# Methamphetamine-Induced Psychosis: To Treat or Not to Treat?

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## Abstract

Substance-induced psychosis is a common presentation in emergency departments. A group of psychiatry residents at McMaster University sought to understand the treatment approach to patients with substance-induced psychosis, specifically secondary to methamphetamine use. We considered the case of a 20-year-old homeless man with a history of methamphetamine use, psychosis and limited community follow-up. The current data for first episode psychosis and clinically high-risk criteria for psychosis, and the conversion to a schizophrenia spectrum from a substance-induced psychosis was considered. There is a paucity of data to support an evidence-based approach to treating a patient with a substance-induced psychosis, therefore it is important to approach this presentation on a case-by-case basis. Further, considering the moderate risk of conversion from substance-induced psychosis to schizophrenia spectrum disorder, there could be value in an approach involving close follow-up and assessment, similar to the model used for the Clinically High-Risk (CHR) population. Taking this into consideration, there may be an expanded role for first-episode psychosis treatment teams in the management and treatment of patients with substance-induced psychosis.


## Introduction

Substance-induced psychosis is a common presentation in emergency departments. A variety of substances can cause substance-induced psychosis, and the prevalence of particular substance-induced psychological disorders may vary based on regional differences in substance abuse patterns and formulations of substances. According to the DSM-V, 7-25% of individuals who present with a first episode of psychosis are reported to have symptoms secondary to substances/medications.[1]

The psychiatry residents at the Waterloo Regional Campus of McMaster University learn in a "one room school house"- a group, problem-based approach to learning psychiatry. As a group, we sought to understand an evidence-based approach to the management of a patient with substance-induced psychosis, specifically secondary to crystal methamphetamine. This particular substance-induced presentation was of particular interest because of its high prevalence in our local emergency departments. Also, our group was interested in how methamphetamine's action on the dopamine pathway may interface with the dopamine hypothesis of psychosis. The pathophysiology of psychosis is believed to be related to increased D2 activity in the mesolimbic pathway and decreased D1 activity in the mesocortical pathway.[2] Methamphetamine has dual action on dopamine, both promoting its release from nerve endings which increases dopamine in the synaptic cleft,[3] and inhibiting its reuptake and degradation.[4] Therefore, increased dopamine transmission in the mesolimbic pathway is similar to the underlying pathophysiology of primary psychotic disorders. These similarities led our resident group to question whether patients presenting to our local emergency department with methamphetamine-induced psychosis should be treated with a dopamine antagonist (i.e. antipsychotic medications) like those presenting with a psychosis attributed to a primary psychotic disorder or if evidence better supports watchful waiting

until the substance clears. Methamphetamine depletes the brain of its dopamine stores and causes damage to the nerve terminal,[5] and therefore we wondered if there was similar efficacy for treatment as those with primary psychotic disorders.

A literature search was undertaken and revealed that there is very little evidence on the treatment of substance-induced psychosis secondary to methamphetamine use. However, this raised further questions among our group: is substance-induced psychosis a predictor of conversion to a primary psychotic disorder? Is this risk of conversion even more significant for those with prodromal symptoms or those in the ultra-high-risk group?

## Case Presentation

A 20-year-old homeless male was referred for psychiatric consultation. His medical history is remarkable for episodic issues such as abscesses and pneumonia, and his psychiatric history is remarkable for multiple visits to the local emergency department related to substance intoxication and possible psychosis. His medical chart reveals that he has been prescribed oral antipsychotics on multiple occasions, though it is unclear whether he has ever filled these prescriptions. He is homeless and has no family physician or psychiatrist following him in the community.

On arrival to the clinic, his outreach worker noted that he has just injected crystal methamphetamine into his neck, and he does this most days. He is pacing in the waiting room and asks that the interview room door be kept open during the interview. On mental status exam, he is restless, pacing at times, and sits for only short intervals of time during the assessment. He appears distracted by internal stimuli. He is preoccupied by a sprinkler head in the ceiling and speaks about "cameras watching." He answers concrete, closed-ended questions appropriately. When asked open-ended questions, his thought process is tangential and preoccupied by persecutory delusional themes. He admits to hearing voices but is unable to further elaborate. He denies thoughts of harming himself, thoughts of harming others or needing to protect himself.

