low cost and potent effects, methamphetamine has emerged as a widely abused drug, especially in the Northwest (NEDTAC, 1998; Hunt, 2006). Other psychostimulants include methylenedioxymethamphetamine, also known as ecstasy, methylphenidate (Ritalin™), and dextroamphetamine (Adderall™). The latter two drugs are used in treating Attention-deficit/hyperactivity disorder (ADHD) and are also increasingly abused (Kaye, Darke and Duflou, 2009; Schifano, 2004; Schifano et al., 2006; Schifano et al., 2010; Dupont et al., 2008; Klein-Schwartz, 2002; DeSantis and Webb, 2008). Nonmedical use of prescription stimulants has been shown to be associated with concurrent illicit polydrug use. (Arria et al., 2008).

Methamphetamine can cause health problems including seizures, cardiac arrhythmias, respiratory failure, brain hemorrhage and death (Darke, 2008). Case reports and population-based studies support a cause-effect relationship between methamphetamine and fatal damage to the cardiovascular, pulmonary, and neurovascular systems (Bashour, 1994; Farnsworth et al., 1997; Westover et al., 2008; Costa et al., 2001; Packe et al., 1990; Ohta et al., 2005; McIntosh et al., 2006; Ho et al., 2009; McGee et al., 2004; Westover et al., 2007; Nestor et al., 1989; Maury et al., 1999). Previous work has been done on cocaine overdose including medical management and death from poisoning (Alaraj et al., 2010; Schwartz et al., 2010; Wood et al., 2009; Xue et al., 2011). Excluding cocaine, little is known about psychostimulant overdose, including the epidemiology of fatal poisoning. Therefore, the focus of the study is to provide new, descriptive information about non-cocaine psychostimulant-related deaths and to compare them to cocaine only-related deaths using a unique cohort of former inmates released from prison followed to death.

The number of adults in the correctional population in the U.S. is increasing. In 2008, over 7.3 million people were on probation, incarcerated, or on parole (Blaze and Bonczar, 2009). Methamphetamine-related crimes rose 4% to 7% from 1997 to 2004 according to the Bureau of Justice Statistics. In 2005, 20% of all drug offenders sentenced in U.S. District Court were due to methamphetamine-related drug offenses (Mumola and Karberg, 2006).

As the U.S. population of former inmates grows, society faces another set of difficulties. People released from incarceration often have a difficult time integrating back into society and engage in risky behavior, such as illicit drug use, which can result in an untimely death (Farrell and Marsden, 2008; Kariminia et al., 2007; Harding-Pink, 1990). A prior study in the northwestern U.S. demonstrated an increased risk of death among former inmates, especially during the first two weeks post-release (Binswanger et al., 2007). Many of these

deaths were attributed to psychostimulants including cocaine and methamphetamine. This study aims to better understand contributing substances and associated health conditions upon death, socio-demographic risk factors, and incarceration risk factors for psychostimulant-related deaths.

Methods

For this retrospective cohort study, we used data from a study of former inmates which included individuals released from the Washington State Department of Corrections (DOC) between July 1, 1999 and December 31, 2003. Of the 30,636 inmates released during the study period, 399 (1%) were excluded from the analysis using previously described exclusion criteria (Binswanger et al., 2007). The final sample consisted of 30,237 former inmates.

Sources of Data

The data were obtained from a retrospective cohort study (Binswanger et al., 2007), which concluded that former inmates released from the Washington State DOC were at a high risk of death after release from prison, especially death related to overdose. The original data set included linkage data from the Washington State DOC with the National Death Index (NDI) which indexes deaths in the U.S. as well as the District of Columbia, The Virgin Islands, and Puerto Rico (National Death Index, 2000). The Washington State DOC provided personal identifiers for all persons released from prison during the study period. These identifiers were linked to the NDI, a computerized database of information abstracted by states from death certificates, using previously described methods (Binswanger et al., 2007). The NDI *Plus* allowed us to determine the underlying and multiple causes-of-death for each deceased former inmate as they translate medical codes listed on death certificates into International Classification of Disease codes, or ICD codes (World Health Organization, 2010). Most cases of death involving drug overdose are certified by a coroner. Many public health and substance dependence studies have used similar methods to link specific databases with NDI to determine cause-of-death information (Bell et al., 2009; Degenhardt et al., 2009; French et al., 2009; Ravndal et al., 2010; Vlahov et al., 2008).

We performed a search of all decedents for the ICD-10 code T43.6, "poisoning by psychostimulants with abuse potential, excluding cocaine." This code was provided by the NDI based on the descriptions listed by the coroner or physician upon death. T43.6 is listed as one of the multiple causes-of-death because poisoning (overdose) deaths cannot be listed as an underlying cause-of-death. In order to determine the underlying cause-of-death, we used the ICD-10 cause-of-death recode set 358. This recode set was established by the National Center for Health Statistics for the purposes of publishing data on causes-of-death from 1999 and beyond. Nineteen of the 25 total deaths due to non-cocaine psychostimulant-related deaths were associated with the underlying cause of death codes for "accidental poisoning by and exposure to drugs and other biological substances" (code 440) or "poisoning by and exposure to drugs and biological substances of undetermined intent" (code 443). Six additional deaths were associated with other underlying causes of death (F15.2, I25, I11.9, Y11, and Y14; see Table 2).

