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## Challenges of Treating Methamphetamine-Positive Patients

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### Abstract

**Background:** Methamphetamines are addictive stimulants that induce dopamine release, a sense of euphoria, and increased libido. The effects of methamphetamine in inhibiting control of cognitive behavior and increasing arousability are thought to augment the potential for violence. Withdrawal from methamphetamine produces symptoms such as depression, fatigue, hypersomnolence, irritability, and agitation. Per the National Survey of Drug Use and Health (NSDUH), abuse of methamphetamine has increased in the past few years from 440,000 in 2012 to 569,000 in 2014. Wider use in the general population has led to an escalation in related emergency department visits and mounting expenditures due to prolonged length of hospitalization.

**Methods:** A literature search following PRISMA guidelines was conducted through PubMed. Studies were selected based on relevance and then categorized. Those that focused on diagnosis and cost of management were included. All studies, regardless of publication date, were considered due to the paucity of literature regarding methamphetamine treatment and withdrawal.

**Results:** A total of 9,792 studies were identified following the initial search. Sixty-three articles were found to be appropriate after screening of the title, abstract, and body of the papers. Of these, 12 retrospective and prospective studies met inclusion criteria and contained information on methamphetamine-positive trauma patients, Injury Severity Score (ISS), hospital resource utilization, and cost. Although methamphetamine-users have a lower overall ISS compared to non-users, various studies documented an increased utilization of hospital resources and, in some cases, prolonged hospital stays in methamphetamine-positive patients.

**Limitations:** Limitations of this article are like all PRISMA-guided review studies: the dependence on previously published research and availability of references as outlined in our methodology. The studies specific to this topic include mostly subjective experiences with very limited Level I or II data.

**Conclusion:** Methamphetamine use has steadily increased since 2012. Use of methamphetamine impairs both executive and cognitive abilities, putting patients and others at risk for injuries in comparison to nonusers. The most common mechanisms of injury are assault and gunshot wounds. Increased length of hospital stays, admission to the Intensive Care Unit (ICU), need for emergent operative intervention, hospital staff resources, and ambulance transport have all been associated with patients who use methamphetamine. Although methamphetamine users exhibit relatively lower Injury Severity Scores compared to nonusers, they utilize greater hospital resources and contribute to escalating health care costs.

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### Keywords

Methamphetamine, Amphetamine, Test, Trauma, ISS

## Introduction

Methamphetamines are addictive stimulants that induce dopamine release, a sense of euphoria, and increased libido. The effects of methamphetamine in inhibiting control of cognitive behavior and increasing arousability are thought to augment the potential for violence [1]. With a half-life of 12 hours [2], methamphetamine's potential for abuse has been a growing problem in most cities. According to the National Survey of Drug Use and Health (NSDUH) from the Substance Abuse and Mental Health Services Administration (SAMHSA), the number of people age 12 or older who are current users of methamphetamine rose from 440,000 in 2012 to 569,000 in 2014 [3,4]. In 1989, 7.4% of trauma patients tested positive for methamphetamine use, and in 1994, the number almost doubled to 13.4% [5]. One study found that 34.9% of methamphetamine users had committed an act of violence while under the influence [1]. Methamphetamines may induce significant neurological manifestations, such as hallucinations, delirium, and seizures [6]. Chronic users of methamphetamine have experienced hallucinations and paranoia [6]. Paranoia with hallucinations was widely reported in both the first and second methamphetamine epidemic in Japan [7]. In the first epidemic from 1945-1957, the incidence of paranoid features with hallucinations was 72%. During the second epidemic from 1970-1992, the incidence increased to 76.3% [7]. Schizophrenia-like symptoms induced by methamphetamine have been attributed to changes in uptake of methamphetamine and dopamine at nerve terminal membranes [7].

Increased use of methamphetamines in the general population has led to greater numbers of trauma patients who are methamphetamine-positive. Furthermore, this patient population requires additional care to manage complications related to methamphetamine while in the hospital, which leads to higher resource utilization and escalating healthcare expenditures.

