Novel Psychoactive Treatment UK Network

NEPTUNE

Guidance on the Clinical Management of Acute and Chronic Harms of Club Drugs and Novel Psychoactive Substances

The Health Foundation
Inspiring Improvement

Club Drug Clinic/CAPS
Central and North West London NHS Foundation Trust (CNWL)
69 Warwick Road
Earls Court
SW5 9HB

http://www.Neptune-clinical-guidance.com

http://www.Neptune-clinical-guidance.co.uk

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Chapter 8

Methamphetamine

Drug group: stimulant

The use of methamphetamine in the UK continues to be relatively uncommon, with its use limited to specific populations and contexts, most particularly men who have sex with men (MSM). However, a discussion of methamphetamine harms and their management is included in this guidance document because of both the level of harms relating to the use of this substance and the lack of experience in the management of its harms in the UK.

Methamphetamine hydrochloride is stable and volatises easily so can be smoked, unlike amphetamine sulphate.

8.1. Street names

Street names at the time of publication include Crystal Meth, Tina, Christine, Ice, Glass, Crank, Yaba and Crazy Medicine. Other street names may be used locally.

8.2. Legal status

Methamphetamine and 4-methylamphetamine are Class A drugs under the Misuse of Drugs Act 1971.

8.3. Quality of the research evidence

There is a much larger and more robust body of evidence on methamphetamine harms and treatment than for other club drugs. This includes a number of well conducted randomised controlled trials (RCTs) and Cochrane reviews, especially in relation to dependence.

However, most of the research evidence on methamphetamine comes from the US, Australia and South East Asia. UK and European research is much more limited, reflecting the currently low rates of use across most of Europe. Some of the findings of international studies may be less relevant in a UK context, especially those relating to epidemiology and trends.

8.4. Brief overview of pharmacology

Methamphetamine is an *N*,α-dimethylphenethylamine and a member of the phenethylamine family. It is a synthetic stimulant and a derivative of amphetamine.[1] Methamphetamine is a potent psychomotor stimulant with strong physiological effects on the peripheral and central nervous systems, resulting in physical and psychological effects.[2] It is typically described as a more potent stimulant than non-methylated amphetamines. It is highly lipophilic, and in comparison with amphetamine at similar doses crosses the blood–brain barrier more easily, is more potent and has a more pronounced and a longer-lasting stimulant effect.[3] Methamphetamine has short-term and long-term effects that are similar to those produced by cocaine, but they last longer and can be more severe.[4]

The action of methamphetamine and other amphetamines have been well described.[2,5,6,7] Methamphetamine increases the activity of the noradrenergic and dopamine neurotransmitter systems. It increases the release and blocks the reuptake of dopamine. It has an active metabolite, amphetamine, and two inactive metabolites, p-OH-amphetamine and noradrenaline. It is oxidised and metabolised in the liver through enzymatic degradation primarily involving cytochrome P450-2D6. Approximately 10% of Caucasians are deficient in this enzyme, and a study has suggested that this makes them particularly sensitive to the effects of methamphetamine, as they lack the ability to metabolise and excrete the drug efficiently.[8]

Chronic methamphetamine alters brain function. Brain imaging studies have shown changes in the activity of the dopamine system that are associated with reduced motor skills and impaired verbal learning.[9] Imaging studies of methamphetamine-dependent individuals have found structural abnormalities: severe grey-matter deficits in the cingulate, limbic and paralimbic cortices, smaller hippocampal volumes, significant white-matter hypertrophy, medial temporal lobe damage and striatal enlargement.[10,11]

Studies have also shown severe structural and functional changes in areas of the brain associated with emotion and memory,[11,12] as well as neurochemical and metabolite changes in the ventral striatum.[13,14] Prolonged use has been reported to lead to down-regulation of dopamine D_2 receptors and uptake sites.[15] A state of hypodopaminergic activity has been reported.[16,17]

The psychiatric consequences of methamphetamine use are theorised to be secondary to its mechanisms of action: methamphetamine enters the synaptic neurons via monoamine transporters and, once in the neurons, displaces the monoamines from vesicular and intracellular locations, pushing the monoamines into the extraneuronal spaces. Long-term use is associated with alterations in the levels of monoamines implicated with stimulant use, which include noradrenaline, serotonin and dopamine.[18,19]

