




Methamphetamine dependence in Australia—why is ‘ice’ (crystal meth) so addictive?

Russ Scott 

West Moreton Prison Mental Health Service, Brisbane, QLD, Australia

Australia has one of the highest rates in the world of the use of the crystalline form of methamphetamine, a highly addictive stimulant that is often associated with a chronic, relapsing dependency. Methamphetamine use is associated with both acquisitive and violent offending, which cause substantial personal and societal costs. Whilst the short-term euphoria and stimulation provide a positive reinforcement to methamphetamine use, the aversive states of withdrawing from methamphetamine and the associated craving, which may last up to five weeks into abstinence, underlie the negative reinforcement to continued methamphetamine use. Although many methamphetamine-dependent users experience high levels of psychological distress, it is likely that less than half engage with treatment or support services, and current intervention and treatment programmes have high discontinuation rates. Stigma and discrimination, even from paramedics and health clinicians, are prominent barriers to methamphetamine-dependent users accessing treatment in Australia.

Keywords: addiction; craving; dependence; discrimination; methamphetamine; stigma.

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Introduction

This selective narrative review begins with a brief overview of the prevalence of methamphetamine use in Australia and the health care and other burdens including violent offending related to methamphetamine dependence. After considering the pharmacology, neurobiology and routes of use, the pleasurable subjective effects of methamphetamine use are distinguished from the features seen in intoxication, confusional states and methamphetamine-induced psychosis. Withdrawal from methamphetamine and the phenomena of cravings are described before the various mechanisms underlying methamphetamine dependence are considered in the context of

the different criteria and terminology used in the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) and the *International Classification of Diseases* (11th Revision). After summarising the limited studies into the pharmacological management of methamphetamine withdrawal and dependence, the cognitive deficits and other factors that are likely to contribute to the high discontinuation rates in methamphetamine treatment programmes are outlined. The current research into psychological interventions, stigma and other internal and external barriers to treatment for methamphetamine-dependent users are reviewed. The article concludes with some broad policy recommendations for treatment services to address the disproportionate burden

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of care and societal costs associated with methamphetamine dependence in Australia.

An ‘ice’ storm in Australia?

Methamphetamine is a potent and highly addictive stimulant, which is easily manufactured. The hydrochloride salt of methamphetamine is a white, odourless, bitter-tasting, water-soluble powder or crystalline substance known colloquially as ‘ice’. Compared to the lower purity forms, crystalline methamphetamine is associated with an increased risk of dependence (Courtney & Ray, 2014). Since the 1990s, methamphetamine has dominated the amphetamine market in Australia (Topp et al., 2002) with a shift to the high-purity crystalline form (N. Scott et al., 2015). From 2006, claims of an ‘ice epidemic’ in Australia prompted the National Amphetamine-Type Stimulant Strategy 2008–2011 and increased investment in law enforcement, drug treatment and public education (Lancaster et al., 2014).

In 2015, methamphetamine first surpassed cannabis as the most commonly reported substance used by Australian prison entrants (Australian Institute of Health and Welfare, AIHW, 2015). In 2018, the Drug Use Monitoring in Australia project found that half of police detainees who provided a urine sample subsequently tested positive to methamphetamine (Voce & Sullivan, 2019).

In 2019, The National Drug Strategy Household Survey found that 1.3% of Australians aged 14 years or over reported having used meth/amphetamines in the previous 12 months (AIHW, 2020a). The survey found that people who used crystal methamphetamine were far more likely to use it monthly or more often than people who used mainly powder forms of amphetamine. Weekly use among people who reported using mainly crystal methamphetamine more than doubled from 12% in 2010 to 29% in 2019.

Since all self-report household surveys are compromised by non-response bias and exclude participants with no current home

address (which includes high-risk populations such as the homeless and those in institutional settings like prisons) and cannot take account of excess mortality in methamphetamine users, the actual prevalence of methamphetamine use in Australia may be considerably higher than estimates derived from household surveys (G. C. K. Chan et al., 2022). Data from the Young People in Custody Health Survey in New South Wales found that 31% of participants reported recent use of crystal methamphetamine (Kaye et al., 2021).

‘Crystal meth’ in Australia

Crystal methamphetamine is mainly imported into Australia, mostly from the United States, Mexico and Southeast Asia (Coyne & Westendorf, 2021; Stoneberg et al., 2018). Crystalline methamphetamine is sold to users for a typical ‘hit’ as a ‘point’ (i.e. 0.1 g) or supplied in larger quantities like an ‘eight ball’ (an eighth of an ounce or 3.5 g). Methamphetamine may be adulterated (‘cut’) with sugar, glucose, ephedrine or ketamine, which may constitute a substantial proportion of the ‘street’ dose. An analysis of 2018–2019 Drug Use Monitoring in Australia data indicated that 64% of police detainees obtained methamphetamine from someone they knew, while 28% bought from a dealer (Doherty & Sullivan, 2020).

In Australia, between 2010 and 2016, there was a 230% increase in demand for methamphetamine-related treatment and a 270% increase in methamphetamine-related hospital admissions (AIHW, 2015). In Queensland from 2009 to 2015, there was a 20-fold increase in methamphetamine-related hospital admissions (Queensland Health, 2017). The Alcohol and Other Drug Treatment National Minimum Data Set shows that between 2003 and 2019, the rate of treatment episodes for methamphetamine in Australia increased more than three-fold (McKetin, Chrzanowska, et al., 2021).

The most recent National Illicit Drug Reporting System study found that nearly half of intravenous users reported that

methamphetamine was ‘easy’ or ‘very easy’ to obtain despite the ‘street’ price doubling since the previous year (Peacock et al., 2021). The study found that two thirds of recent crystal methamphetamine users reported using weekly or more frequently. In 2020, the New South Wales Special Commission of Inquiry into crystal methamphetamine estimated that approximately \$7.3 billion worth of crystal methamphetamine is consumed per year in Australia (Howard, 2020).

Wastewater testing for substances suggests that methamphetamine usage occurs more commonly throughout the week compared with cocaine and methylenedioxymethylamphetamine (MDMA, ‘ecstasy’), which are known as ‘recreational’ or ‘party drugs’ and demonstrate a more prominent spike in usage over weekends (Lai et al., 2016).

Societal costs of methamphetamine use in Australia

Methamphetamine use is associated with significant health harms and imposes a considerable burden on Australian society (Gordon & de Jong, 2018; McKetin et al., 2018) particularly ambulance services, emergency departments and mental health services (Darke et al., 2017; Isoardi et al., 2019; Jones et al., 2019). The prevalence of methamphetamine use is likely to be even higher in rural (Monahan & Coleman, 2018; Roche & McEntee, 2017) and Indigenous communities in Australia (MacLean et al., 2017; Snijder & Kershaw, 2019; Reilly et al., 2020), and methamphetamine-related suicide makes a large contribution to methamphetamine-related mortality (Darke et al., 2019; Lewis et al., 2021). The Australian drug harms ranking study found that crystal methamphetamine was the third most harmful substance to users and the second most harmful substance to others (Bonomo et al., 2019). When the two part-scores were combined, alcohol and crystal methamphetamine were the two most harmful substances in Australia. In

2018, the costs of methamphetamine to the Australian community were estimated to be up to \$7 billion annually, which included, in descending order, criminal justice system costs, premature mortality, workplace costs (including accidents and absenteeism), health care costs, child protection services costs, road crashes costs, prevention and harm reduction measures (Tait et al., 2018).