## Methods

A literature search was conducted through PubMed following PRISMA guidelines (Figure 1). Key phrases that were searched for included "methamphetamine and pediatrics", "methamphetamine and pregnant adults", "methamphetamine and adults", "methamphetamine treatment", "methamphetamine and withdrawal", "methamphetamine and trauma", "methamphetamine and severity score", "methamphetamine and test", and "methamphetamine and urine". After reviewing the title and abstract of all studies, those in English were selected based on relevance, especially those that focused on the diagnosis, demographics, and cost of management. Studies were categorized as well based on the PRISMA checklist. Due to the paucity of published

work, all studies, regardless of date of publication, were considered.

## Results

The PubMed search yielded the following results for each search term: "methamphetamine and pediatrics"-111 results, 2 relevant, 0 selected; "methamphetamine and pregnant adults"-47 results, 3 relevant, 0 selected; "methamphetamine and adults"-859 results, 9 relevant, 2 selected; "methamphetamine and treatment"-763 results, 10 relevant, 2 selected; "methamphetamine and withdrawal"-429 results, 3 relevant, 1 selected; "methamphetamine and severity score"-38 results, 1 relevant, 1 selected; "methamphetamine and trauma"-252 results, 20 relevant, 4 selected; "methamphetamine and urine"-962 results, 16 relevant, 2 selected. A total of 9,772 studies were identified following the initial search. After removing duplicates, 4,657 articles remained, and then 63 studies were deemed appropriate after screening of the title, abstract, and body of the papers. Articles were excluded that were published in non-English languages, discussed animal models, or did not discuss a correlation between methamphetamine-positive patients and Injury Severity Score or hospital costs. Of these, 12 studies on methamphetamine-positive trauma patients included complete information on Injury Severity Score, hospital resource utilization, and cost. The selected studies contained both retrospective and prospective reports that identified demographic information and clearly correlated methamphetamine use to Injury Severity Score, hospital length of stay, and cost of hospital resources.