8.5. Clinical and other legitimate uses of methamphetamine

Methamphetamine has been used in the treatment of narcolepsy and attention deficit hyperactivity disorder (ADHD). There is also some research on other therapeutic uses of methamphetamine. A rat study looked at whether low-dose methamphetamine could prevent neuronal loss and improve functional behaviour after severe traumatic brain injury (TBI). It found that low doses elicited a robust neuro-protective response, resulting in significant improvements in behavioural and cognitive function.[20]

8.6. Prevalence and patterns of use

Methamphetamine is one of the most widely misused drugs in the world, with over 35 million users estimated. However, at a European level, the use of methamphetamine has historically been low, with some exceptions, notably in the Czech Republic and, more recently, Norway and Slovakia. However, there are some indications that meth-amphetamine is increasing in availability and data from some European countries suggest that it may be replacing amphetamine.[21,22]

In the UK, methamphetamine use is still limited, and amphetamine sulphate continues to be much more available and widely used. Data from the Crime Survey for England and Wales (CSEW) on the use of methamphetamine have been collected since 2008/09 and show the following, with no statistically significant changes over the years. Use of methamphetamine in the last year was reported by 0.1% of adults (16–59 years) in all six annual surveys, with no significant differences between young adults and all 16–59-year-olds in the proportion of people reporting its use.[23]

Other UK data also suggest its limited use. A retrospective study on the number of enquiries to the poison centres of two large inner-city hospitals from 2000 to the end of 2006, as well as the National Poisons Information Centre 2005/06, reported that there was no evidence of increasing use of methamphetamine or that acute methamphetamine poisoning was a significant clinical problem in comparison with other established, drugs such as MDMA.[24]

The prevalence of methamphetamine use is higher among some sub-groups (e.g. 'clubbers'), although there rates still remain lower than for other club drugs. Among the UK sample from the Global Drug Survey in 2012 3.8% of respondents reported ever trying methamphetamine, with 0.8% reporting use in the last 12 months and 0.2% in the last month. The percentage of methamphetamine users among those described as 'regular clubbers' was higher, with 1% reporting use in the last 12 months.[25]

There is some evidence that methamphetamine use is more common among MSM than it is among the general population and that its use is mainly concentrated in this population. This was shown by the 2013/14 CSEW, which analysed responses by sexual orientation where this was self-reported (these data have to be treated with caution because of the small number of respondents involved). The results are presented in Table 8.1.

Table 8.1. *Proportion of 16–59-year-olds reporting methamphetamine use in the past year (3-year combined data-sets 2011/12, 2012/13 and 2013/14)*[23]

Heterosexual: all	Male heterosexual	Female heterosexual	Gay or bisexual: all	Male gay or bisexual	Female lesbian or bisexual
0.0%	0.1%	0.0%	0.6%	1.1%	0.0%

Other data from targeted surveys also suggest that in the UK the use of methamphetamine may be higher among MSM than the general population. These surveys, although not comparable, suggest rates of use that are higher than those reported by the CSEW,[26–28] with for example a 2007 survey of London MSM estimating use of methamphetamine in the past year at 7.8%[29] and a survey carried out in 2010 reporting 8.7%.[30]

Studies have also shown differences in the use of methamphetamine within populations of MSM. Like other international research, UK studies have reported that HIV-positive men are more likely to use methamphetamine than other MSM.[30–34] US studies have shown that the incidence of HIV among MSM who use methamphetamine is more than double that among MSM who do not use methamphetamine.[35]

There are also differences based on geography, with methamphetamine found in metropolitan areas mainly (e.g. London and Manchester). In the UK methamphetamine is more widely used by gay men in London than elsewhere in the country.[29,30] A recent study also showed differences within London, with higher prevalence in areas such as Lambeth, Southwark and Lewisham (LSL), which are home to large populations of gay and bisexual men, and have a large gay commercial scene and sex-on-premises venues. In these locations methamphetamine use in the past four weeks (4.9% of LSL respondents) was higher than among gay men elsewhere in London (2.9%) and substantially higher than elsewhere in England (0.7%).[30] Methamphetamine is associated with 'chemsex', as discussed in greater detail in section 8.10.2.

There is no evidence that the use of methamphetamine is becoming more widespread among MSM in the UK, although one report suggested that its use appears to be increasing, albeit slowly and certainly not exponentially.[30] There is also no evidence that its use is becoming more mainstream in the UK, or whether it will ever expand to the wider population. Drug-using cultures differ and methamphetamine use may not follow the same pathways as in other parts of the world, including the US and Australia, where its use has expanded beyond MSM populations.