We also examined cocaine only-related death by performing the analogous search using the ICD code T40.5, "poisoning by cocaine." There were 55 total deaths related to poisoning by cocaine (Table 3). Six deaths had both T40.5 and T43.6 listed among their causes-of-death, meaning that upon death, they had both cocaine and another psychostimulant in their system. These deaths were included in the group of 25 inmates who died from psychostimulants (described above), and thus excluded from our final group of 49 inmates

who died with cocaine only. The original study listed 50 deaths with an underlying cause-of-death of overdose who had cocaine also listed among their multiple causes of death. These 50 deaths were not exclusive for cocaine and included some deaths which included stimulants other than cocaine in their system upon death (Binswanger et al., 2007).

We examined demographics among our two study groups (non-cocaine psychostimulant-related deaths and cocaine only-related deaths) compared to the total study population (N=30,237). We tabulated causes-of-death of interest including the underlying cause-of-death listed as contributors to death for both non-cocaine psychostimulant-related deaths and cocaine only-related deaths. Among those who died with non-cocaine psychostimulants, we examined poly-drug abuse, as well as a concurrent diagnosis of mental/behavioral disorders due to the use of multiple drugs.

Statistical Methods

A primary aim is to compare persons whose death was related to psychostimulants to those who did not over variable time at risk. Cox proportional-hazards regression examined whether certain factors were related to survival time. All 30,237 subjects are included in the analyses. The data are right-censored as data on subjects were only obtained through December 31st, 2003, resulting in the majority of subjects not experiencing the outcome of death.

Three separate analyses examined the risk factors for three specific types of death: non-cocaine psychostimulant-related deaths (N = 25), cocaine only-related deaths (N = 49), and the combination of death related to either non-cocaine psychostimulant use or cocaine use (N = 74). Risk factors tested were the demographic variables sex, race, and age, type of release, and length of incarceration (expressed in years). Race was dichotomized into two groups (white and non-white) because some of the race categories did not contain any death events, making the estimation of a hazard ratio for such race categories futile. Otherwise, race and ethnicity were combined to create the following mutually exclusive groups: Latino, Non-Latino White, Non-Latino African American, Non-Latino American Indian/Eskimo/Aleutian, Non-Latino Asian/Pacific Islander, and Other. Groups which include multiple races were combined into “other” due to small numbers of deaths in this category.

Data on potential risk factors for death came from the electronic administrative records of the DOC. Generally, race and ethnicity were self-reported upon intake. Age is analyzed in decade units in order to facilitate easier interpretation of the resultant hazard ratios. Release status was categorized as release into the community under supervision of community custody staff (“community supervision”) or release into the community without any custody supervision (“without community supervision”). Community supervision is also known as parole. We generated hazard ratios (HR) and 95% confidence intervals (CI). Analysis was conducted using Stata 10.1 (College Station, Texas, USA) and SAS 9.2 (SAS Institute Inc., Cary, NC, USA).

In order to assess the risk of death during each 2-week interval, we calculated incident mortality rates (IMR) for each interval, defined as deaths occurring in the given interval per 100,000 person-years of risk. The exact number of days-at-risk in the interval for each subject was calculated, then summed over the cohort of subjects and divided by 365.25 to find the total number of years-at-risk. The number of deaths was divided by the years-at-risk, then multiplied by 100,000 to give the estimated IMR.

It is assumed that the number of deaths, X , follows a Poisson (λ) distribution, where λ is estimated based on the observed data. In order to estimate the confidence interval (CI) for

the IMR, we used large-sample methods for the situations where the number of events is at least 10, for which it is reasonable to assume that the normal approximation to the Poisson distribution holds. Recalling that the mean and variance for X are both λ , we first calculate the 95% CI for λ for the observed years-at-risk as $X \pm z_{1-\alpha/2} \sqrt{X}$, we then simply re-scale this to give the 95% CI for the number of deaths per 100,000 person years-at-risk. When the number of deaths is less than 10, it is not reasonable to assume that the normal approximation to the Poisson distribution holds. In these situations, we used exact methods, first obtaining the 95% CI for the expectation of a Poisson variable given the observed number of deaths from a table, then again re-scaling this to obtain the 95% CI for the IMR per 100,000 person years-at-risk.

Results

Non-Cocaine Psychostimulant-Related Deaths

Of the 30,237 persons released from Washington State DOC, 443 died during a mean follow up period of 1.9 years. Twenty-five (6%) of the 443 inmates had non-cocaine psychostimulants (ICD-10 T43.6) listed as a condition contributing to death (Table 1). Six of these 25 former inmates had both a non-cocaine psychostimulant and cocaine listed among their causes-of-death. Twenty-one (84%) of the former inmates with non-cocaine psychostimulants listed among their causes-of-death were male and 21 (88%) were non-Hispanic white. The mean age at time of release was 35.9 years and the mean number of releases was 1.28. The mean length of stay in prison was significantly shorter for those inmates who died with non-cocaine psychostimulants compared to the overall prison population (0.67 years versus 1.72 years). Among those who died with non-cocaine psychostimulants, the mean years to death post release was 1.08 years compared to 1.17 years in the full cohort. Most deaths occurred in Washington State (n=22, 88%), as in the overall population (n=379, 86%).

Cocaine-Only Related Deaths

There were 49 inmates who died with cocaine listed as a condition of death in the absence of other non-cocaine psychostimulants (Table 1). Seventy-one percent were male (n=35) and the majority were non-Hispanic white (55%, n=27). The mean length of prison stay for those who died with cocaine was shorter than the total prison population (1.30 years versus 1.72 years). The mean time to death post release was much shorter for those who died with cocaine as compared to the large inmate population (0.68 years versus 1.17 years). Similar to the other groups, 94% of the inmates who died with cocaine died in Washington.