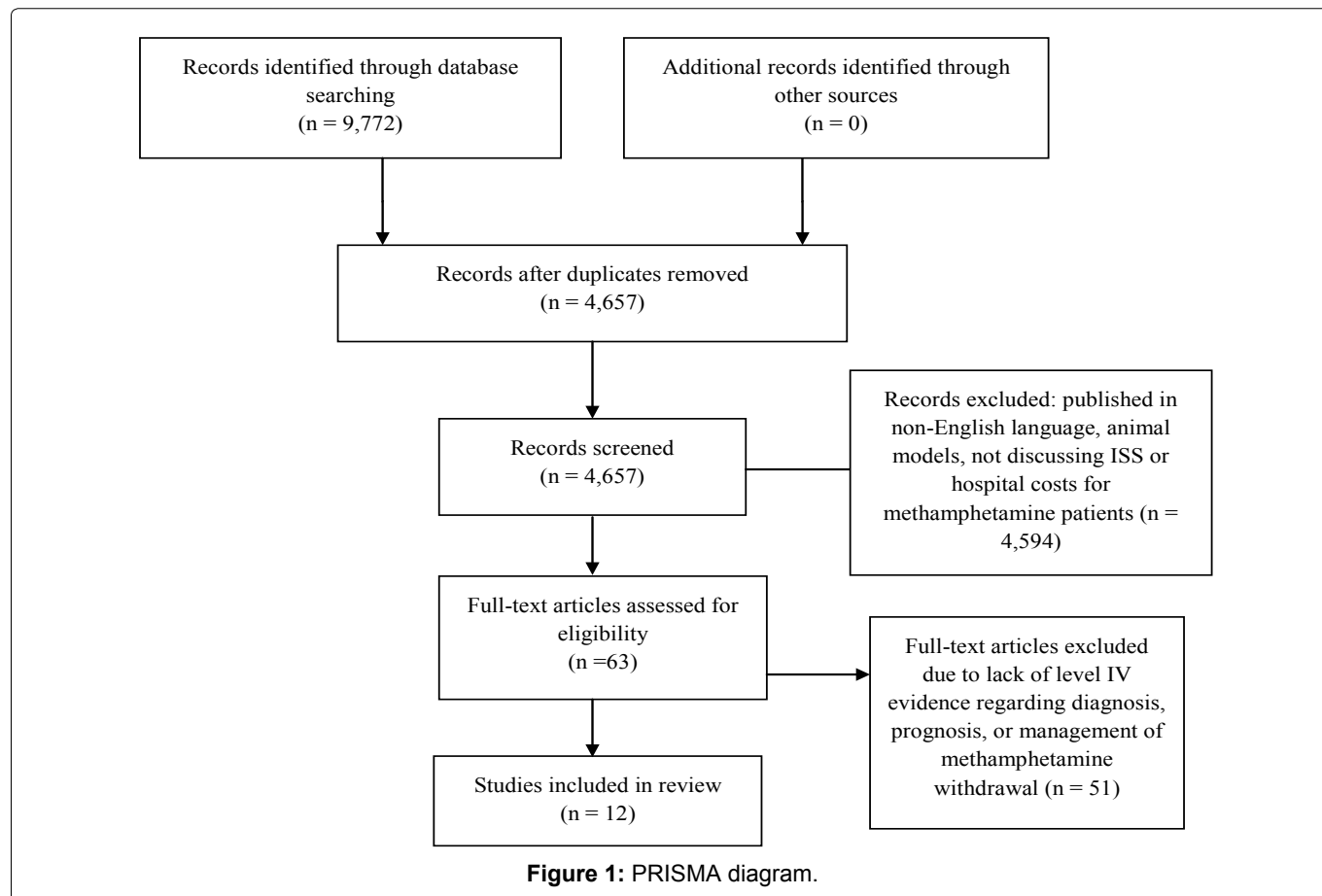
## Discussion

Methamphetamine use increases the risk for injury by promoting risk-taking behavior [8]. While operating a vehicle under the influence of methamphetamine, a person's driving behavior typically includes drifting, weaving in and out of lanes, and high speed collisions [9]. In addition, the withdrawal symptoms of methamphetamine, such as depression, fatigue, hypersomnolence, irritability, and agitation, have been shown to contribute to motor vehicle collisions [5,8]. One study found that common injuries included blunt assault and gunshot

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wounds [8]. Methamphetamine users are predominantly male and with an average age in the mid-thirties [8]. Studies have also shown that Caucasians and Latinos are more likely to test positive for methamphetamine compared to African Americans [8]. Methamphetamine users are more likely to lack health insurance [8]. The University of California-Davis Medical Center found that the most common demographic of methamphetamine use was uninsured Caucasian males in their late 30s. Tobacco use was also a common comorbidity in this group. This same study reported an upward trend in methamphetamine use among females due to perceived effects of wakefulness, weight loss, and enhanced libido [9].

Patients admitted to trauma centers are assigned an Injury Severity Score (ISS). This score is determined from six body regions based on the significance of the associated injury: head, face, chest, abdomen, extremities, and external. Each region is then assigned an Abbreviated Injury Score (AIS). The highest three AIS regions are each squared and added together to form the overall ISS, which ranges from a value of 0 to 75. The ISS has been shown to predict morbidity, mortality, and length of hospitalization following trauma [10]. In an interesting study from 2009, methamphetamine-positive patients had noticeably higher face and lower chest AIS values than those who did not use methamphetamine [8]. Methamphetamine users were more likely to have trauma-

ma-related complaints than non-users (37% vs. 21%). Altered level of consciousness and chest and abdominal pain were other common complaints by methamphetamine-positive patients [9]. Glasgow Coma Scale (GCS) scores however, were only slightly lower in methamphetamine users than in non-users [8].