US and other studies have shown a change over time in the sociodemographic characteristics of methamphetamine users. A study of treatment admissions from the California Alcohol and Drug Data System from 1992 to 2002 showed not only a five-fold increase of methamphetamine admission, but also a shift towards usage by minority ethnic groups and a more vulnerable population in terms of homelessness, chronic mental health problems and disability. There was also a substantial increase in people reporting a legal supervision status (criminal justice intervention).[36] In the UK, this vulnerable population is currently typically more associated with crack cocaine and opiate use.

8.7. Routes of ingestion and dosing

The most common form of methamphetamine is a hydrochloride salt, which comes as a white or off-white bitter-tasting powder, or as purer crystals that are soluble in water. It can also come in tablets, which carry logos similar to those on ecstasy tablets.

Most of the methamphetamine used in the UK is in the crystalline form. It is currently mainly smoked but it is also snorted, injected intravenously (known as 'slamming' among MSM in the UK), used anally (known as 'booty bumping') or inserted into the urethra. It has been noted that if too much methamphetamine is inserted anally, it may not all be completely dissolved and there is a risk of abrasion of condoms resulting from friction with this undissolved methamphetamine, which can contribute to the condom breaking.[37]

There is some evidence that smoking methamphetamine has more harmful psychological effects and a higher addictive potential than snorting or swallowing the drug, and that smokers have levels of dependence approaching those seen among methamphetamine injectors.[38,39]

Methamphetamine is rapidly absorbed after ingestion and its half-life is 8–13 hours.[40] The stimulant effects depend on a number of factors, including route of ingestion and dose; they may last between 6 and 12 hours, but longer durations have been reported.[41] Intravenous injection and smoking have a rapid onset of action. Following oral administration, peak concentrations are seen in 2.6–3.6 hours and the mean elimination half-life is 10.1 hours (range 6.4–15 hours). Following intravenous use the mean half-life is slightly longer (12.2 hours).

Methamphetamine is expensive in the UK, with a cost of up to £260 per gram, which is much above the cost in countries where it is more highly prevalent.[42] It is also considerably more expensive than other stimulant drugs, including cocaine, at approximately £50–£100 per gram.

8.8. Desired effects for recreational use and unwanted effects

The effects of methamphetamine result from a surge in newly synthesised catecholamines and serotonin; these include excitation, well-being, increased alertness, energy and confidence, highly focused attention and decreased appetite. Methamphetamine use creates feelings of increased confidence, sociability and euphoria.[43] In methamphetamine-naïve individuals, acute doses can improve cognitive processing. Studies show that single low to moderate doses increase arousal and alertness, and improve attention and concentration, particularly among those who are sleep-deprived. Methamphetamine has an apparent aphrodisiac effect, with increased sexual drive, decreased fatigue and loss of sexual inhibition. It can delay ejaculation, assist longer intercourse and decrease humoral secretions.[44,45] Paradoxically, there is evidence that long-term use is associated with decreased sexual functioning in some men.[46]

Higher dose of methamphetamine can cause dysphoria, restlessness and anxiety, and are associated with tremors and dyskinesia. In binge use of methamphetamine, the euphoric effects decrease over time, while dysphoria and compulsive behaviour increase. Bingeing has also been reported to induce sleeplessness, hallucinations and paranoia.[47]

The negative psychological effects of methamphetamine use may include anxiety, restlessness, insomnia, grandiosity, paranoia, psychosis, hallucinations (including delusional parasitosis), depression, unprovoked aggressive or violent behaviour and irritability. Individuals can talk excessively, be agitated, aggressive and restless, and may be observed performing repetitive meaningless tasks.[8]

Unwanted effects of methamphetamines have been reported to be common. A US study of 350 individuals found that the majority reported problems associated with methamphetamine use, which included weight loss (84%), sleeplessness (78%), financial problems (73%), paranoia (67%), legal problems (63%), hallucinations (61%), work problems (60%), violent behaviour (57%), dental problems (55%), skin problems (36%) and high blood pressure (24%).[48] In the UK Gay Men's Sex Survey 2007, 40.4% of men who had used methamphetamine in the past year reported concerns about this drug.[26]

The 'come-down' from methamphetamine is one of the most common unwanted effects reported by users.[49] Users may feel irritable, restless, anxious, depressed and lethargic, and there are reports of the use of benzodiazepines or heroin to soften the come-down. It has been reported in New Zealand that it is often sold in a package with GHB/GBL to help with its come-down effects.[50] Anecdotal evidence from the UK suggests that the two substances are sometimes used together.