Characteristics and Causes of Death

Of the twenty-five former inmates who died with non-cocaine psychostimulants, 22 had overdose (poisoning) listed as the primary cause-of-death (Table 2). Overdose was defined as “accidental” or “of undetermined intent.” “Accidental” poisonings accounted for 19 (76%) all of the psychostimulant-related deaths. Most of the former inmates who died with cocaine only had overdose (n=45) as the underlying cause-of-death.

The physiologic outcomes for the 25 inmates who died with non-cocaine psychostimulants are reported in Table 3. Trends existed among the additional causes-of-death listings. More than half (52%, n=13), had three or more drug types listed among the contributors of death, such as alcohol, cocaine, and/or heroin. Alcohol was listed as an additional condition of death in four non-cocaine psychostimulant-related deaths. Mental/behavioral disorder due to the use of substances was another frequent condition of death (n=12).

Trends for increased risk of death

Men were less likely to die from a cocaine-only related death as compared to women (HR=0.41, CI=0.22–0.77; Table 4). A similar pattern was observed when the non-cocaine psychostimulant-related deaths and the cocaine only-related deaths were combined (n=74, HR 0.55, CI 0.32–0.94). Increasing age was associated with increased risk of death for both the cocaine only-related deaths (HR=1.70, CI=1.31–2.21 for each decade increase in age) and the combination of cocaine and non-cocaine psychostimulant-related deaths (HR 1.59, CI=1.28–1.98). Increased length of incarceration was associated with a decreased risk of death from non-cocaine psychostimulants (HR 0.42, CI=0.22–0.80 for each increasing year of incarceration) and for the combined groups of cocaine-only deaths and non-cocaine psychostimulant deaths (all psychostimulants) (HR=0.76, CI=0.63–0.92).

Time of Release to Death

For all three groups examined, non-cocaine psychostimulant-related deaths, cocaine only-related deaths, and all cause mortality, the incidence mortality rate (IMR) was the highest during the first two weeks post-prison release (Table 5). The proportion of all-cause deaths occurring in the first two weeks was 38/(9%), whereas for cocaine deaths, 14/49 (29%) died in the first two weeks, and for non-cocaine stimulants, 20% of the deaths occurred in the first two weeks. Of the non-cocaine psychostimulant-related deaths, 5 of the 25 total deaths occurred in the first two weeks post prison discharge (IMR=437.1, CI 142–1,020).

Discussion

We found that psychostimulants, including cocaine, were important contributors to drug-related mortality in former inmates. Seventeen percent of deaths among former inmates had non-cocaine psychostimulants (T43.6) or cocaine (T40.5) listed as a contributor to death. A systematic review of the literature showed that prevalence estimates of drug abuse and dependence in male prisoners upon reception into custody is 10–48% in male prisoners and 30–60% in female prisoners (Fazel et al., 2006). These findings show that substance abuse and dependence is significantly more prevalent in the prison population as compared to the general population.

The vast majority of deaths in our study occurred in men. However, women who used cocaine had a higher risk of death than males. This was also seen among the combined cocaine-only and non-cocaine psychostimulant-associated deaths (all psychostimulant-related deaths). Male gender was not statistically significant in regards to an increased risk of death among those who died from a non-cocaine psychostimulant-related death. These findings are in contrast to national death rates related to non-cocaine psychostimulants. According to the CDC Wonder Database, a national database that provides cause-of-death data for all deaths in the United States, during 1999–2004, males aged 15–64 years old have a higher age-adjusted death rate related to non-cocaine psychostimulants as compared to females (males=0.83 [CI 0.80–0.85] per 100,000 person-years [p-y] versus females= 0.32 [CI 0.31–0.33] per 100,000 p-y). This trend continued during 2005–2006 (males=1.42 [CI 1.36–1.47] per 100,000 p-y versus females=0.52 [CI 0.50–0.57] per 100,000 p-y) (CDC Wonder Database). However, two previous studies have reported a higher, but not statistically significant, standardized mortality ratio (SMR) in women versus men who abuse amphetamine/methamphetamine. The first study showed increased mortality for females (SMR= 6.22, CI=4.59–8.25) who were dependent on amphetamine versus males (SMR= 5.87, CI=4.13–8.09) (Lejckova et al., 2007). A second study examining mortality among methamphetamine dependent users had similar findings. Mortality was higher among females (SMR=8.69, SE=0.53) versus males (SMR=5.85, SE=2.11) (Kuo et al., 2010).

The majority of deaths related to psychostimulants were seen in non-Hispanic white males, which reflects use patterns in the United States (Ititani et al., 2007). Non-white race was not protective for a death related to non-cocaine psychostimulants, but did show a trend in that direction.

Two of the most commonly reported co-occurring diagnoses upon death among those who died with non-cocaine psychostimulants were mental disorders due to the use of drugs and accidental overdose. Psychosis, depression, and anxiety disorders have been reported with use of methamphetamine. (Salo et al., 2010; Glasner-Edwards et al., 2009; Yen et al., 2006). It is possible that when a former inmate is released from prison, he is more vulnerable to the effects of the drug, and has an increased risk of developing a substance-related mental disorder. Alternatively, ex-inmates with mental disorders likely have more severe drug use diatheses. Increased vigilance may be needed if a former inmate with a known substance abuse history shows signs of a mental disorder during the post discharge period.