Methamphetamine use and associated violent offending and victimisation

In 2016, 58% of adult police detainees in Australian capital cities reported using methamphetamine in the previous 12 months, a two-fold increase compared to 5 years previously (Ticehurst & Sullivan, 2018). Forty-two percent of interviewees said they were dependent on methamphetamine. Of those who reported that methamphetamine contributed to their detention, half said that they were ‘high’ at the time of arrest.

Methamphetamine-related offending, including both acquisitive and violent offending, causes substantial personal and societal costs (Cumming et al., 2020; McKetin et al., 2020; Spivak et al., 2020).

Methamphetamine dependence is also associated with high rates of domestic violence (Morgan & Gannoni, 2020). A recent longitudinal birth cohort study found that a history of any methamphetamine use was associated with an increased adjusted risk of violence perpetration, intimate partner violence perpetration and violence victimisation (Foulds et al., 2020). Those who are homeless and use methamphetamine are particularly vulnerable to violence victimisation (Carrillo Beck et al., 2022).

A brief history of methamphetamine

Amphetamine-type stimulants were developed as synthetic alternatives to ephedra from the *Ephedra* plant, which has been used for over 5000 years in traditional Chinese medicine. In 1885, ephedrine, the active alkaloid

present in ephedra, was extracted and was later recognised to be similar to epinephrine (adrenaline). Ephedrine had the advantage of being able to be inhaled or taken orally, which had a longer duration of action and produced more pronounced and dependable central nervous stimulation. In 1919, methamphetamine was first synthesised in Japan using ephedrine as a precursor. In 1932, Benzedrine (dextroamphetamine) was first marketed as an inhaler for the treatment of asthma and nasal congestion. Benzedrine was later used to reduce behavioural problems in children with attention deficit hyperactivity disorder and to treat narcolepsy and depression and as an anorexic.

In 1940, methamphetamine was marketed in tablet form as Methedrine. During the Second World War, Benzedrine and Pervitin (methamphetamine) were used by the military to improve alertness and performance and reduce fatigue in pilots and soldiers. Following the war, both the United States and Japan experienced epidemics of methamphetamine-related morbidity (Morelli & Tognotti, 2021).

The current estimated global prevalence of amphetamine and methamphetamine use is 0.7%, with dependence affecting 11% of those users (Farrell et al., 2019). The United States and Canada followed by Australia have the highest prevalence of methamphetamine use (United Nations Office on Drugs & Crime, 2022). A recent study from the United States found that approximately 1.6 million adults used methamphetamine each year yet fewer than a third received treatment (Jones et al., 2021). It is estimated that over the past 10 years, the mortality related to methamphetamine use has doubled (Edinoff et al., 2022).

The molecular pharmacology of methamphetamine

Methamphetamine (N-methyl-alpha-methylphenethylamine) belongs to the phenethylamine and amphetamine-type class of potent

central nervous stimulants sharing properties similar to those of naturally occurring cocaine (Moszczynska & Callan, 2017). Methamphetamine causes the release and partially blocks the reuptake of the monoamine neurotransmitters dopamine, noradrenaline, adrenaline and serotonin, which stimulate post-synaptic monoamine receptors. Unlike cocaine, which principally blocks plasma membrane transporters that re-uptake monoamines, methamphetamine exerts multiple pharmacological effects via different processes including attenuating the metabolism of monoamine neurotransmitters by inhibiting monoamine oxidase, which contributes further to the accumulation of circulating neurotransmitters (Paulus & Stewart, 2020).

The neurobiology of methamphetamine

In the dopaminergic pathways of the brain, methamphetamine activates the mesolimbic, mesocortical circuit and the nigrostriatal pathways, which have been related to the euphoric effects observed immediately after ingestion (Courtney & Ray, 2014). In the noradrenergic pathway, methamphetamine is active in the medial basal forebrain, the hippocampus and the prefrontal cortex which subserve functions related to arousal, memory consolidation and cognitive processing, respectively (Mather et al., 2016). The serotonergic pathways regulate diverse functions including pain perception, sexual drive, reward and higher order cognitive processing (Carhart-Harris & Nutt, 2017).

The wide distribution and interactions of monoamine neurotransmitters throughout the central nervous system and the peripherally mediated effects of methamphetamine contribute to the intricacy of methamphetamine effects. The potentiation of dopaminergic neurotransmission within the mesocorticolimbic circuit has been implicated in the risky decision-making and reinforcing properties of dependency-producing methamphetamine (Kohno et al., 2014).

Routes of use of methamphetamine

In contrast to alcohol, cannabis and other substances, methamphetamine can be used by a number of different routes. Intravenous injection is the fastest route of administration. Following intravenous use, peak plasma levels of methamphetamine are achieved in less than 15 min (Cruickshank & Dyer, 2009). Following intravenous use, the acute subjective effects may diminish over 4–6 hr but may persist for up to 12 hr or more (Huestis & Cone, 2007).

Smoking (vapour inhalation) of the crystalline solid form of methamphetamine is the next fastest route of administration. Smoking has the advantage of convenience as compared to intravenous injection and produces an almost immediate and intense effect with none of the risks inherent in intravenous use. Subjective effects may occur within 15 min after smoking, and peak plasma levels are reached between 2 and 3 hr as the methamphetamine is more slowly absorbed from the upper respiratory tract (Harris et al., 2003). Methamphetamine easily crosses the nasal mucosa after snorting (insufflation), and peak concentrations occur at approximately 4 hr (Hart et al., 2008). Methamphetamine may also be taken orally or by anal or vaginal suppository.

Bioavailability of methamphetamine

The methyl group makes methamphetamine highly lipid soluble, which allows it to cross the blood brain barrier more rapidly than other stimulants including amphetamine and makes methamphetamine more stable against enzymatic degradation. The basic nitrogen moiety in the chemical structure of methamphetamine, its relatively high lipophilicity and its low plasma–protein binding influence its distribution and excretion.

Elimination of methamphetamine

Substances are removed from the body after 8 half-lives (since only approximately 1/164 of

the substance dosage will remain in the body after that time). Methamphetamine from intravenous use is typically detectable in the plasma for 36–48 hours.

As a molecule, methamphetamine exists in two optically active forms. The two stereoisomers or enantiomers share the same atomic particles but differ in their structural arrangements and biological properties. Of the two stereoisomers, d-methamphetamine is a more powerful central nervous stimulant than l-methamphetamine. At normal urine pH, the elimination half-life of d-methamphetamine, between 10.2 and 10.7 hours, is marginally shorter than the elimination half-life of l-methamphetamine, which is between 13.3 and 15.0 hr (Mendelson et al., 2006).

Methamphetamine is metabolised in the liver, and the main metabolites are amphetamine (an active metabolite), 4-hydroxymethamphetamine and noradrenaline. The primary mode of elimination of methamphetamine is renal excretion (Schep et al., 2010). Approximately 70% of a methamphetamine dose is excreted in the urine within 24 hours, 30–50% as unchanged methamphetamine, up to 15% as 4-hydroxymethamphetamine and 10% as amphetamine (Kim et al., 2004).