8.9. Mortality

A study of cohorts of individuals in California hospitalised from 1990 to 2005 with a diagnosis of disorders relating to methamphetamine, cocaine, alcohol, opiates and cannabis and followed up for 16 years (74,139 individuals and 4122 deaths) found that hospitalised methamphetamine users had a higher mortality risk than the users of all substances, except for opiates. The standardised mortality rate for methamphetamine found by the study was 4.67, which is similar to rates found by studies in inpatient or treatment settings in the Czech Republic,[51] Denmark[52] and Taiwan,[53] but slightly larger than those reported by a community-based sample of amphetamine users in Sweden.[54]

Deaths associated with methamphetamine have been attributed to homicide, suicide, motor vehicle accidents, manufacturing, distribution and sales of the drug as well as its direct toxic effects.[55] Biologically based causes include stroke and cerebral haemorrhage, cardiovascular collapse, pulmonary oedema, myocardial infarction, hyperpyrexia and renal failure.[56,57]

For up-to-date guidance on the management of methamphetamine acute toxicity, it is recommended that information be sought from the National Poisons Information Service (NPIS), specifically the NPIS 24-hour telephone service and the poisons information database TOXBASE®:

http://www.toxbase.org/Poisons-Index-A-Z/M-Products/Methamphetamine/

It is recommended that relevant clinicians and departments are registered to receive these facilities.

Non-UK readers should consult their local or national guidelines.

8.10. Acute harms

8.10.1. Acute toxicity

The features of acute toxicity are summarised in Box 8.1. The relevant literature is discussed in section 8.11.

8.10.1.1. Cardiovascular and respiratory harms

The acute (and chronic) use of methamphetamine can severely affect the cardiovascular system.[8] It causes an acceleration of heart and lung action through vasoconstriction and bronchodilation, while muscle activity is primed via transient

Box 8.1. *Feature of acute methamphetamine toxicity*

Cardiovascular and respiratory
Narrow-complex tachycardias (common)
Chest pain
Palpitations
Systemic hypotension or hypertension
Ventricular tachycardia or ventricular fibrillation.
Dyspnoea

Gastrointestinal and urological
Abdominal pain
Vomiting
Metabolic acidosis

Neurological, psychiatric and central nervous system
Tremor
Sweating
Dilated pupils
Agitation
Confusion
Headache
Anxiety
Seizures
Hallucinations or delusions
Hyperpyrexia (may be severe)
Serotonin syndrome (especially if more than one stimulant drug has been used) (serotonin syndrome is discussed in depth in section 7.7.2).

hyperglycaemia and dilation of blood vessels in skeletal muscles.[58] Some non-essential physiological activity is inhibited (e.g. stomach and intestinal function); levels of stress hormones – including cortisol and adrenocorticotropic hormone – are increased by 200% in humans following ingestion[59] and remain elevated for hours.[2] Tachycardia and hypertension are common features of methamphetamine toxicity.[4]

Chest pain is a common complaint associated with methamphetamine use,[60] with one study reporting that they account for 38% of emergency department visits and 28% of admissions among patients using methamphetamine.[61] It has also been suggested that although in some patients chest pain is due to methamphetamine-induced hypertension, tachycardia or anxiety, acute coronary syndrome (ACS) is common among methamphetamine users. One study recommended that patients with chest pain in the context of methamphetamine use should be evaluated for ACS.[62] The prevalence of ACS was found to be 25% in a small series of patients presenting to an emergency department with chest pain after methamphetamine use.[63]

Methamphetamine users have significantly higher rates of coronary artery disease than the general population.[64] Even those with normal coronary arteries are at risk of methamphetamine-induced myocardial infarction, because of coronary spasm, which may be refractory to intracoronary vasodilator therapy.[65] The putative mechanisms of myocardial infarction in the context of methamphetamine use include accelerated atherosclerosis, rupture of pre-existing atherosclerotic plaques, hypercoaguability and epicardial coronary artery spasm.[65,66] Acute myocardial infarction following methamphetamine use can be severe and can result in cardiogenic shock and death.[67]

There is an association between methamphetamine use and cardiomyopathy, with different levels of problems reported by studies in areas where the prevalence of methamphetamine use is high. A study in Hawaii (where methamphetamine use is high) reported that methamphetamine use accounts for 40% of all admissions of patients under the age of 45 years with cardiomyopathy. More than 20% of with heart failure were former or current methamphetamine users.[68] A US registry containing information on more than 11,000 patients with decompensated heart failure reported that more than 5% were stimulant users.[69]