The other commonly reported co-occurring cause-of-death among those who died with non-cocaine psychostimulants was accidental drug overdose, or overdose of undetermined intent. This finding was also observed to be a common co-occurring cause of death among those who died with cocaine-only. Former inmates show a highest risk of death 1–2 weeks post prison discharge. The excess rates of acute drug-related mortality observed in the initial post-release period among former inmates is thought to be due to many factors. Two important contributors to death include decreased drug tolerance after an extended period of abstinence and the concurrent use of multiple drugs (O'Neil et al., 2006; Møller et al., 2010). These findings are reported more commonly among opioid users and their applicability to stimulant users remains unclear. Inmates likely engage in high risk behavior immediately post discharge, which increases their risk of death. Over an eight week period post prison discharge, risk of death stabilizes.

Longer length of stay in prison was found to be protective in two outcome measures: non-cocaine psychostimulant-related deaths and the combined groups of non-cocaine psychostimulant-related deaths and cocaine only-related deaths. In the cocaine only-related deaths, an increased prison stay was not found to be significantly protective, but the trend was toward this effect. This association has been observed for overdose deaths of all types in the original cohort (Binswanger et al., 2011). This protective finding may be related to drug rehabilitation programs offered to inmates incarcerated in the Washington State DOC. In Washington, offenders are screened for addiction and given substance abuse treatment, including long term treatment, known as a therapeutic community (TC), which lasts from 6–12 months in a structured, residential setting. Outpatient treatment is offered to former inmates and provides a minimum of 3 months of transitional care at designated community-based sites. According to Washington DOC, approximately 85% of offenders complete treatment through the TC program, 90% complete intensive outpatient treatment, and 67% complete outpatient treatment in the community (Patty Noble-Desy, Washington DOC). It is not clear if this finding would be observed in other states with less access to treatment. Further study is needed to determine if resources dedicated to identifying and treating substance abusing inmates may reduce the risk of death among inmates. One can further speculate whether longer sentences allow healing of prior health effects of psychostimulants, especially development of collateral coronary circulation, or lower tolerance among subjects who have completed longer sentences allows access to euphoria at lower dose of the drug.

Further research is needed on the mechanism by which psychostimulants result in death and whether it differs by type of psychostimulant used. There appear to be multiple mechanisms by which methamphetamine causes death and our study population reflects a few them, specifically neurovascular and cardiovascular pathology (Table 3). Acute coronary

syndrome causing myocardial infarction from amphetamine/methamphetamine is described in the literature (Bashour, 1994; Farnsworth et al., 1997; Westover, Nakonezny and Haley, 2008; Costa et al., 2001; Packe et al., 1990; Turnspeer et al., 2003). Methamphetamine-associated cardiomyopathy and decompensated heart failure have also been described (Kaye et al, 2007; Diercks et al., Wijetunga et al., 2003; Yeo et al., 2007; Diercks et al., 2007), along with ischemic strokes, artery dissections, and hemorrhagic strokes. (Ohta et al., 2005; McIntosh et al., 2006; Ho et al., 2009; McGee et al., 2004; Westover et al., 2007). Methamphetamine has also been shown to cause pulmonary complications, notably acute pulmonary edema (Nestor et al., 1989; Maury et al., 1999). ICD-10 codes were limited in their ability to provide a more refined pathologic mechanism of psychostimulant-related cause-of-death.

Multiple drugs reported as contributing causes-of-death was a common finding in our study. Fifty-two percent of the former inmates who died with non-cocaine psychostimulants listed as a cause-of-death had three or more drug types listed among the contributors to death. Polysubstance abuse makes it difficult to determine whether the psychostimulant was a proximate cause-of-death, a key interaction drug potentiating the effects of other drugs simultaneously abused, or just an epiphenomenon. According to the Surveillance for the National Vital Statistics Reports, the number of overdose deaths from cocaine has risen from 1999 to 2007 (3,000 deaths in 1999-5,000 in 2007). In contrast, deaths from heroin overdose have remained steady, about 1,700 in 1999 and 1,900 in 2007, possibly due to the implementation of naloxone training programs in heroin users (CDC 2010; Tobin et al., 2009). A better understanding of the physiologic mechanism of psychostimulant-related deaths would permit the development of preventive therapies, antidotes, or appropriate medical management of psychostimulant-related toxicity. Unlike opioids, in which naloxone can reverse toxicity, there is no known antidote for cocaine or methamphetamine toxicity.

Our study was limited by the ambiguity of the ICD-10 code T43.6. Psychostimulants of abuse can refer to methamphetamine, amphetamine, MDMA, methylphenidates, and ephedrine. In our study population psychostimulants most likely referred to methamphetamine; its abuse is on the rise and is more prevalent than other psychostimulants across the Northwest. To better understand methamphetamine-related morbidity and mortality, a specific ICD code should be created to distinguish methamphetamine from other psychostimulants currently listed as drugs of abuse under the T43.6 code.

We do not know specifically how many of the 25 former inmates' deaths were certified by a coroner versus a physician. This represents a limitation which may have led to underascertainment of psychostimulant-related deaths. Suicides, homicides, overdoses, and people who are found dead outside of the hospital generally go to the coroner for a full investigation. When a person dies in a hospital of a known medical cause, an investigation is not necessarily done, and additional causes-of-death may be missed, biasing our results towards the null. For instance, former inmates may have had cardiac disease secondary to methamphetamine abuse hastening a death from heart failure. Methamphetamine may not be in their system at death, but was a major contributor to death. Methamphetamine may have been used by the perpetrators of violence against former inmates who died of homicide (or from motor vehicle accidents). The conditions listed on a death certificate do not define mechanism of death by psychostimulants, but provide information which may lead to a better understanding of the mechanism of death. Our results may not be generalizable to areas of the country where methamphetamine abuse is less common (eg. East Coast), nor may it apply to deaths among individuals not recently released from prison. However, as methamphetamine use continues to rise across the country, our results may gain greater relevance. While our study was limited by the small number of deaths from psychostimulants which may have limited our ability to detect statistically significant risk

factors, to our knowledge, the study included the largest cohort of methamphetamine-related deaths in the United States.