Methamphetamine is a weak base with a pKa of 9–10. Renal excretion of methamphetamine increases with reduced urinary pH. An acidic diet will increase excretion thereby reducing the half-lives of the metabolites whilst an alkaline diet will increase the half-life to between 16 and 31 hours.

Urine drug screens by immunoassay detect the presence of methamphetamine and its metabolite amphetamine up to 3 days following occasional use depending on several factors including the dose, duration of use, hydration of the user and the analytic method. False-positive results are produced by other stimulants, anorexiant and chemically related compounds like MDMA. Any positive immunoassay result will require confirmation by gas chromatography–mass spectrometry.

With a long terminal urinary half-life of 25 hours, methamphetamine accumulates in the urine with repeated dosing and, depending on the cut-off value, may be detected in urine for up to 7 days in heavy users (Oyler et al., 2002).

Since metabolism of methamphetamine does not appear to be altered by chronic exposure, dose escalation appears to arise from pharmacodynamic rather than pharmacokinetic tolerance. The effects of methamphetamine do not demonstrate a predictable dose-related progression, and there is no method by which the level of methamphetamine in the circulation or urine can be correlated with that user's behaviour or functioning (Goldfeder et al., 2023; Weber et al., 2017).

The subjective effects of methamphetamine

The psychological effects of methamphetamine depend on several variables:

- the dose and route of administration;
- the duration (chronicity) and frequency of use;
- the user's tolerance;
- the period of time since last used;
- the context in which the methamphetamine is used;

There are also a number of confounding factors that complicate the determination of dose-effect relationships, including reporting bias and the co-morbid use of other substances (including other stimulants or sedatives).

Methamphetamine users typically describe a distinctive pattern of experiences over the course of two or more stages: the 'high', the 'binge' (or 'run'), the 'tweak' and the 'crash'. After administration of methamphetamine, the stimulant phase may last between 6 and 8 hours and up to 12 hours. The 'high' is characterised by an immediate 'rush' of pleasure often of only minutes duration followed by a euphoria (also sometimes described colloquially as being 'fried'). As the individual's

methamphetamine use increases, tolerance to the euphoric effect may develop, and the user may escalate the dose or frequency of use to 'chase' the 'rush' effect. The user may also 'binge' or 'run', which is characterised by repeated administration over days or even a week.

After smoking or intravenous use, plasma concentrations of methamphetamine remain elevated well after the acute subjective effects subside. Binging is facilitated by the development of acute tolerance, coupled with the memory of the previous 'rush', which produces the intense desire to reinstate the stimulant effect by repeated administration.

A typology of methamphetamine users in Australia

During the 'high' experienced in intoxication, methamphetamine users report increased sociability, energy and talkativeness as well as arousal, elevated or euphoric mood, heightened confidence and assertiveness (Brookfield et al., 2021), attentiveness and curiosity, improved concentration and cognitive performance and increased libido (B. Green et al., 2020). Indeed, those employed in a number of vocations including long-haul truck driving, hospitality and the entertainment industry may use methamphetamine to improve their physical performance and their ability to work long hours.

One recent study of methamphetamine initiation identified narratives that corresponded to three constructs from the theory of 'planned behaviour': attitude (needing energy to work, wishing to escape pain, wanting to have fun and aspiring to a thinner body), subjective norms (ubiquity of methamphetamine use, yearning for closer relationships and wanting to fit in) and perceived behavioural control (believing addiction is inevitable, feeling forced to fit in and having no real control; Schmidt et al., 2019).

An earlier study of patterns of usage within Australian populations of methamphetamine

users identified three distinct behavioural contexts (Department of Health, 2008). The ‘social user’ was motivated by the disinhibitory effects of methamphetamine and identified sharing the experience of methamphetamine use at parties, clubs and social events as the critical element of the appeal. In comparison to other user groups, social users also appeared to place greater importance on maintaining goals and an interest in non-substance activities such as their employment or studies, and in circles of friends who were not regular users.

The ‘functional user’ was motivated by the enabling effects of methamphetamine including enhanced confidence, alertness, concentration, energy and stamina or the suppression of appetite resulting in weight loss. Increases in any of these characteristics effectively enabled the user to achieve a task more quickly or more efficiently. To avoid the stigma and being labelled negatively, methamphetamine users may construct symbolic boundaries by depicting themselves as ‘functional users’ (Webb et al., 2017).

The ‘dependent user’ was motivated by the perception of normality from reliance on methamphetamine and exhibited compulsive methamphetamine seeking and use, even in the face of negative health and social consequences. The dependent user described uncontrollable, compulsive cravings that caused them to use methamphetamine repeatedly. The craving was for either the methamphetamine or the act of taking the methamphetamine.

A recent Australian study found that compared to methamphetamine users who injected, those who smoked methamphetamine were younger and less likely to be unemployed, have a prison history or live alone (McKetin, Quinn, et al., 2021). Whilst younger users may be more typically ‘social’ or ‘functional users’, some from the younger cohort and those initiating from early or middle adulthood may use methamphetamine to ‘self-medicate’ in the context of pre-existing factors including a

history of childhood abuse or neglect (Chen et al., 2019; Kittirattanapaiboon et al., 2017; Svingen et al., 2016) and current stressful life events (Chen et al., 2014; Yimsaard et al., 2018).

Methamphetamine use and co-morbid mental illness

Serious mental illness (Akindipe et al., 2014; Chang et al., 2018; Eslami-Shahrbabaki et al., 2015) or other substance use (Baker et al., 2021; Crummy et al., 2020; Ellis et al., 2018) are common co-morbidities in methamphetamine dependence. In 2020, the National Drug Strategy Household Survey found that among adult Australians who recently used substances, 26% had been diagnosed with or treated for a mental health condition in the previous 12 months, and people with a mental health condition were 2.2 times as likely to have used amphetamine or methamphetamine. (AIHW, 2020b).

Methamphetamine intoxication

During intoxication users may exhibit affective changes, changes in sociability, hypervigilance, interpersonal sensitivity, anxiety, tension or anger and impaired judgment. Physical signs or symptoms may include palpitations, changes in blood pressure, perspiration or chills, nausea or vomiting, psychomotor agitation or retardation, muscle weakness, respiratory depression or chest pain.

Methamphetamine intoxication may also be associated with stereotyped or compulsive behaviours (known as ‘tweaking’ or ‘tinkering’), in which the user may engage in meaningless repetitive or compulsive behaviours including dismantling and re-assembling devices or sorting of objects. Other unpleasant physical symptoms associated with methamphetamine intoxication include involuntary body movements including twitching of fingers and body muscles, lip-smacking, tongue protruding and grimacing (orofacial dyskinesia), tremor, tightening of jaw muscles

(trismus) and teeth grinding (bruxism). Methamphetamine intoxication may also be associated with pruritis (itching), reduced tolerance to sound (hyperacusis), headaches and elevated body temperature (Darke et al., 2008). More extreme physical signs or symptoms include confusion, dyskinesias, dystonias, seizures or coma.