One case series reported that more than a quarter (27.2%) of methamphetamine-intoxicated patients had a prolonged corrected QT interval (QTc>440ms), suggesting that methamphetamine-induced alterations in cardiac conduction may be partly responsible for the drug's dysrhythmogenic effects.[70]

Other conditions related to methamphetamine intoxication include premature ventricular contractions, premature supraventricular contractions, accelerated atrioventricular conduction, atrioventricular block, intraventricular conduction delay, bundle branch block, ventricular tachycardia, ventricular fibrillation, and supra-ventricular tachycardia.[63,70,71] Methamphetamine-induced dysrhythmias may also occur because of myocardial ischaemia or infarction.[60]

Methamphetamine use may also be associated with aortic dissection and carries a greater risk for that than cocaine; it may be second only to hypertension in its importance as a risk factor for aortic dissection.[72] Methamphetamine can cause

cerebral stroke, haemorrhage and hypertension.[40,73] Like other drugs injected, the injection of methamphetamine has been associated with endocarditis.[60] Cardiovascular events are often involved in medical complications and death associated with methamphetamine.[74] The ingestion of large quantities of methamphetamine has been associated with cerebrovascular haemorrhage.[75,76,77]

The risks associated with the long-term use of methamphetamine are discussed in section 8.12.

8.10.1.2. Hyperthermia

The ingestion of large quantities of methamphetamine has been associated with hyperthermia, above 41°C.[75–77]

8.10.1.3. Rhabdomyolysis

A five-year US study found that 43% of patients who presented to an emergency department with rhabdomyolysis were positive for methamphetamine.[78]

8.10.1.4. Urological

The ingestion of large quantities of methamphetamine has been associated with renal and liver failure.[75–77]

8.10.2. Methamphetamine use and high-risk sexual behaviours

There are current anecdotal reports in the UK of high-risk behaviours associated with methamphetamine among a minority of gay men,[79] with this drug most commonly associated with what is referred to as 'chemsex', or sometimes as 'party and play', which is used to describe sex between men that occurs under the influence of drugs taken immediately before and/or during the sexual session.[30] Three patterns of behaviour are associated with methamphetamine use: high-risk sex, sexualised injecting and the sharing of injecting equipment.

The use of club drugs in a sexual context has been described.[80,81] Methamphetamine is one of the drugs most commonly used in a sexual context (chemsex) in the UK[79] and elsewhere. In a US study of 60 MSM, 68% reported using methamphetamine during sex more than 50% of the time.[82]

A relatively large body of evidence shows the heightened sexual risk-taking associated with methamphetamine use[83–89] and a relationship has been observed between increased severity of methamphetamine use and HIV risk.[88] Methamphetamine use has also been associated with sexually transmitted infections (STI), with studies showing that MSM who use methamphetamines, regardless of their HIV status, have a greater risk of STIs than those who do not.[32,90]

There is some evidence that compared with use of other drugs, methamphetamine use is a particularly strong predictor of unprotected anal sex among MSM.[91,92] It has

also been associated with increased rates of STIs,[35,93,94] including HIV infection.[80,95–103] Men who use methamphetamine are 1.5–2.9 times more likely to acquire HIV than those who do not.[87,104–107] There is also an association between methamphetamine use and rates of HIV and hepatitis C.[108–115]

Studies also suggest that HIV-positive MSM who use methamphetamine are significantly more likely than MSM who do not use methamphetamine (regardless of their HIV status) to engage in unprotected anal sex,[32,116–118] and group sex,[119] to have multiple sexual partners,[29,32,116,120,121] to find sexual partners on the internet,[32] to have sex with an injecting drug user[116] and to be intoxicated during sex.[32,116] Among HIV-infected MSM men who have a sero-discordant partner (i.e. HIV negative, or status unknown), the use of methamphetamine is significantly associated with unprotected anal sex.[33,122,123]

A number of factors and sub-groups of methamphetamine users have been associated with particularly high-risk behaviours for transmission of HIV and STIs. These include methamphetamine users who use sildenafil (Viagra)[91–93,123,124] or other illicit drugs during sex,[125,126] those who exchange sex for methamphetamine,[127] those who report high levels of sexual compulsivity,[123,128] those who engage in sexual encounters in public spaces[34,129] and those who report methamphetamine binges.[130]