We conclude that criminal justice populations should be warned about the risk of death due to psychostimulants, especially in the context of poly-drug abuse and during the transition from prison to the community. Providing treatment for methamphetamine abuse to inmates, and continuing treatment upon release, may help prevent the trends illustrated by this study. Further research focused on understanding the mechanism of death caused by psychostimulants may allow for the development of an antidote to prevent death caused by acute intoxication. Educating people about the dangers of methamphetamine use and providing high quality drug treatment programs are essential for prevention and treatment.

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Abbreviations

DOC	Department of Correction
NDI	National Death Index
ICD	International Classification of Disease
HR	Hazard ratio
CI	Confidence interval
SAMHSA	Substance Abuse and Mental Health Services

References

- HSA Treatment Episode Data Sets (TEDS). 2007 Oct. <http://www.oas.samhsa.gov>
- Alaraj A, Wallace A, Mander N, Aletich V, Charbel FT, Amin-Hanjani S. Effect of acute cocaine use on vasospasm and outcome in aneurysmal subarachnoid hemorrhage. *World Neurosurg.* 2010 Apr; 73(4):357–360. [PubMed: 20849793]
- Arria A, Caldeira K, O'Grady K, Vincent K, Johnson E, Wish E. Nonmedical use of prescription stimulants among college students: associations with attention-deficit-hyperactivity disorder and polydrug use. *Pharmacotherapy.* 2008; 28:156–169. [PubMed: 18225963]
- Bashour T. Acute myocardial infarction resulting from amphetamine abuse: A spasm-thrombus interplay? *Am Heart J.* 1994; 128:1237–1239. [PubMed: 7985607]
- Bell J, Trinh L, Butler B, Randall D, Rubin G. Comparing retention in treatment and mortality in people after initial entry to methadone and buprenorphine treatment. *Addiction.* 2009 Jul; 104(7): 1193–1200. [PubMed: 19563562]
- Binswanger IA, Blatchford P, Lindsay R, Stern M. Risk factors for all-cause, overdose and early deaths after release from prison in Washington state. *Drug Alcohol Depend.* 2011

- Binswanger IA, Merrill J, Krueger P, et al. Gender differences in chronic medical, psychiatric, and substance-dependence disorders among jail inmates. *Am J Public Health*. 2010; 100(3):476–482. [PubMed: 19696388]
- Binswanger IA, Stern M, Deyo R, Heagerty P, Cheadle A, Elmore J, et al. Release from prison—a high risk of death among former inmates. *N Engl J Med*. 2006; 356(2):157–165. [PubMed: 17215533]
- Bureau of Justice Statistics. Number of state prisoners declined by almost 3,000 during 2009; Federal prison population increased by 6,800. Justice Programs. Press Release June 23, 2010. <http://bjs.ojp.usdoj.gov/content/pub/press/pim09stpy09acpr.cfm>
- CDC's Issue Brief: Unintentional Drug Poisoning in the United States. 2010. <http://www.cdc.gov/HomeandRecreationalSafety/pdf/poison-issue-brief.pdf>
- CDC Wonder Database. <http://wonder.cdc.gov/>
- Costa G, Pizzi C, Bresciani B, Tumscitz C, Gentile M, Bugiardini R. Acute myocardial infarction caused by amphetamines: a case report and review of the literature. *Ital Heart J*. 2001; 2(6):478–480. [PubMed: 11453588]
- Darke S, Kaye S, McKetin R, Duffou J. Major physical and physiological harms of methamphetamine use. *Drug and Alcohol Review*. 2008; 27:253–262. [PubMed: 18368606]
- Degenhardt L, Randall D, Hall W, Law M, Butler T, Burns L. Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: risk factors and lives saved. *Drug Alcohol Depend*. 2009 Nov 1; 105(1–2):9–15. Epub 2009 Jul 15. [PubMed: 19608355]
- DeSantis A, Webb E, Noar S. Illicit use of prescription ADHD medications on a college campus: a multimethodological approach. *Journal of American College of Health*. 2008; 57(3):315–324.
- Diercks D, Fonarow G, Kirk J, Jois-Bilowich P, Hollander J, Weber J, et al. Illicit stimulant use in a United States heart failure population presenting to the emergency department (from the acute decompensated heart failure national registry emergency module). *Am J Cardiol*. 2008; 102:1216–1219. [PubMed: 18940295]
- Diercks D, Kirk J, Turnipseed S, Amsterdam E. Evaluation of patients with methamphetamine- and cocaine-related chest pain in a chest pain observation unit. *Crit Pathways in Cardiol*. 2007; 6:161–164.
- Dupont R, Colemann J, Bucher R, Wilford B. Characteristics and motives of college students who engage in nonmedical use of methylphenidate. *American Journal of Addiction*. 2008; 17(3):167–171.
- Farnsworth T, Brugger C, Malters P. Myocardial infarction after intranasal methamphetamine. *Am J Health-Syst Pharm*. 1997:586–587. [PubMed: 9066872]
- Farrell M, Marsden J. Acute risk of drug-related death among newly released prisoners in England and Wales. *Addiction*. 2008; 103(2):251–255. [PubMed: 18199304]
- Fazel S, Bains P, Doll H. Substance abuse and dependence in prisoners: a systematic review. *Addiction*. 2006; 101:181–191. [PubMed: 16445547]
- French AL, Gawel SH, Hershov R, Benning L, Hessol NA, Levine AM, Anastos K, Augenbraun M, Cohen MH. Trends in mortality and causes of death among women with HIV in the United States: a 10-year study. *J Acquir Immune Defic Syndr*. 2009 Aug 1; 51(4):399–406. [PubMed: 19487953]
- Glasner-Edwards S, Marinelli-Casey P, Hillhouse M, et al. Depression among methamphetamine users: Association with outcomes from the Methamphetamine Treatment Project at 3-year follow up. *J Nerv Men Dis*. 2009; 197(4):225–231.
- Glaze, L.; Bonczar, T. Bureau of Justice Statistics. Bulletin: Probation and Parole in the United States, 2008. U.S. Department of Justice. Office of Justice Programs; 2009 Dec. NCJ 228230. <http://bjs.ojp.usdoj.gov/content/pub/pdf/ppus08.pdf>
- Harding-Pink D. Mortality following release from prison. *Med Sci Law*. 1990; 30(1):12–16. [PubMed: 2304391]
- Ho E, Josephson S, Lee H, Smith W. Cerebrovascular complications of methamphetamine abuse. *Neurocrit Care*. 2009; 10(3):295–305. [PubMed: 19132558]
- Hunt D. Methamphetamine Abuse: Challenges for Law Enforcement and Communities. National Institute of Justice. 2006; 254:24–27.
- Iritani B, Hallfors D, Bauer D. Crystal Methamphetamine use among young adult in the USA. *Addiction*. 2007; 102(7):1102–1113. [PubMed: 17567398]