Methamphetamine intoxication may be associated with irritability, paranoia and aggression (Leamon et al., 2010), over-valued ideas (solitary, abnormal beliefs that are neither delusional nor obsessional in nature, but which are preoccupying to the extent of dominating the person's thinking) and ideas of reference (abnormal or erroneous beliefs about a real incident or observation that is neither delusional nor obsessional in nature, which ascribes special individual meaning to those random, neutral or irrelevant incidents or observations), which may also be accompanied by perceptual disturbances (auditory, visual or tactile illusions), which usually occur with intact reality-testing (Zweben et al., 2004). Methamphetamine users may also experience tactile illusions or formication, the feeling that 'bugs' are crawling on or under the skin ('meth mites'), which causes them to compulsively scratch or pick at themselves, producing sores and ulcers. A dry mouth and poor dental care may also result in caries and loss of dentition ('meth mouth').

Intoxicated methamphetamine users experiencing emotional dysregulation and paranoia have an increased propensity for aggression and violence (Addison et al., 2021). A large study from the United States found that a majority of methamphetamine users reported that their use resulted in violent behaviour (Brecht & Herbeck, 2013).

Methamphetamine 'binging'

The rapid increase in the release of dopamine and the receptor activation caused by methamphetamine elicit a reward signal that triggers

associative conditioning (Volkow et al., 2016). By this type of Pavlovian learning, repeated experiences of reward from methamphetamine use become associated with the environmental stimuli that preceded them (Koob & Volkow, 2016). It is theorised that with repeated exposure to the same reward, dopamine cells stop firing in response to the reward itself and instead fire in an anticipatory response to the conditioned stimuli or 'cues' that predict the delivery of the reward (Altshuler et al., 2020; Schultz, 2015).

By this mechanism, environmental stimuli that are repeatedly paired with methamphetamine use – including the environments, contexts and other persons with whom the methamphetamine has been taken, the ritual of preparing to use the methamphetamine (making up the 'fit') and the user's mental state before the use of methamphetamine – may all come to elicit conditioned, fast surges of dopamine release that trigger craving for methamphetamine and motivate the substance-seeking behaviours and may lead to the 'binge' use seen with methamphetamine use (Weiss, 2005). As these conditioned responses become deeply entrenched, they can trigger strong cravings for methamphetamine use even after a period of treatment or forced abstinence – for example, whilst the user was imprisoned.

By motivational learning in substance use, the greater the attribute associated with the reward from using the substance, the greater the effort a user is willing to exercise and the greater the negative consequences or sequelae the user is willing to tolerate in order to obtain the reward (Volkow et al., 2019). Whilst dopamine cells stop firing after repeated consumption of a 'natural reward' like food or sex gratification, thereby satiating the drive to further pursue that reward, methamphetamine circumvents the natural satiation and continues to directly increase dopamine levels, which partly explains why compulsive behaviours including 'binging' are more likely to emerge in methamphetamine users (Wise, 2008).

Clinical studies have shown that chronic methamphetamine use triggers much smaller increases in dopamine levels in dependent users than in persons who have not previously used methamphetamine, and it is this attenuated release of dopamine and down-regulation of the dopamine signalling that renders the brain reward system much less sensitive to stimulation by both substance-related and non-substance-related rewards (Zhang & Volkow, 2019). As a result, dependent users no longer experience the same degree of euphoria from methamphetamine use as they did from their earlier use, and this phenomenon may also explain why methamphetamine-dependent users experience anhedonia and are often less motivated by everyday stimuli that they had previously found rewarding.

Methamphetamine confusional state

During methamphetamine intoxication, particularly after sustained or repeated use, the user may develop an acute confusional state (delirium) as a result of sleep deprivation, exhaustion, dehydration and poor nutrition. The confusional state in methamphetamine intoxication ('overamping') may have a fluctuating course with disturbances in attention and cognition, changes in arousal, disturbed sleep-wake cycle and disorganised behaviour (Harding et al., 2022).

The confusional state in methamphetamine intoxication is often associated with grossly impaired judgement in which the user may make impulsive decisions that risk serious self-harm or harm to others. The syndrome described as an 'excited (or agitated) delirium' (Gonin et al., 2018) is associated with an elevated risk of harm including death (Kunz et al., 2021).

Methamphetamine-induced psychosis

Positive symptoms of paranoia, persecutory delusions and auditory and visual hallucinations are by far the most commonly reported

features of methamphetamine-induced psychosis, and aggression and depression are also common (Voce et al., 2019). The features of methamphetamine-induced psychosis may be indistinguishable from acute paranoid schizophrenia (Wearne & Cornish, 2018). Psychosis may be more prevalent among users of crystalline methamphetamine (Lappin et al., 2016), which may be related to the purity compared to other forms of methamphetamine and the self-selection of those who use this form of methamphetamine.

An early study of the Sydney methamphetamine market found that although rates of psychosis among regular methamphetamine users were 11 times that seen among the general population, very few methamphetamine users who experienced psychosis attended hospital (McKetin et al., 2005). A later study of methamphetamine users found that almost a quarter had experienced a clinically significant symptom of at least moderate severity in the past 12 months (McKetin et al., 2006).

A longitudinal prospective study of 278 methamphetamine-dependent users from Brisbane and Sydney found that even abstinent methamphetamine users had a 7% risk of experiencing psychotic symptoms, and the risk of experiencing psychotic symptoms increased to 48% when participants were using methamphetamine heavily (McKetin et al., 2013).

The prevalence of methamphetamine-induced psychoses is up to 26% in community settings and up to 46% in dependent users in treatment settings (Chiang et al., 2019). A recent meta-analysis produced a composite event rate of 43% for a methamphetamine-induced psychotic disorder over a lifetime (Lecomte et al., 2018).

The prognosis of methamphetamine-induced psychosis is variable and may relate to doses and patterns or route of use (Yang et al., 2020). There are subsets of users who appear to not develop psychotic symptoms even with frequent use and, conversely, some who experience chronic psychosis following only limited use (Arunogiri et al., 2020).

Although methamphetamine-induced psychosis is usually seen only when high doses are used or for prolonged periods, psychoses can occur in apparently vulnerable persons even after relatively low doses used for short periods. Some individuals who have experienced a methamphetamine-induced psychosis may experience an acute psychosis on re-exposure to small doses (Bramness et al., 2012; Sato, 1992), which would not have induced frank psychotic episodes in the early stages of abuse (Dore & Sweeting, 2006). Other subjects with a previous history of methamphetamine-induced psychosis may become psychotic in response to stressful life events even whilst abstinent from methamphetamine (Yui, Goto, et al., 2000; Yui, Ikemoto, et al., 2000). One early study demonstrated that when two doses of a stimulant were given to volunteers without psychosis, the second dose produced a greater psychotic response, described as a 'sensitised' response or 'reverse tolerance' effect (Strakowski et al., 1997). Repeated psychotic episodes may also lead to relative 'treatment resistance' with symptoms being less responsive to medication following successive relapses and, in some cases, residual symptoms developing that were not present before the relapse (Meredith et al., 2005; Rognli & Bramness, 2015; Yui et al., 2002).

Long-term outcomes for methamphetamine-induced psychosis

Whilst methamphetamine-induced psychotic symptoms are typically transitory, generally lasting less than a week, psychotic symptoms can last substantially longer than a month.

An early study of 104 Japanese methamphetamine users with no previous history of schizophrenia found that 15% experienced active psychotic symptoms for up to 3 months, and symptoms persisted beyond 3 months in 16% (Iwanami et al., 1994). A later study found that psychotic symptoms persisted for more than a month among 40%, including

nearly 30% who exhibited symptoms after more than 6 months of abstinence (Ujike & Sato, 2004).