A recent review of outcomes among MSM who use methamphetamines has reported a low adherence to medication by HIV-positive MSM who use methamphetamine. This, the authors believe, may contribute to the transmission of HIV virus resistant to medication which has been seen in newly infected MSM who use methamphetamine.[89]

However, it is important to note that a *causal* link between methamphetamine use and STIs, HIV and other blood-borne viruses (BBV) has not been established. There is some evidence that individuals who engage in high-risk sexual activity are more likely to use recreational drugs[131] and evidence that among MSM recreational drug use in general (rather than methamphetamine use specifically) is associated with high-risk activity.[132,133]

The link between methamphetamine use and high-risk sexual activities is not unique to MSM, although most of the research has been carried out among MSM and less evidence is available for heterosexuals.[134] Studies of male and female heterosexual populations also suggest that methamphetamine users have a higher frequency of sexual activity, have more sexual partners and engage in higher-risk sexual behaviours (unprotected vaginal sex and anal sex) than the users of any other drugs.[135–139]

8.10.3. Injecting risks

There is some anecdotal evidence of injecting methamphetamine among a minority of MSM in London (sometimes in combination with mephedrone), taking place at sex parties or other social gatherings, where people may share injecting equipment. For some people, injecting appears to have become sexualised. This combination of factors has been described as 'a perfect storm for transmission of both HIV and HCV [hepatitis C], as well as a catalogue of ensuing mental health problems'.[79]

It has been noted that HIV-positive men are more likely to inject psychoactive substances (including methamphetamine) than other MSM, with injecting increasingly common with older age, peaking among men in their 40s.[30] There are some reports from methamphetamine users of increased sexual desires with injecting methamphetamine, in comparison with other forms of methamphetamine use.[140,141]

Injecting is a serious public health concern, as well as heightening risks and harms to the individual user.[142] The evidence on the elevated injecting-related risk behaviours among methamphetamine users in comparison with other injectors has been ambiguous.[84,143–145] Regardless, methamphetamine injecting has been identified as a significant risk factor and injectors often present with more complex needs. Studies have shown that methamphetamine injectors are more dependent than non-injectors,[146] are at increased risk of non-fatal overdose,[147] are more likely to engage in HIV-risk behaviours;[143,148–150] and a study has reported a higher prevalence of STIs than among non-injecting methamphetamine users.[151]

Methamphetamine injectors are more likely to have co-morbid psychiatric disorders than are non-injecting methamphetamine users.[152,153] There is also evidence that methamphetamine injectors may be more likely to attempt suicide than those who smoke or snort the drug,[153,154] with a seven-year study reporting that people who injected methamphetamine had an 80% greater risk of attempting suicide than those who did not inject, even after taking into account a wide range of potential confounders. The study also showed a dose–response relationship between frequency of injecting methamphetamine and suicidal behaviour. The conclusion was that individuals who inject methamphetamine should be considered at high risk of suicide among populations of methamphetamine users, as well as the broader injecting population.[155]

8.10.4. Acute harms of poly-drug use and drug interactions

The high level of poly-drug use among methamphetamine users has been well established.[156] Cross-sectional population surveys suggest that the concurrent use of alcohol and cocaine is particularly common.[157] This can cause harm as it increases blood pressure. Methamphetamine can also mask the effects of alcohol, which may increase the risk of alcohol poisoning and accidents due to false feelings of being sober. Concurrent use of amphetamine and cannabis can increase psychotic symptoms in some users. Methamphetamine used with heroin can lead to respiratory depression and can increase the risk of heroin overdose.[1] The combination of methamphetamine and cocaine has been shown to increase substantially the cardiotoxic effects of both drugs.[158]

The co-ingestion of GHB and methamphetamine might increase the risk of GHB overdose, as methamphetamine can mask the signs of acute toxicity. There are also risks associated with the use of methamphetamine with other serotonergic substances. Informal reports from specialist UK 'club drug' clinics and some UK research[30] suggest that methamphetamine is often used in combination with mephedrone, another stimulant, leading to a potential risk of serotonin toxicity (on which, see section 7.7.2).

The potential for drug interactions with CYP2D6 inhibitors is high and co-administration of these agents may increase the toxicity of methamphetamine. Well known CYP2D6 inhibitors include: amiodarone, citalopram, codeine, fluoxetine, haloperidol, methadone, paroxetine and valproic acid. Among the antiretrovirals, while low-dose ritonavir does not seem to affect CYP2D6 activity,[159] the newer booster cobicistat is included in the list of CYP2D6 inhibitors.