## Diagnostic Focus and Assessment

Several studies have investigated the conversion rate to primary psychosis following an episode of substance-induced psychosis. The strongest evidence is for cannabis, amphetamines and alcohol as substances that induce psychosis.[6] One of the largest studies that looked at this concept was a register-based study of 18,478 Finnish inpatient cases. Dr. Niemi-Pynttari and his group collected data from the nationwide Finnish Hospital Discharge Register, which included diagnosis at initial presentation as well as at follow-up. Of the 18,478 patients discharged after their first admission with a diagnosis of substance-induced psychosis, 825 (4.5%) had amphetamine-induced psychosis. They found that these patients had a 30% chance of being diagnosed with a schizophrenia spectrum disorder in the eight years following admission.[6] They also found gender differences in conversion from methamphetamine-induced psychosis to schizophrenia spectrum disorders, with men converting at a higher rate than women. This difference did not exist for other substances in their study. The group postulated that there may be a dose-dependent effect on the risk of developing a schizophrenia spectrum disorder. In summary, it appears that patients who present with methamphetamine-induced psychosis are at high-risk for developing a schizophrenia spectrum disorder, but causation is still unclear. It remains difficult to determine, based on initial presentation, which presentations will continue to a

schizophrenia spectrum disorder and which will be fully attributed to the psychoactive properties of the substance. Further, the differential diagnoses for patients that present with disordered thought content and/or perceptual abnormalities is vast. The DSM-V lists the various schizophrenia spectrum disorders (delusional disorder, schizophrenia, brief psychotic disorder) as well as various medical conditions (delirium, malignancies), substance-related disorders, mood disorders and obsessive-compulsive disorder.[1] Differentiating between these causes remains important as prognosis varies based on etiology and timely intervention.

## Therapeutic Focus and Assessment

The types and intensity of interventions vary based on the etiology of psychosis. The application of early and intensive treatment interventions in first episode psychosis in schizophrenia is based on the hypothesis that early intervention leads to better outcomes. This hypothesis is based on data that has shown that by six months, there are statistically significant correlations between duration of untreated psychosis and positive symptoms, negative symptoms, symptoms of depression/anxiety, overall functioning and number of patients achieving remission. In general, a longer duration of untreated psychosis is associated with worse outcomes.[7] This evidence base has led to funding and associated infrastructure for first-episode psychosis clinics and treatment teams, which also provide service to those patients in the Clinically High-Risk category.

Currently, Clinically High-Risk (CHR) criteria for psychosis consists of genetic risk/family history of psychosis combined with a decline in social functioning, transient psychotic symptoms or attenuated psychotic symptoms.[8] Treatment has shown some benefit in terms of psychological, pharmacological and neuroprotective agents. Treatment guidelines from various international organizations recommend close follow-up and monitoring of this group.[9] The Canadian Schizophrenia guidelines specifically recommend that all patients with Clinically High Risk of developing schizophrenia be referred to a specialist for evaluation and offered psychological interventions, such as CBT for psychosis, but offer no conclusive recommendations around pharmacological agents. Additionally, long-term antipsychotic treatment with a primarily preventive purpose is not recommended. A recent meta-analysis showed that 36% of participants that met ultra-high-risk criteria transitioned to a schizophrenia spectrum disorder after 3 years.[10] These rates are similar to those who present with a substance-induced psychosis and transition to a schizophrenia spectrum disorder. However, those with substance-induced psychosis do not receive this level of follow up and are often excluded from intensive programming, such as first episode programs.[11] This raises the question of whether there is a role for those with substance-induced psychosis to be followed more closely, similar to the delivery models of care for those within the Clinically High-Risk category, bearing in mind the funding implications for such an endeavour.

Patients with methamphetamine-induced psychosis are often excluded from these services, which led our group to wonder if we are missing a key window of opportunity to intervene and provide treatment during this vulnerable period, which could possibly decrease long-term morbidity and mortality. It is noteworthy that despite the high-prevalence of comorbid substance use among patients presenting with first-episode psychosis, there is little research that considers whether early intervention also reduces substance use. One study found that in patients with first-episode psychosis and substance use, there were significant reductions in drug and alcohol use over the 12-month period in the program.