Two subsequent longitudinal studies from Japan found prisoners who remained psychotic or exhibited spontaneous recurrence of psychosis whilst abstinent from methamphetamine during incarcerations ranging between 5 and 12 months (Akiyama, 2006; Akiyama et al., 2011). A more recent study from Iran found that of 152 inpatients with methamphetamine-induced psychosis, 31% took more than one month to respond to anti-psychotic medication (Zarrabi et al., 2016).

Withdrawal from methamphetamine

During the 'crash', the acute phase of methamphetamine withdrawal is characterised by increased sleeping (somnia) and increased appetite, depression, anxiety and craving (Khani et al., 2018; McGregor et al., 2005). Following the acute withdrawal phase, the user may experience headaches, cramps and vomiting and a prolonged insomnia that may last for up to 15 days (Zhao et al., 2021). The 'crash' may also be marked by affective blunting with dysphoria, irritability, fatigue and social withdrawal. Unlike in alcohol and opioid withdrawal, there are no objective measurable parameters like heart rate, blood pressure or pupil diameter that can be used to evaluate the methamphetamine withdrawal stage or severity.

Chronic or frequent use of methamphetamine results in a depletion of pre-synaptic monoamine stores, a down-regulation of receptors (Proebstl, Kamp, et al., 2019) and neurotoxicity (Shin et al., 2017), which underlie the significant withdrawal symptoms and intense cravings for methamphetamine (Zorick et al., 2010). Methamphetamine use is associated with cognitive impairment in complex decision-making and flexibility and working memory, which may persist even after a month of abstinence (Proebstl, Krause, et al., 2019; Simon et al., 2010).

The pattern of cumulative dosing seen particularly with methamphetamine smoking appears to facilitate tolerance to the drug. Although plasma concentrations may remain high for several hours after smoking (Cho & Melega, 2002), the subjective euphoria appears to wane rapidly. Although there are likely to be contextual factors that reinforce dependent use patterns among methamphetamine users, including the social ritual particularly associated with smoking methamphetamine, the re-instatement of euphoria with repeated inhalations is likely to occur because of acute behavioural tolerance to methamphetamine (McKetin et al., 2006). Although the severity of the withdrawal syndrome appears to be related to the frequency of use and usually resolves spontaneously within 14 days of abstinence, protracted withdrawal may take up to five weeks to dissipate (Zorick et al., 2010).

Criteria in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition

In the *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition, Text Revision (DSM-IV; American Psychiatric Association, APA, 2000) there were two methamphetamine-related mental health disorders—abuse and dependence. For methamphetamine dependence, the DSM-IV required a maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of seven criteria occurring at any time in the same 12-month period.

In May 2013, the American Psychiatric Association promulgated the fifth revision of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; APA, 2013). In a further effort to harmonise with the World Health Organization *International Classification of Diseases* (ICD; World Health Organization, WHO, 2022), the DSM-5 combined the abuse and dependence criteria to form a single

‘methamphetamine use disorder’. In the DSM-5, methamphetamine use disorder is defined as a pattern of use occurring within a 12-month period leading to clinically significant impairment or distress, as manifested by at least two of 11 criteria:

- methamphetamine is often taken in larger amounts or over a longer period than was intended;
- there is a persistent desire or unsuccessful efforts to cut down or control use;
- a great deal of time is spent in activities necessary to obtain and use methamphetamine, or recover from its effects;
- craving, or a strong desire or urge to use;
- recurrent use resulting in a failure to fulfil major role obligations at work, school, or home;
- continued use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of methamphetamine;
- important social, occupational, or recreational activities are given up or reduced because of methamphetamine use;
- recurrent use in situations in which it is physically hazardous;
- methamphetamine use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by methamphetamine tolerance, as defined by either of the following:
 - a need for markedly increased amounts of methamphetamine to achieve intoxication or desired effect;
 - a markedly diminished effect with continued use of the same amount of methamphetamine, and;

- withdrawal, as manifested by either of the following:
 - the characteristic withdrawal syndrome;
 - methamphetamine (or a closely related substance) is taken to relieve or avoid withdrawal symptoms;

The DSM–5 has also adopted combinations of the diagnostic criteria to define three severity specifiers:

- mild—the presence of two to three criteria;
- moderate—the presence of four to five criteria;
- severe—the presence of six or more criteria;

The two most noteworthy changes in the DSM–5 were the removal of ‘legal problems’ from the symptom list and the addition of ‘drug craving’ as a criterion. Clinicians now also eschew pejorative terms like ‘drug habit’ or ‘substance abuse’ (McGinty & Barry, 2020).

Whilst the DSM–5 offers a simplified diagnostic system and avoids the problem of ‘diagnostic orphans’ (when a person fulfilled two DSM–IV substance dependence criteria but no substance abuse criteria), having a substance use disorder defined by any two of 11 diagnostic criteria creates a very broad and heterogeneous condition, which may be less useful in assessing risk and treatment needs in clinical practice (Lago et al., 2016; Saunders, 2017). Importantly, the DSM–5 does not consider classification of a substance use disorder based on harm caused to the person’s physical or mental health or harm to the health of others (Matone et al., 2022).

Criteria in the International Classification of Diseases, 11th Revision

Compared to the DSM–5, the ICD–11 (WHO, 2022), which came into effect in January 2022, arguably gives greater emphasis to issues of clinical utility in a broad range of

contexts. The ICD–11 has global applicability for health recording and statistics in primary, secondary and tertiary care. Diagnostic guidance linked to categories of the ICD–11 also standardises data collection and enables large-scale research.

The ICD–11 retains the well-established distinction between harmful use and dependence as separate diagnostic categories. The characteristic feature of methamphetamine dependence is the strong internal drive to use, which is manifested by impaired ability to control use, increasing priority given to use over other activities and persistent use despite harm or negative consequences. The ICD–11 criteria emphasise how experiences are often accompanied by a subjective sensation of urge or craving to use methamphetamine and the prominent withdrawal symptoms. In the ICD–11, although the features of dependence are usually evident over a period of at least 12 months, the diagnosis may also be made if the methamphetamine use is continuous (daily or almost daily) for at least three months. In the ICD–11, all the items related to a substance taking over in daily life activities described in the DSM–5 are represented in only one category: increasing precedence of substance use over other aspects of life (First et al., 2021).

‘Craving’ in methamphetamine dependence

Craving, the subjective experience of wanting a substance, derives from positive outcome expectancies whereby, based on their past experiences, the subject self-administers a substance like methamphetamine in anticipation of a physical and/or psychological reward—either a pleasurable ‘high’ or relief from unpleasant sensations (Hartz et al., 2001). Craving often intrudes significantly into the daily lives of substance users and may dominate their thoughts and cause considerable distress.

Substance users may develop compulsive patterns of drug-seeking and drug-taking behaviour that take place at the expense of most other activities and from which the user

cannot desist (Lüscher et al., 2020). This process of ‘incentive-sensitisation’ has four major tenets: dependency-producing drugs share the ability to alter brain organisation, the brain systems that are altered include those normally involved in the process of incentive motivation and reward, the critical neuroadaptations (Seger, 2010) render these brain reward systems hypersensitive (‘sensitised’) to drugs and drug-associated stimuli, and the brain systems that are sensitised do not mediate the pleasurable or euphoric effects of drugs (drug ‘liking’), but instead mediate a sub-component of reward termed incentive salience or drug ‘wanting’ (Robinson & Berridge, 2008). These cognitive performance deficits appear to be more pronounced in methamphetamine users (Guerin et al., 2021) who also demonstrate craving, which is associated with behavioural measures of self-control (Dakhili et al., 2022; Grodin et al., 2019) and social cognition (Zhong et al., 2016).