8.10.5. Acute withdrawal

For withdrawal see section 8.12.2.

8.10.6. Emergency hospital admissions

In countries where rates of methamphetamine use are high, admissions to emergency departments (EDs) are reportedly very common. US data demonstrate that regular users of methamphetamine have a high rate of presentation to ED[61,160,161] and there is some evidence that adult methamphetamine users use ED and other hospital resources more than the users of other substances.[61,162] A Canadian study of homeless and street-based youth reported that frequent injecting of methamphetamine was associated with increased risk of ED utilisation.[155] Studies have shown that 1–2% of all ED visits are related to methamphetamine in endemic areas, with psychiatric conditions being the most common complaints.[154,163–173]

No such data are available for the UK, where the prevalence of methamphetamine use is low. However, 0.46% of drug-related presentations to an inner city hospital ED between 1 October 2005 and 31 December 2006 were related to self-reported methamphetamine use.[24]

In comparison with other patients presenting to EDs for toxicology-related issues, some studies have shown that those presenting with methamphetamine-related problems are more agitated, violent and aggressive and more likely to present on arrival with tachycardia and hypertension.[174,175]

In terms of mental health presentations, a study of psychiatric admissions to EDs reported that there were no differences in heart rate, admission route or cost of care of methamphetamine-related visits and other visits. This, according to the study, suggests that methamphetamine users presenting for psychiatric problems are clinically similar to non-amphetamine users with psychiatric problems.[176]

Studies have also shown relatively high levels of methamphetamine-related hospital presentations for psychiatric problems. Psychiatric symptoms, including acute psychosis, depression and anxiety disorders, have been associated with both acute and chronic methamphetamine use.[154,163–176]

Some studies have also suggested that more amphetamine-related presentations to EDs were for psychiatric problems than for other problems; 18% of methamphetamine-related ED visits were associated with psychiatric complaints or diagnosis, representing the largest patient sub-group visiting EDs with psychiatric issues.[163,176]

In the US, where rates of methamphetamine use are significantly higher than in the UK, a study reported that methamphetamine-related psychiatric visits to EDs represented 7.6% of all psychiatric attendances at EDs, a percentage which the authors described as 'disproportionate'. In comparison, 1.8% of all trauma visits were methamphetamine-related and 2.1% of presentations with chest pain were methamphetamine-related.[176]

8.11. Management of acute harms

TOXBASE® recommends that where a patient has impaired consciousness, emergency clinicians should ensure clear airways and adequate ventilation. As with other amphetamines, in the event of cardiac arrest, resuscitation should be continued for at least 1 hour and only stopped after discussion with a senior clinician. Prolonged resuscitation for cardiac arrest is recommended following poisoning, as recovery with good neurological outcome may occur.

TOXBASE® also suggests that the benefit of gastric decontamination is uncertain. Clinicians should consider oral activated charcoal if methamphetamine has been ingested within 1 hour, provided the airway can be protected. Asymptomatic patients should be observed for at least 4 hours, or 8 hours for patients who have ingested sustained-release preparations. Agitated adults can be sedated with an initial dose of oral or intravenous diazepam.

8.12. Harms of chronic use and dependence

8.12.1. Dependence

The risk of dependence with methamphetamine use is high. Tolerance to methamphetamine takes place when the drug is taken frequently, leading to users taking higher doses or using more frequently or changing the route of administration in order to get the desired effect.* There is some emerging evidence that craving to methamphetamine cues can be measured in dependent individuals[177–179] and that cue-elicited methamphetamine craving is a strong predictor of subsequent use.[180]

There is some evidence that methamphetamine-dependent users show a decrease in everyday functioning, disruption in everyday activities and increased errors in planning a daily schedule. Methamphetamine dependence has also been linked to impairments in the domains of communication, work and recreation.[181,182] There is also evidence that the chronic use of methamphetamine causes cognitive deficits after withdrawal.[183–185] Studies have also shown that this may be associated with disruptions of the dopaminergic and serotonergic systems.[183,186–189] Chronic use of methamphetamine causes neurochemical and neuroanatomical changes, which includes memory impairment.

* Section 7.9.1 has discussed ICD-10 criteria for harmful use and dependent use and should be referred to when reading the present chapter. It also offers additional information on dependence on amphetamine-type substances.