- Kariminia A, Law M, Butler T, Levy M, Corben S, Kaldor J, et al. Suicide risk among recently released prisoners in New South Wales, Australia. *Med J Aust*. 2007 Jan; 187(7):387–390. [PubMed: 17908000]
- Kayes S, Darke S, Duflou J. (MDMA)-related fatalities in Australia: demographics, circumstances, toxicology and major organ pathology. *Drug and Alcohol Dependence*. 2009; 104(3):254–261. [PubMed: 19604654]
- Kaye S, McKetin R, Duflou J, Darke S. Methamphetamine and cardiovascular pathology: a review of the evidence. *Addiction*. 2007; 102:1204–1211. [PubMed: 17565561]
- Klein-Schwartz W. Abuse and toxicity of methylphenidate. *Current opinion in Pediatrics*. 2002; 14(2): 219–223. [PubMed: 11981294]
- Kuo CJ, Liao YT, Chen W, et al. Causes of death of patients with methamphetamine dependence: A record-linkage study. *Drug and Alcohol Review*. 2010
- Lejckova P, Mravcik V. Mortality of hospitalized drug users in the Czech Republic. *J Drug Issues*. 2007; 37:103–118.
- Maury E, Darondel, Buisinne A, Guitton C, Offenstadt G. Acute pulmonary edema following amphetamine ingestion. *Intensive Care Med*. 1999; 25(3):332–333. [PubMed: 10229175]
- McGee S, McGee D, McGee M. Spontaneous intracerebral hemorrhage related to methamphetamine abuse. *Am J Forensic Med Path*. 2004; 25(4):334–337. [PubMed: 15577524]
- McIntosh A, Hungs M, Kostanian V, Yu W. Carotid artery dissection and middle cerebral artery stroke following methamphetamine use. *Neurology*. 2006; 67:2259–2260. [PubMed: 17190959]
- Møller LF, Matic S, van den Bergh BJ, et al. Acute drug-related mortality of people recently released from prisons. *Public Health*. 2010; 124:637–639. [PubMed: 20888607]
- Mumola, C.; Karberg, J. Bureau of Justice Statistics Special Report. Drug Use and Dependence, State and Federal Prisoners, 2004. 2006 Oct. NCJ 213530. <http://bjs.ojp.usdoj.gov/content/pub/pdf/dudsfp04.pdf>
- National Death Index Plus: coded causes of death. Supplement to the National Death Index user's manual. Hyattsville, MD: National Center for Health Statistics; 1999.
- National Death Index user's manual. Hyattsville, MD: National Center for Health Statistics; 2000.
- National Evaluation Data and Assistance Center (NEDTAC). Epidemiology and Treatment of Methamphetamine Abuse in California: A Regional Report. 1998 Feb. <http://www.icpsr.umich.edu/SAMHDA/NTIES/NTIES-PDF/REPORTS/epidmlgy.pdf>
- Nestor T, Tamamoto W, Kam T, Schultz T. Acute pulmonary oedema caused by crystalline methamphetamine. *Lancet*. 1989; 25:1277–1278. 2(8674). [PubMed: 2573788]
- Ohta K, Mori M, Yoritaka A, Okamoto K, Kishida S. Delayed ischemic stroke associated with methamphetamine use. *J Emerg Med*. 2005; 28(2):165–167. [PubMed: 15707812]
- O'Neil ML, Kuczenski R, Segal DS, Cho AK, Lacan G, Melega WP. Escalating dose pretreatment induces pharmacodynamic and not pharmacokinetic tolerance to a subsequent high-dose methamphetamine binge. *Synapse*. 2006 Nov; 60(6):465–473. [PubMed: 16897726]
- Packe G, Garton M, Jennings K. Acute myocardial infarction caused by intravenous amphetamine abuse. *British Heart J*. 1990; 64:23–24.
- Pitts WR, Lange RA, Cigarroa JE, Hillis LD. Cocaine-induced myocardial ischemia and infarction: pathophysiology, recognition, and management. *Prog Cardiovasc Dis*. 1997 Jul-Aug;40(1):65–76. [PubMed: 9247556]
- Ravndal E, Amundsen EJ. Mortality among drug users after discharge from inpatient treatment: an 8-year prospective study. *Drug Alcohol Depend*. 2010 Apr 1; 108(1–2):65–69. [PubMed: 20022184]
- Reding, N. *Methland-The Death and Life of an American Small Town*. New York: Bloomsbury; 2009.
- Salo R, Flower K, Kielstein A, et al. Psychiatric comorbidity in methamphetamine dependence. *Psychiatry Research*. 2010
- Schifano F. A bitter pill. Overview of ecstasy (MDMA, MDA) related fatalities. *Psychopharmacology*. 2004; 173(3–4):242–248. [PubMed: 14673568]
- Schifano F, Corkery J, Deluca P, Oyefeso A, Ghodse AH. Ecstasy (MDMA, MDA, MDEA, MBDB) consumption, seizures, related offences, prices, dosage levels and death in the UK (1994–2003). *Journal of Psychopharmacology*. 2006; (3):456–463. [PubMed: 16574720]