Craving may last up to three months into abstinence (Lopez et al., 2015; Wang et al., 2013), and craving beliefs, or interpretations and decisions about cravings, have been shown to predict relapse in methamphetamine users (Galloway & Singleton, 2009; Lee et al., 2010).

Methamphetamine dependence—‘positive reinforcement’

Substance use was conventionally understood as providing an immediate short-term reward. When the positive effects of the use of the substance outweigh the risks or negative consequences, the substance-seeking behaviour is said to be ‘positively reinforced’. Methamphetamine dependence appears to be strongly associated with injecting and smoking and the use of the high-potency crystal methamphetamine.

Methamphetamine dependence—‘negative reinforcement’

Substance use may also be reinforced by alleviating uncomfortable or aversive states. By

‘negative reinforcement’, a person may continue to use a substance despite negative consequences, because the substance use assuages adverse states such as negative mood states, tension, cravings or other withdrawal symptoms (Koob & Le Moal, 2005). For some methamphetamine users, even the initial use of the substance may be a maladaptive coping mechanism to alleviate depression or anxiety that existed prior to the substance use.

The role of negative reinforcement in perpetuating methamphetamine was demonstrated in a study of 73 non-treatment-seeking users who were surveyed to examine their reasons for continued use (Newton et al., 2009). The reasons were categorised as (a) positive reinforcement, (b) negative reinforcement or (c) inhibitory control dysfunction or impulsivity. While questions pertaining to positive reinforcement or ‘pleasure seeking’ were endorsed more frequently, a significant proportion of the sample endorsed questions pertaining to negative reinforcement, ‘pain avoidance’ and to reduce dysphoria, ‘bad feelings’ or withdrawal symptoms. Significantly, the majority of the cohort who endorsed negative reinforcement items perpetuating their methamphetamine use did not endorse questions related to positive reinforcement. Social deficits may also be a risk factor for continued use, and while methamphetamine can reduce social anxiety and irritability acutely (Maxwell, 2014), continued use may cause interpersonal problems resulting in stress and negative mood states for which the user again defaults to using methamphetamine to alleviate discomfort.

Methamphetamine dependence—‘the three-stage cycle’

By a more recent conceptualisation, substance dependence develops as a three-stage cycle of binge/intoxication, withdrawal/negative affect and pre-occupation/anticipation marked by varying dysfunction within motivation, reward, stress and executive function systems

(Koob, 2013). Whilst the initial state of binge/intoxication is driven by the rewarding effects of the substance, in which an increased incentive salience is attributed to the substance and new substance-seeking behaviours develop, during the withdrawal/negative affect stage, the substance user experiences increases in negative emotional states and an overall increased stress-response. The third stage of preoccupation/anticipation consists of increased craving characterised by obsessive thinking about substances, which triggers compulsive drug-seeking behaviour and deficits in executive functioning. The three stages are theorised to feed into one another and increase in intensity, ultimately resulting in the substance dependence.

As an evolving process, while the development of dependence begins with the initial use, which is positively reinforced by the rewarding effects, the substance use is subsequently sustained and becomes negatively reinforced as it eases the adverse states of irritability, withdrawal symptoms, physical discomfort and pain and emotional symptoms like anxiety, alexithymia, depression and blunted responsivity to natural or everyday rewards (Koob & Volkow, 2016). With prolonged exposure, the rewarding effects of the substance decreases as reflected by hypo-activation within the reward regions of the ventral striatum and over-active stress-systems reflected by amygdala hyperactivation (Volkow et al., 2016). This evolves into the third stage of preoccupation/anticipation, a key contributor to relapse in which altered functioning within frontal regions results in executive dysfunction when presented with a salient cue signalling substance use. The deficits in executive function impact upon decision making, self-regulation and inhibitory control, resulting in the substance user's inability to inhibit maladaptive behaviours and, instead, persist in their substance-seeking behaviours despite the negative consequences.

The concept of the negative reinforcement cycle in motivating and maintaining

methamphetamine dependence continues to evolve. Studies of subjective experience, behaviour and functional brain imaging have been integrated to demonstrate that methamphetamine users appear to have impaired cognitive control and emotion processing, loss of reward and interoceptive information different from those of non-using individuals, which suggests that users have an altered experience of negative outcomes, difficulties employing effective emotion regulation and difficulty engaging in adaptive or goal-directed decision-making (May et al., 2020).

Pharmacological management of methamphetamine dependence and withdrawal

By protracting the study duration and compromising statistical power and generalisability from Type II errors and 'missing data', high drop-out rates hamper the accumulation of quality evidence of the efficacy of treatment options for methamphetamine dependence. Small sample sizes and multiple co-morbidities are also common limitations of clinical trials of treatments for methamphetamine dependence.

Even aside from these limitations, there is no good evidence of any robust efficacy of pharmacotherapy for methamphetamine dependence (B. Chan et al., 2019). A recent systematic review of 43 studies found that none yielded convincing results, and most studies were underpowered and had low treatment completion rates (Siefried et al., 2020). There is currently insufficient evidence that any stand-alone pharmacologic interventions have any efficacy in the treatment of methamphetamine dependence (Moszczynska; Hussain et al., 2021).

Another recent systematic review considered 26 systematic reviews of two psychological interventions (contingency management and cognitive behavioural therapy) and eight pharmacological treatments concluded that none of five pharmacotherapies studied had

sufficient evidence to support or discount their use (Ronsley et al., 2020).

Another recent systematic review considered 26 systematic reviews of two psychological interventions (contingency management and cognitive behavioural therapy) and eight pharmacological treatments concluded that none of five pharmacotherapies studied had sufficient evidence to support or discount their use (Ronsley et al., 2020).

Although *N*-acetylcysteine has been shown to be effective in reducing craving and promoting abstinence and medication adherence among cannabis-dependent users (Sharma et al., 2022), a recent randomised control study of 153 methamphetamine users in Victoria found that *N*-acetylcysteine did not significantly reduce craving, severity of dependence, withdrawal, suicidality, depression, hostility or psychotic symptoms relative to placebo (McKetin, Quinn, et al., 2021). Lisdexamfetamine, a pharmacologically inactive prodrug of dexamphetamine, is approved in Australia for the treatment of attention-deficit/hyperactivity disorder and binge eating disorder. The results of an early study of the efficacy of lisdexamfetamine for the treatment of acute methamphetamine withdrawal appear to be promising (Acheson et al., 2022).