Further, the rates of involuntary hospitalizations and arrests decreased to match those who were not using substances. However, this study had several major limitations, such as no control group, and its generalizability to our particular question is limited by its exclusion of patients with substance-induced psychosis. [11]

# Conclusions and Implications for Clinical Practice

There is a dearth of evidence to inform a clinical approach to treating substance-induced psychosis. This may be a result of a rapidly changing landscape of substance use patterns, regional differences in the prevalence and formulation of culprit substances, or the common exclusion of individuals with substance-induced psychosis in research studies. However, the current literature clearly demonstrates that patients with substance-induced psychosis, in particular methamphetamine-induced psychosis, are a vulnerable population group given their rate of conversion to a primary psychotic disorder. A lack of research in the domain of substance-induced psychosis may heighten this vulnerability by contributing to a lack of evidence-informed treatment interventions, which can ultimately lead to exclusion from services directed toward patients with non-substance-induced psychosis. Further complicating the matter, there is a difficulty in promoting the shared decision-making approach as the nature of the illness can lead to altered mental states which could result in lack of capacity to make decisions. Further, busy emergency departments and walk-in clinic settings may not be conducive to building rapport and support trusting, long-term relationships. This may lead physicians to approach patients in a very paternalistic and at times dismissive manner. Supportive, trusting relationships become equally important in fostering discussions about substance use and its implications.

We sought to explore the evidence for early and intensive treatment interventions provided to the Clinically High Risk (CHR) and First Episode Psychosis (FEP) population groups could be valuable for those with substance-induced psychosis, and although no research exists to support their efficacy in this patient group, we feel that this represents an important future research direction. We also recognize that treating substance induced psychosis challenges physicians to use their clinical acumen to differentiate between various etiologies of psychosis, make decisions in the context of limited evidence and often limited resources available to treat this vulnerable population and at the same time balance the best interest of the patient while preserving their autonomy as individuals.

# Learning Points

- There is a paucity of data to support an evidence-based approach to treating a patient with a substance-induced psychosis, therefore it is important to approach this presentation on a case-by-case basis.
- Considering the moderate risk of conversion from substance-induced psychosis to schizophrenia spectrum disorder, there could be value in an approach involving close follow-up and assessment, similar to the model used for the Clinically High-Risk (CHR) population.
- There may be an expanded role for first-episode psychosis treatment teams in the management and treatment of patients with substance-induced psychosis, bearing in mind the limitations in funding opportunities.

- Physicians must be mindful of their paternalistic approach to decision making in patients with psychosis and attempt to engage the patient in a shared-decision making approach as much as possible.

## References


1. American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*. American Psychiatric Pub.
2. Sadock, B. J., Sadock, V. A., & Ruiz, P. (2015). *Kaplan & Sadock's synopsis of psychiatry: Behavioral Sciences/Clinical Psychiatry* (11th ed.). Philadelphia: Wolters Kluwer.
3. Kish, S. J. (2008). Pharmacologic mechanisms of crystal meth. *Canadian Medical Association Journal*, *178*(13), 1679-1682.
4. Bramness, J. G., Gundersen, Ø. H., Guterstam, J., Rognli, E. B., Konstenius, M., Løberg, E. M., ... & Franck, J. (2012). Amphetamine-induced psychosis-a separate diagnostic entity or primary psychosis triggered in the vulnerable?. *BMC Psychiatry*, *12*(1), 221.
5. Rusyniak, D. E. (2011). Neurologic manifestations of chronic methamphetamine abuse. *Neurologic Clinics*, *29*(3), 641-655.
6. Niemi-Pynttäri, J. A., Sund, R., Putkonen, H., Vorma, H., Wahlbeck, K., & Pirkola, S. P. (2013). Substance-induced psychoses converting into schizophrenia: a register-based study of 18,478 Finnish inpatient cases. *The Journal of Clinical Psychiatry*, *74*(1), e94-9.
7. Marshall, M., Lewis, S., Lockwood, A., Drake, R., Jones, P., & Croudace, T. (2005). Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: a systematic review. *Archives of General Psychiatry*, *62*(9), 975-983.
8. Addington, J., Addington, D., Abidi, S., Raedler, T., & Remington, G. (2017). Canadian treatment guidelines for individuals at clinical high risk of psychosis. *The Canadian Journal of Psychiatry*, *62*(9), 656-661.
9. Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., ... & Valmaggia, L. (2013). The psychosis high-risk state: a comprehensive state-of-the-art review. *JAMA Psychiatry*, *70*(1), 107-120.
10. Fusar-Poli, P., Bonoldi, I., Yung, A. R., Borgwardt, S., Kempton, M. J., Valmaggia, L., ... & McGuire, P. (2012). Predicting psychosis: meta-analysis of transition outcomes in individuals at high clinical risk. *Archives of General Psychiatry*, *69*(3), 220-229.
11. Archie, S., Rush, B. R., Akhtar-Danesh, N., Norman, R., Malla, A., Roy, P., & Zipursky, R. B. (2007). Substance use and abuse in first-episode psychosis: prevalence before and after early intervention. *Schizophrenia Bulletin*, *33*(6), 1354-1363.