- Schifano F, Corkery J, Naidoo V, Oyefeso A, Ghodse H. Overview of amphetamine-type stimulant mortality data—UK, 1997–2007. *Neuropsychobiology*. 2010; 61(3):122–130. [PubMed: 20110737]
- Schwartz B, Rezkalla S, Kloner R. Cardiovascular effects of cocaine. *Circulation*. 2010 Dec 14; 122(24):2558–2569. [PubMed: 21156654]
- Tobin K, Sherman S, Beilenson P, Welsh C, Latkin C. Evaluation of the Staying Alive programme: training injection drug users to properly administer naloxone and save lives. *International Journal of Drug Policy*. 2009; 20(2):131–136. Epub 2008 Apr 22. [PubMed: 18434126]
- Treatment Episode Data Set: The TEDS Report. Trends in Methamphetamine Admission to Treatment: 1997–2007. <http://www.oas.samhsa.gov/2k9/209/209MethTrends2k9.html>
- Turnipseed S, Richards J, Kirk J, Diercks D, Amsterdam E. Frequency of acute coronary syndrome in patients presenting to the emergency department with chest pain after methamphetamine use. *J Emerg Med*. 2003; 24(4):369–373. [PubMed: 12745036]
- U.S. Drug Enforcement Administration. Methamphetamine. 2010. <http://www.justice.gov/dea/concern/meth.html>
- Washington State Department of Corrections. Offender Life-Substance Abuse Treatment. <http://www.doc.wa.gov/family/offenderlife/substanceabuse.asp>
- Westover A, McBride S, Haley R. Stroke in young adults who abuse amphetamines or cocaine. *Arch Gen Psychiatry*. 2007; 64:495–502. [PubMed: 17404126]
- Westover A, Nakonezny P, Haley R. Acute myocardial infarction in young adults who abuse amphetamines. *Drug and Alcohol Dependence*. 2008; 96:49–56. [PubMed: 18353567]
- Wijetunga M, Seto T, Lindsay J, Schatz I. Crystal methamphetamine-associated cardiomyopathy: Tip of the iceberg? *J of Toxicology*. 2003; 41(7):981–986.
- Wood D, Dargan P, Hoffman R. Management of cocaine-induced cardiac arrhythmias due to cardiac ion channel dysfunction. *Clin Toxicol (Phila)*. 2009 Jan; 47(1):14–23. [PubMed: 18815938]
- World Health Organization. International Classification of Disease. 2010. <http://www.who.int/classifications/icd/en/>
- Vlahov D, Wang C, Ompad D, Fuller CM, Caceres W, Ouellet L, Kerndt P, Jarlais DC, Garfein RS. Collaborative Injection Drug User Study. Mortality risk among recent-onset injection drug users in five U.S. cities. *Subst Use Misuse*. 2008; 43(3–4):413–428. [PubMed: 18365941]
- Xue L, Ko MC, Tong M, Yang W, Hou S, Fang L, Liu J, Zheng F, Woods JH, Tai HH, Zhan CG. Design, preparation, and characterization of high-activity mutants of human butyrylcholinesterase specific for detoxification of cocaine. *Mol Pharmacol*. 2011 Feb; 79(2):290–297. Epub 2010 Oct 22. [PubMed: 20971807]
- Yen CF, Chong MY. Comorbid psychiatric disorders, sex, and methamphetamine use in adolescents: a case-control study. *Comprehensive Psychiatry*. 2006; 47:215–220. [PubMed: 16635651]
- Yeo K, Wijetunga M, Ito H, Eford J, Tay K, Seto T, et al. The association of methamphetamine use and cardiomyopathy in young patients. *The Am J of Med*. 2007; 120:165–171.

Table 1

Demographics of the 30,237 former inmates release from the Washington State DOC July 1999–2003, those that died with T43.6 as an associated causes of death, and those that died with T40.5 as an associated cause of death.