The most recent systematic review and meta-analysis of randomised controlled trials concluded that there was insufficient evidence to indicate that any medication is effective for the treatment of methamphetamine withdrawal (Acheson et al., 2023)

Cognitive deficits and discontinuation in methamphetamine dependence treatment

The typical chronic, relapsing course of methamphetamine use indicates that there is likely to be a neuro-degenerative component that may prove relatively refractory to treatment in the long term. Impaired cognitive function in methamphetamine users (Huckans et al., 2021; Potvin et al., 2018), particularly attentional and memory deficits and impulsivity

(Fitzpatrick et al., 2020; Moallem et al., 2018), may also be implicated in the reduced motivation to engage in treatment (Hussain et al., 2021; Rubenis et al., 2018a) and the poorer outcomes in treatment (Basterfield et al., 2019; Rubenis et al., 2018b; Wang et al., 2020).

All intervention programmes for methamphetamine users have high discontinuation rates. One study of 42 methamphetamine users receiving a 12-week relapse prevention programme from an outpatient clinic found that nearly 70% of participants had at least one positive urine screening for methamphetamine during the programme, and 40% quit the programme before completion (Chen et al., 2015).

In a subsequent larger programme, 51% of 440 enrollees dropped out within the first two weeks, and the mean number of days that enrollees stayed in the programme was only 60 (Cook et al., 2017). Long-term recovery from methamphetamine is also difficult. One study found that 61% of users relapsed 1 year after receiving treatment from outpatient clinics while an additional 25% relapsed between 2 and 5 years later (Brecht & Herbeck, 2014).

Abstinence-based residential rehabilitation programmes typically adopt a therapeutic community model in which better treatment outcomes are predicted by factors including client-centred approaches to decision-making and goal-setting, motivation to change, therapeutic alliance and treatment satisfaction. However, a recent prospective study of 176 methamphetamine-dependent users who stayed in residential rehabilitation for a median of 8 weeks found that only 23% remained abstinent at 1 year (McKetin et al., 2018). The only independent predictors of abstinence were more weeks in treatment, better rapport with treatment providers and the provision of individual counselling.

A subsequent study of 108 patients with a history of methamphetamine abuse who commenced a six-month inpatient rehabilitation found a drop-out rate of 41% (Kamp et al.,

2019). The main reason for premature discontinuation of treatment was unreported relapse and subsequent disciplinary dismissal, followed by violation of other clinic rules.

Psychological interventions in the management of methamphetamine dependence

The results of recent studies of behavioural interventions for methamphetamine dependence are encouraging (AshaRani et al., 2020; Stuart et al., 2020). Contingency management (CM) is a relatively novel intervention based on the principles of operant conditioning, which aims to initiate abstinence by systematically arranging consequences that are designed to weaken substance use and strengthen abstinence (Brown & DeFulio, 2020; Pfund et al., 2022). The community reinforcement approach (CRA) is a broad-spectrum cognitive-behavioural treatment with the premise that a person's environment can play a powerful role in discouraging substance use and that adjustments can be made that make abstinence more rewarding than substance use (Meyers et al., 2011). A recent network meta-analysis compared interventions with 'treatment as usual' found that only CM plus CRA increased the number of patients abstinent from methamphetamine at the end of treatment (De Crescenzo et al., 2018). Other studies of brief cognitive behavioural therapy have shown reasonable reductions in the frequency of methamphetamine use and the number of days of methamphetamine use at weeks 4 and 12 (Alammehrjerdi et al., 2019). A recent systematic review found consistently positive results across five systematic reviews demonstrating the effectiveness of CM compared to 'treatment as usual', as well as other interventions including CRA and cognitive behaviour therapy (CBT; Ronsley et al., 2020).

The most recent overview of systematic reviews of the psychosocial interventions for amphetamine-type stimulant use disorder

found that relative to 'usual care' (only counselling or self-help materials), membership of a psychological intervention group was associated with an important reduction in substance use (Tran et al., 2021). Patients in psychological interventions used intravenous substances substantially less, and the risk of unsafe sex was lower than in the control group. The combination of therapies reduced substance use in the preceding 30 days compared to cognitive behavioural therapy intervention alone. CM may also be supplemented with CRA (Lee & Rawson, 2008). However, despite these positive results, CM programmes are difficult to implement, and their long-term outcomes have not been established. Barriers to their use include the cost of training of providers (Kirby et al., 2006; Murphy et al., 2015).

Behavioural activation aims to maximise activities that are not substance related but are positively valued by the subject. A 2018 systematic review found that behavioural activation was associated with abstinence of methamphetamine use in seven of the eight reviewed studies and improved mood states over time in six of the eight studies (Martinez-Vispo et al., 2018).

Given the evidence for their effectiveness and in the absence of other similarly effective interventions, it would appear that CM augmented by CBT or CRA may be most efficacious for methamphetamine-dependent users (Oluwoye et al., 2020). Group cohesion and mutual peer support are also increasingly recognised as predictors of retention in any abstinence treatment programmes (Raftery et al., 2020). The SMART (Self-Management and Recovery Training) Recovery model uses principles of motivational interviewing and techniques taken from rational emotive behaviour therapy and cognitive-behavioural therapy (SMART Recovery Australia, 2021). With a strong focus on accessibility through open enrolment, no cost or waiting lists and the option to attend online or face-to-face across cities, regional and rural locations (Beck et al.,

2021), the SMART Recovery model may offer a ‘best practice’ template for operationalising psychological interventions for methamphetamine dependence.

Barriers to treatment for methamphetamine users in Australia

Rates of methamphetamine-related harms including emergency department presentations, hospitalisations and deaths in Australia have risen substantially over the last 5 years (Darke et al., 2017; Degenhardt et al., 2017), which is likely to be partly attributable to the availability of high-purity crystalline methamphetamine (AIHW, 2020a; Karlsson & Burns, 2018; Man et al., 2022).

However, despite many methamphetamine-dependent users experiencing high levels of psychological distress, it is likely that less than half of those with methamphetamine dependence in Australia engage with treatment or support services (Lanyon et al., 2019; Quinn et al., 2021).

The primary barriers to accessing treatment are psychosocial and internal (Kenny et al., 2011). Four of the most commonly endorsed barriers are embarrassment or stigma, belief that treatment was unnecessary, preferring to withdraw alone without assistance and privacy concerns (Cumming et al., 2016). Inadequate resources were also commonly reported, including insufficient capacity to meet demand in treatment services, issues around treatment location and affordability and a lack of co-ordination between alcohol and other drugs services and mental health services.

A later qualitative study found that six perceived barriers emerged from the narratives of methamphetamine users (Alexander et al., 2018). The first three perceived barriers—low self-efficacy, conflicting thoughts about methamphetamine use and the side effects of withdrawal—were related to internal barriers, while the other three perceived barriers—escaping the drug environment, friends and family

prevented recovery and inadequate drug rehabilitation programmes—were related to external barriers.

Stigmatisation of methamphetamine users in Australia

Stigma is the social process by which individuals with negative attributes, identities or conditions are devalued by others. The prominent stigma experienced by methamphetamine users can take different forms. Enacted or structural stigma refers to the direct experience of discrimination (Kershaw et al., 2021; McKenna, 2013). Self or internalised stigma refers to negative thoughts about the self, based on membership of the methamphetamine user group (Cama et al., 2016; Luoma et al., 2014). Perceived stigma refers to an individual reporting that most of the public believes the negative stereotypes about their methamphetamine users, whilst social or public stigma refers to negative views held by the public toward methamphetamine users generally, which often leads to discrimination (Crapanzano et al., 2019; Woodhead et al., 2019).