Generally, ISS has been shown to correlate with higher hospital costs secondary to longer lengths of stay [8]. Although methamphetamine patients often suffer minimal traumatic injuries and have overall lower ISS values, they incur much higher hospital costs compared to patients with a higher ISS [8]. One prospective study found a significant difference in hospital admission rates between methamphetamine users and non-users (58% vs. 22%) [9]. Another year-long study at a regional tertiary trauma center [6] corroborated this finding: a greater use of hospital resources was found in methamphetamine-positive patients. Length of hospital stay was one day longer for positive patients ( $2.7 \pm 0.4$  vs.  $1.7 \pm 0.1$ ). A significant difference in billing charges for methamphetamine-positive patients ( $\$15,617 \pm \$1866$ ) versus methamphetamine-negative patients ( $\$11,600 \pm \$648$ ) was also reported [6].

One retrospective review study examined the relationship between methamphetamine testing and hospital admissions. From an initial population size of 5,372

people, 526 individuals tested positive for methamphetamine [2]. Although this study did not find a significant difference in Intensive Care Unit (ICU) days between the methamphetamine positive patients and negative patients (6.7 vs. 7.9), it did find a difference in ISS scores greater than or equal to 16 (28.2% for methamphetamine positive vs. 24.3% for methamphetamine negative). The study also found that methamphetamine intoxication was twice as likely to require ambulance transport to the hospital (69% vs. 22%) [9] as well as hospital admission [2]. Since the physical examination in this patient population is often unreliable, greater use of diagnostic testing may lead to increased costs and longer hospitalization. Symptoms such as tachycardia, diaphoresis, and/or altered sensorium are frequent methamphetamine-induced effects which often require ongoing clinical evaluation, diagnostic testing, and continued monitoring in an acute care environment. Both hospital and ICU stays are often prolonged until these symptoms abate to a level where a patient can be safely and thoroughly evaluated [6]. At times, this clinical effect can last for days. In our experience, we routinely observe a “five-day methamphetamine” effect in our methamphetamine positive trauma patients.

In the study by London, et al. conducted in 2009, 557 of 6,193 patients tested positive for methamphetamine. After analyzing the Length of Hospital Stay (LOS), they found that overall LOS was actually similar between methamphetamine users and nonusers. Methamphetamine-positive patients incurred 16% higher hospital costs compared to nonusers-most of this related to diagnostic testing. Methamphetamine-positive patients required greater utilization of the emergency department, CT/MRI, and radiology in general compared to methamphetamine-negative patients. Increases in overall cost were also attributed to the unreliable physical examination in such patients, which led surgeons to operate more often. The authors estimated that if 10% of ICU admissions were due to minimally injured methamphetamine-positive patients, their annual direct costs would amount to more than four million dollars [8]. A comparison of burn patients from methamphetamine lab explosions supported this opinion that users often present additional challenges to the clinicians because of greater initial resuscitation requirements when compared to similar burn patients who were methamphetamine-negative [11].

Methamphetamine withdrawal has variable symptomatology and clinical manifestations. The acute phase is characterized by hypersomnolence, polyphagia, agitation, fatigue, and depression for 7-10 days following use of methamphetamine. Beyond 10 days, symptoms of sleep and appetite irregularities can last up to 2 weeks. The most common withdrawal symptoms in untreated users

were moderate depression, decreased attention span, and increased irritability [12]. Additional symptoms of palpitations, chest pain, and difficulty breathing have been reported [6]. Pneumomediastinum, pneumothorax, pulmonary hypertension, myocardial infarction, and acute pulmonary edema have also been reported in methamphetamine-positive patients without a clear underlying traumatic etiology [6,13]. Methamphetamine users are also more likely to develop coronary artery disease and subarachnoid hemorrhage [2].

Correctly identifying patients who are methamphetamine positive is important for proper care and management in the hospital, especially in cases of withdrawal. Currently, many trauma centers and hospitals use a seven-panel urinalysis drug screen, which does not distinguish between methamphetamines and other chemically similar compounds in the same class of drugs. For example, medications such as brompheniramine, phenylpropanolamine, bupropion, trazodone, chlorpromazine, promethazine, and ranitidine have been reported to cause false-positive results of amphetamine in urine drug screens [14]. If a patient has an amphetamine-positive urine toxicology screen, physicians should consider further confirmatory testing with an expanded drug screen aimed to specifically detect methamphetamines. Due to the high number of false positive screens related to amphetamines in general, a confirmatory test should be conducted using gas chromatography/mass spectrometry or high-performance liquid chromatography. False-negatives from urine drug analysis may occur when small drug quantities are ingested, with prolonged time since drug administration, and when large quantities of fluid have been ingested by the patient. The manipulation of urine testing with household products such as vinegar, bleach, and table salt should also be considered, as these products interfere with antigen-antibody binding in urine drug analysis. Further analysis with pH testing and urine density can help elucidate if a sample has been chemically altered (Table 1) [15].