Demographics	Total cohort released from 1999–2003 (N=30,237)	Total cohort with non-cocaine psychostimulants listed as a contributor of death (n=25)	Total cohort with cocaine only listed as a contributor of death in absence of other psychostimulants (n=49)
Sex, % (n)			
Male	87% (26,270)	84% (21)	71% (35)
Female	13% (3,967)	16% (4)	29% (14)
Race, % (n)			
White	62% (18,836)	84% (21)	55% (27)
African American	20% (5,932)	8% (2)	39% (19)
Hispanic	13% (3,803)	4% (1)	4% (2)
Native American, Alaska Native, non-Hispanic	3% (1,021)	4% (1)	2% (1)
Asian or Pacific Islander, non-Hispanic	2% (576)	0	0
Other or Unknown	0% (69)	0	0
Age (years)			
Mean	34.0+/-9.8	35.9+/-8.5	38.9+/-10.1
Median	32.9	36.3	39.3
Release type, % (n)			
Discharged	26% (7,842)	48% (12)	31% (15)
Other	3% (810)	0	0
Community Custody	71% (21,585)	52% (13)	69% (34)
Characteristics of the 443 inmates who died			
State where death occurred, % (n)			
Washington	86% (379)	88% (22)	94% (46)
Oregon	4% (17)	8% (2)	0
California	4% (17)	4% (1)	2% (1)
Other	6% (30)	0	4% (2)
Mean number of releases	1.28	1.28	1.29
Mean length of prison stay (years)	1.72	0.67	1.30
Mean time to death post release (years)	1.17	1.08	0.68

Table 2

Underlying cause of death for 25 former inmates who died with non-cocaine psychostimulants and 64 former inmates who died with cocaine only.

Underlying Cause of Death associated with T43.6*	Definition of ICD code	Number of deaths with Specified ICD code (X=25)
F15.2	Mental and behavioural disorders due to psychoactive substance use.	2***
I11.9, I25.0	Heart disease	2
Y11, Y14	Poisoning by and exposure to substances, undetermined intent	3
X41, X44	Accidental poisoning by and exposure to substances	19
Underlying Cause of Death associated with T40.5**	Definition of ICD code	Number of deaths with Specified ICD code (X=49)
I21.9	Acute myocardial infarction, unspecified	2
W69	Drowning	2
Y14	Poisoning by and exposure to substances, undetermined intent	2
X42, X44	Accidental poisoning by and exposure to substances	45

* T43.6=Poisoning by psychostimulants with abuse potential

** T40.5=Poisoning by cocaine

*** Values 2 are not reported to avoid identifying study participants

Table 3

Characteristics of former inmates who died with the ICD-10 code T43.6

Most frequent co-occurring reasons for death*	Number of deaths with code T43.6
Three or more drug types listed among contributors of death	13
Mental/behavioral due to the use of multiple drugs listed as a condition of death	12
Cocaine and psychostimulants dually listed as conditions of death	6
Anoxic brain injury	2
Intracerebral hemorrhage or subarachnoid hemorrhage/stroke	2
Cardiac arrest	2**

* Condition may be listed more than once for each death reported

** Values 2 are not reported to avoid identifying study participants

Among former inmates (N=30,257), potential risk factors for each of three outcomes: psychostimulant-related deaths (excluding cocaine), cocaine only-related deaths, and the combined group

Table 4

	Non-Cocaine Psychostimulant Related Death(N=25) *	Cocaine only Related Death(N=49) **	Combined Psychostimulant and Cocaine Related Deaths (n=74) ***			
	Hazard Ratio	Hazard Ratio	Hazard Ratio			
	95% Lower and Upper Confidence Interval	95% Confidence Interval	95% Confidence Interval			
Male	1.05	0.36-3.09	0.41	0.22-0.77	0.55	0.32-0.94
Non White race	0.35	0.12-1.04	1.48	0.84-2.61	0.98	0.60-1.58
Age (Decade)	1.38	0.93-2.05	1.70	1.31-2.21	1.59	1.28-1.98
On community custody after release	0.52	0.23-1.14	0.91	0.49-1.67	0.75	0.46-1.20
Increasing length of prison stay (by year)	0.42	0.22-0.80	0.85	0.71-1.02	0.76	0.63-0.92

* Includes six T40.5 related deaths

** Includes T40.5, exclusive of T43.6

*** Includes all T40.5 and T43.6

Incidence mortality rate per 100,000 person-years for each group, non-cocaine psychostimulant-related deaths, cocaine only-related deaths, and all cause mortality by weeks post-prison discharge

Table 5

Interval	N At Risk	Deaths	Tot Days at Risk in Interval	Tot Yrs at Risk in Interval	Incidence Mortality Rate (IMR)*	95% CI for IMR
Non-Cocaine Psychostimulant-Related Deaths (T43.6)						
Weeks 1-2	30,237	5	417,777	1,143.81	437.1	(142, 1,020)
Weeks 3-4	29,519	1	409,692	1,121.68	89.2	(2, 497)
Weeks 5-6	28,961	0	402,091	1,100.87	0.0	(0, 335)
Weeks 7-8	28,437	0	394,560	1,080.25	0.0	(0, 342)
All Weeks	30,237	25	18,519,091	50,702.51	49.3	(30, 69)
Cocaine only-Related Deaths (T40.5)						
Weeks 1-2	30,237	14	417,777	1,143.81	1,224.0	(583, 1865)
Weeks 3-4	29,519	2	409,692	1,121.68	178.3	(22, 644)
Weeks 5-6	28,961	3	402,091	1,100.87	272.5	(56, 797)
Weeks 7-8	28,437	3	394,560	1,080.25	277.7	(57, 812)
All Weeks	30,237	49	18,519,091	50,702.51	96.6	(70, 124)
All Cause Mortality						
Weeks 1-2	30,237	38	417,777	1,143.81	3,322.2	(2,266, 4,379)
Weeks 3-4	29,519	13	409,692	1,121.68	1,159.0	(529, 1,789)
Weeks 5-6	28,961	8	402,091	1,100.87	726.7	(313, 1,432)
Weeks 7-8	28,437	11	394,560	1,080.25	1,018.3	(417, 1,620)
All Weeks	30,237	443	18,519,091	50,702.51	873.7	(792, 955)

* Incidence Mortality Rate = Deaths per 100,000 Person Years-at-Risk