Public stigma appears to be more prevalent for methamphetamine users (Deen et al., 2021; Waller & Clifford, 2020). Methamphetamine users are stigmatised because their problematic substance use is commonly considered ‘anti-social’, and dependent users are often characterised as responsible for their predicament (Ozkok et al., 2022; Yang et al., 2017) even amongst paramedics (Jones et al., 2021), emergency department physicians (Mendiola et al., 2018) and mental health clinicians (Avery et al., 2016; Salani et al., 2020; Usher et al., 2017).

By stereotyping and labelling (using pejorative epithets like ‘addicts’, ‘junkies’ or ‘meth heads’), stigma negatively impacts users’ access to health care, support and safety (Gray, 2010; Selseng, 2017). By social disapproval and discrimination, stigma attached to substance users is even greater than that for

other mental health disorders (Rao et al., 2009) and often leads to the emotional experience of shame, which may exacerbate substance use and other high-risk behaviours including needle sharing and multiple substance use (von Hippel et al., 2018) and discourage substance users accessing or staying in treatment (Luoma et al., 2019; Rahim & Patton, 2015).

Health care providers find caring for substance users complex, stressful and often unrewarding, and these patients are frequently perceived as aggressive, manipulative and poorly motivated (Murphy et al., 2020; Petersén et al., 2021; Richards et al., 2019). A study of patients with recent methamphetamine use presenting to the St Vincent's Hospital in Melbourne found that 65% were described as aggressive toward emergency department staff, and 50% were described as aggressive toward staff in the acute inpatient service (Unadkat et al., 2019).

Whilst interdisciplinary providers regularly endorse negative attitudes towards substance users (Francis et al., 2020; Nieweglowski et al., 2018), they also often demonstrate deficient knowledge, training and support to treat this cohort of patients (Arya et al., 2020; Van Boekel et al., 2013). Negative attitudes towards these patients may translate to disempowerment and suboptimal care, including reduced patient–provider collaboration, shorter encounters and the adoption of an impersonal task-oriented approach to management (Bielenberg et al., 2021; Sussman, 2021).

In 2015, the Australian government launched the confronting *Ice Destroys Lives* media campaign, which evoked concern in the community by linking crystal methamphetamine use to violence, criminal activity and deviance (Ayres & Jewkes, 2012; Dobson & Rose, 2022; Douglass et al., 2017). A quantitative media content analysis examining print media portrayals of methamphetamine found that the largest number of articles were published in 2015 with a higher proportion of these articles framed as a 'crisis' associated

with violent and dangerous users (Rawstorne et al., 2020). A study of federal parliamentary speeches in 2015 found that politicians framed methamphetamine use as a 'crisis' or 'epidemic' even more frequently than the media (Cohn et al., 2020).

As well as contributing to the public stigma and marginalisation, the hysteria and moral panic (Fredrickson et al., 2019) in the media coverage around the so-called 'ice epidemic' and related harms (Pisarski, 2021) were likely to have contributed to the under-reporting of usage and low presentation rates for treatment (Chalmers et al., 2016; G. C. K. Chan et al., 2022). Unfortunately, although the National Drug Strategy 2017–2026 acknowledged the imperative to reduce stigma as a key component to reducing substance use in Australia, no explicit programmes or interventions were proposed (Adams & Volkow, 2020).

National Ice Action Strategy 2015

In April 2015, following reports of the increasing prevalence of methamphetamine use particularly in young people in regional and remote Australian communities, the Commonwealth government established the National Ice Taskforce chaired by a former Victoria Police commissioner to provide advice on addressing methamphetamine-related harms in Australia. In October 2015, the final report containing 38 generic recommendations was published (Commonwealth of Australia, 2015a). The two-page response of the Australian government to the final report (Australian Government, 2015) was disappointing. The response was marked by a lack of policy detail or strategy and inexact funding arrangements (McKetin, 2016) and had a surprisingly disproportionate investment of \$241.5 million for the delivery of treatment services by primary health networks (Hamilton & Dunlop, 2016). The subsequent National Ice Action Strategy agreed upon by the Council of Australian Governments

contained no strategy or funding details or any co-ordination of response across jurisdictions (Commonwealth of Australia, 2015b). More recently, the exigencies caused by the COVID pandemic have dominated public health priorities. But in the face of the increasing availability and purity of methamphetamine and the continued under-funding for interventions and treatment programmes for all substance users, including those in correctional custody, reducing the disproportionate burden of care and societal costs associated with methamphetamine dependence remains a significant challenge for health clinicians in Australia.

Policy recommendations for treatment services in Australia

Given the high incidence of co-morbid mental illness, mental health services and alcohol and other drug services need to be flexible and well integrated, and this is particularly important in correctional settings where prison primary health and mental health clinicians together with correctional service psychologists have the opportunity to engage with those who disclose their recent history of methamphetamine use in the community. Community primary health networks also need to offer accessible and comprehensive continuity of care by linkages with specialist outpatient alcohol and other drug services and residential rehabilitation services (Ward et al., 2021), and, in turn, these services must provide proactive relapse prevention by assertive follow-up in the community (Orjiakor et al., 2023) and peer support (Bryant et al., 2022).

To reduce stigmatising and marginalising methamphetamine users and to encourage them to engage in treatment, more balanced and nuanced public education campaigns as well as educational interventions for health care providers (Avery et al., 2019) are needed to provide practical information particularly about the phenomenology of craving and the mechanisms of negative re-enforcement that underlie methamphetamine dependence

and the strong association between methamphetamine use and serious mental illness. Primary health care providers (Quinn et al., 2013; Sanatkar et al., 2022; Ward et al., 2021), emergency department and front-line mental health clinicians need to develop practice guidelines and treatment pathways to support and manage those who present in crisis or who are contemplating addressing their methamphetamine dependence.

As well as increased funding for day programmes and residential rehabilitation capacity in Australia, further research must be undertaken into emotion-focused psychological interventions directed at the negative mood symptoms that maintain and exacerbate methamphetamine dependence (Hamel et al., 2020).

Methamphetamine users often have a history of childhood adversity and other vulnerabilities and often recruit further social disadvantage including unemployment and homelessness. Methamphetamine use is also a common co-morbidity in serious mental illness. Imprisonment has been shown to have both a weak general deterrent effect (Bun et al., 2020; Chalfin & McCrary, 2017) and a weak specific deterrent effect (D. P. Green & Winik, 2010; Mitchell et al., 2017) particularly in relation to drug offender recidivism (Plettinckx et al., 2018). Spain, Portugal and Croatia were the first countries to decriminalise possession of psychoactive substances (Tomaz et al., 2023), and research has found that liberalising drug policies may encourage substance users to adopt harm reduction strategies including engaging with community health services (Benfer et al., 2018; Berryessa, 2021; Moniruzzaman et al., 2022). Given the better understanding of the phenomenology of craving and methamphetamine dependence, there are compelling arguments for more nuanced sentencing discretion, particularly for low level substance-related offending such as possession and small-scale supply of methamphetamine to adults, which takes into account the personal circumstances of the dependent

user (Foulds & Nutt, 2020) and prioritises diversion and community-based rehabilitation over the punitive sanction of imprisonment.

Ethical standards

Declaration of conflicts of interest

Russ Scott has declared no conflicts of interest

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

ORCID

Russ Scott  <http://orcid.org/0000-0002-9037-0333>

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