## Limitations

Limitations of this article are like all PRISMA-guided review articles: the dependence on previously published research and availability of references. In addition, the volume of Level I, II, and III evidence regarding this specific issue in trauma patients is minimal. These types of evidence are preferred as they represent strong correlation between variables through rigorous research, as Level I and II research represent randomized double-blind control trials, Level III represents retrospective or case control studies or systematic reviews while Level IV represents case series and Level V represents expert opinion and specific case reports (Table 2) [16].

**Table 1:** Methamphetamine withdrawal, 1995-Present.

Year	Author	N	Study design	Outcome
1995	Richards	1,679	Retrospective	Significant increase in pre-hospital respiratory rate in methamphetamine-positive patients, but otherwise no other significant differences in vital signs when controlling for age.
1999	Schermer	10,298	Retrospective	Most common mechanism of injury for methamphetamine-positive patients was MVA/MVC. Significant increase from 1984 to 1994.  Mechanisms of trauma for alcohol and methamphetamine were similar. There were similar intervention programs for methamphetamine trauma compared to alcohol.
1999	Richards	461	Retrospective	Demographically, there was a larger inclusion of uninsured patients who were also more likely to use ambulance transport and be admitted to the hospital. Methamphetamine-positive patients had greater utilization of pre-hospital and hospital resources.
2004	Tominga	544	Retrospective	Methamphetamine-positive patients were more likely to have intentional self-injury/assaults, longer hospital stay, and greater hospital charges. They were also more likely to be admitted to the hospital despite having lower ISS scores.
2006	Sommers	106	Prospective, Survey	34.9% of patients with greater than 3 months of methamphetamine use had a history of violence and were more likely involved in private domestic domains.
2007	Yegiyants	971	Retrospective	Methamphetamine-positive patients had higher rates of assault, increased admission for ISS 1-5, and increased length of stay for ISS 6-10. There was no reported difference in total ICU or ventilator days.
2009	London	4,340	Retrospective cohort	Stimulant users less likely to use behavioral health services than opioid users and more likely to use urgent/emergent care and inpatient care compared to non-users. Integrated medical and mental healthcare and drug treatment may reduce utilization of costly healthcare services.

**Table 2:** Levels of evidence.

Level of evidence	Description
I	High-quality randomized controlled trials
II	Lesser-quality randomized controlled trials
III	Retrospective comparative study; case control study; systematic review
IV	Case series
V	Expert opinion or case report

Adapted from Chung, et al. [16].

## Conclusions

This thorough review of the literature regarding methamphetamine use in trauma patients identified a paucity of available literature on the subject. Methamphetamine use has increased since 2012 and continues to rise to epidemic proportions. Use of methamphetamine can affect cognitive abilities and perception resulting in an increase in risk-taking behavior, which may manifest in either intentional or unintentional injuries. Although methamphetamine positive patients typically present with lower Injury Severity Scores compared to nonusers, research has revealed that their length of hospitalization is longer. Indeed, studies have shown that length of hospital stay, ICU admission, probability of emergent operative intervention, use of hospital staff resources, and overall healthcare-related costs are much higher in methamphetamine users. Unfortunately, the use of methamphetamine and related substances appears to be increasing on a global scale. It is therefore strongly recommended that healthcare providers become knowledgeable with the scope of

methamphetamine use, as well as its physiological effects, symptoms of acute intoxication, and withdrawal. Given a lack of published studies specific to this topic, we urge political leaders, healthcare administrators, and national organizations to study this problem formally.

## Conflict of Interest

All authors declare no conflict of interest.

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