



## Review

# Methamphetamine: An update on epidemiology, pharmacology, clinical phenomenology, and treatment literature



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## ABSTRACT

**Background:** Despite initial reports of a decline in use in the early 2000s, methamphetamine remains a significant public health concern with known neurotoxic and neurocognitive effects to the user. The goal of this review is to update the literature on methamphetamine use and addiction since its ascent to peak popularity in 1990s.

**Methods:** We first review recent epidemiological reports with a focus on methamphetamine accessibility, changes in use and disorder prevalence rates over time, and accurate estimates of the associated burden of care to the individual and society. Second, we review methamphetamine pharmacology literature with emphasis on the structural and functional neurotoxic effects associated with repeated use of the drug. Third, we briefly outline the findings on methamphetamine-related neurocognitive deficits as assessed via behavioral and neuroimaging paradigms. Lastly, we review the clinical presentation of methamphetamine addiction and the evidence supporting the available psychosocial and pharmacological treatments within the context of an addiction biology framework.

**Conclusion:** Taken together, this review provides a broad-based update of the available literature covering methamphetamine research over the past two decades and concludes with recommendations for future research.

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## 1. Introduction

Methamphetamine use remains a significant public health concern in the United States (U.S.) and worldwide. Research has greatly advanced our knowledge of the epidemiology, consequences, and treatment of methamphetamine use disorders since methamphetamine's peak in popularity in the 1990s. Thus, the goal of this review is to update the literature on methamphetamine use and addiction since its ascent to popularity. To do so, we cover recent epidemiological reports, methamphetamine pharmacology, and briefly outline the neurocognitive deficits associated with chronic methamphetamine use. We also discuss the clinical presentation of methamphetamine addiction and the evidence supporting the available psychosocial interventions and pharmacological treatments.

This review is intended to supplement recent, more comprehensive reviews of pharmacologic treatments for methamphetamine addiction (i.e., [Brackins et al., 2011](#); [Brensilver et al., 2013](#); [Rose and Grant, 2008](#)) by distinguishing medications that have been tested clinically for reducing methamphetamine use from medications that may be promising based on their anti-craving effects – yet, clinical trials are ultimately needed. A number of other areas of potential interest to the field are also expanded upon, such as the trends in methamphetamine use/abuse rates, associated costs to the individual and society, and recent debates regarding methamphetamine-related neurocognitive impairments. Furthermore, the present review differs from other methamphetamine reviews (e.g., [Panenka et al., 2013](#)) by incorporating this wide range of domains of interest and by highlighting the increasingly recognized role for the opioidergic system in the development (i.e., reinforcement), maintenance (i.e., craving), and treatment (i.e., naltrexone) of methamphetamine addiction as an area for greater study in methamphetamine-related research. Taken together, this review provides a broad-based update of the available literature covering methamphetamine research over the past two decades and concludes with recommendations for future research.

Articles for inclusion in this review were identified through an extensive literature search conducted in January 2014 (and repeated in March, April, and July 2014) in PubMed and national survey databases. Search terms included “methamphetamine” (or “amphetamine” where appropriate) and domain specific terms such as “pharmacokinetics,” “neurocognition,” and “treatment.” Efforts were made to include the most recent reports within each section in order to provide an updated summary of the current knowledge of the field.

### 1.1. Epidemiology of methamphetamine

Methamphetamine remains a widely used illicit drug in the U.S. Estimates from 2012 suggest over 12 million people in the U.S., ages 12 years and older (4.7% of total responders) have used methamphetamine in their lifetimes, 1.2 million people (0.4%) reported using methamphetamine in the past year, and approximately 440,000 (0.2%) of those identified as past month users ([Substance Abuse and Mental Health Services Administration \(SAMHSA\), 2013a](#)). Amphetamine-type stimulants (ATS), of which

methamphetamine is the most frequently used, are the second most commonly used class of illicit drugs worldwide ([United Nations Office on Drugs and Crime \(UNODC\), 2012](#)); approximately 0.7% of the global population (33.8 million people) aged 15–64 years-old, reported using an ATS in 2010 ([UNODC, 2013](#)). Importantly, these estimates appear to be growing, as stated in the 2013 World Drug Report, “The market for ATS appears to be expanding in terms of locations of manufacture and trafficking routes, as well as in terms of demand” ([UNODC, 2013](#)).

### 1.2. History of methamphetamine use in the United States

ATS have a long history of use in the U.S., going as far back as World War II when soldiers used ATS to reduce fatigue and suppress appetite. ATS were widely prescribed in the 1950s and 1960s as a medication for depression and obesity, reaching a peak of 31 million prescriptions in the U.S. in 1967 ([Anglin et al., 2000](#)), with a roughly estimated 9.7 million Americans identified as past-year users of amphetamines in 1970 ([Rasmussen, 2008](#)). The rates of ATS use declined following the passage of the Comprehensive Drug Abuse Prevention and Control Act of 1970, which reclassified amphetamine to a more restrictive schedule, thereby limiting its accepted medical use ([Gonzales et al., 2010](#)). After amphetamine was rescheduled, illicit manufacturers began making methamphetamine using phenyl-2-propanone (“P2P”) and methylamine. However, after P2P became a Schedule II controlled substance in 1980, ephedrine and pseudoephedrine became the predominant precursors and large quantities of these chemicals were smuggled from Mexico into the U.S. ([Maxwell and Brecht, 2011](#)). The increase in production was followed by a dramatic increase in use, with methamphetamine specifically increasing in popularity during the 1990s and early 2000s ([Rawson et al., 2002](#)). For example, estimates from the 2002 U.S. National Survey on Drug Use and Health (NSDUH) suggest that over 210,000 individuals ages 12 and older tried methamphetamine for the first time in 1991, whereas 454,000 individuals did so in 1998 ([SAMHSA, 2003](#)). Following the passage of the Combat Methamphetamine Epidemic Act in 2005 which restricted public access to products containing pseudoephedrine, the rates of methamphetamine use finally began to decrease ([Gonzales et al., 2010](#); [Maxwell and Brecht, 2011](#); [Maxwell and Rutkowski, 2008](#)), as evinced by a drop to 192,000 of new methamphetamine users in 2005 ([SAMHSA, 2006](#)).

This decline in methamphetamine use was short lived however, as illicit manufacturers of methamphetamine began to use the P2P processes once again ([Maxwell and Brecht, 2011](#)). Estimates from the 2012 NSDUH identify over 130,000 individuals as new methamphetamine users in 2012, and the number of past month users in 2012 (440,000 people or 0.2%) remained consistent with reports from the last five years (0.1–0.2%) ([SAMHSA, 2013a](#)).

Recent reports of production and supply indicate a probable rise of methamphetamine use in the near future. For example, the number of methamphetamine laboratories reported in the U.S. quadrupled from 2,754 in 2010 to 11,116 in 2011, and the amount of methamphetamine seized by the U.S. government increased from 15 tons in 2010 to 23 tons in 2011 ([UNODC, 2013](#)). Furthermore, production methods are refined on an ongoing basis to produce

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