Dependence results in deficits in memory and in decision-making and verbal reasoning.[22] There is limited evidence that this functional deficit continues several months after abstinence.[182,190] One study has reported deteriorating cognitive performance during the first three months of abstinence from methamphetamine, with abstinent patients or abstinent patients with a recent lapse scoring worse on neuropsychological testing than patients with on-going methamphetamine use. This reflects the difficulties in attention, understanding and memory often encountered in methamphetamine patients in treatment settings.[184] Although it needs to be substantiated by larger studies, Henry et al. suggest that this may have important implications for treatment interventions, as individuals with poor functional ability may have difficulty responding to cognitive-behavioural therapy (CBT) and the cognitive enhancement techniques commonly used in the treatment of methamphetamine misuse.[190]

8.12.2. Withdrawal

Methamphetamine is associated with a clear withdrawal syndrome. A time-limited withdrawal syndrome may occur within 24 hours of the last dose when heavy chronic users of methamphetamine cease to use the drug abruptly. The withdrawal syndrome is common and severe enough to cause relapse outside a contained environment.[191]

Chapter 7 (the overview of amphetamine-type substances) has discussed in greater detail the phases of amphetamine withdrawal and should be read in conjunction with this present one. Phases of withdrawal symptoms have also been identified with methamphetamine users. For example, a study of 21 inpatients suggested that methamphetamine withdrawal has two phases: an acute phase lasting 7–10 days, in which overall symptom severity declines in a linear pattern from a high initial peak; and a sub-acute phase lasting at least a further 2 weeks, with some studies reporting much longer periods.[192] Withdrawal from methamphetamine has been described as more characterised by psychological and psychiatric symptoms than physical symptoms.[56]

Table 8.2. *The two phases of methamphetamine withdrawal.*

Acute withdrawal symptoms	Longer-term withdrawal symptoms (can last up to 12 months)
Severe dysphoria	Anhedonia
Irritability	Impaired social functioning
Melancholia	Intense craving
Anxiety	Hyper-arousal
Hypersomnia and marked fatigue,	Vegetative symptoms
Intense craving	Anxiety-related symptoms
Paranoia	Severe dysphoria
Intensity of post-binge dysphoria can lead to suicide ideation and attempts have also been linked to withdrawal[56,197] (for more information on the withdrawal syndrome see Chapter 7)	Mood volatility
Akathisia/restless legs	Irritability
	Sleep pattern disruption

Table 8.2 outlines the two phases of methamphetamine withdrawal, according to the reported symptoms.[48,56,76,153,193–197]

Greater severity of withdrawal symptoms in methamphetamine-dependent individuals has been reported among those who are older, who have been using methamphetamine longer and who have more severe methamphetamine use disorder.[192,197]

8.12.3. Physiological, psychological and psychiatric effects of long-term use and dependence

Chronic use has been associated with malnourishment.[198]

8.12.3.1. Cardiovascular effects

Long-term use of methamphetamine can result in severe cardiovascular complications related to chronic hypertension and cardiovascular disease, such as angina, arrhythmias, valvular disease, haemorrhagic/ischaemic strokes and a high incidence of myocardial infarction.[67,68,76,199–203]

8.12.3.2. Neurological effects

The chronic CNS hyperstimulation can lead to frequent headaches, tremors, athetoid movements and seizures.[8] There is evidence that users of amphetamine-type substances, including methamphetamine, may have an above-normal risk of developing Parkinson's disease (PD) because of enduring damage to the brain's dopamine neurons. This was shown by a retrospective population-based cohort study of inpatient hospital episodes and death records from 1990 through to 2005 in California. Patients at least 30 years of age were followed for up to 16 years. The study found that methamphetamine users had a 76% increased risk of developing Parkinson's disease in comparison with the matched population proxy control group. The authors noted that this finding may be limited to high-dose, chronic methamphetamine users and only when they reach middle and older age, when they have suffered age-related loss of dopamine neurons.[204]

8.12.3.3. Pulmonary and respiratory harms

The smoking of methamphetamine can cause respiratory symptoms and disorders such as pulmonary oedema, bronchitis, pulmonary hypertension, haemoptysis and granuloma.[8] Methamphetamine is associated with pulmonary arterial hypertension (PAH),[205] although its precise role remains unclear.[60]

8.12.3.4. Blood-borne infections, and haematological, gastrointestinal and urological effects

Methamphetamine has been reported to cause acute liver injury, with hepatic necrosis and centrilobular degeneration, even in the absence of hepatitis.[206] Mesenteric infarction,[207] segmental ischaemic colitis, vasculitis or vasospasm with spontaneous

resolution have been reported.[208] Severe acute necrotic haemorrhagic pancreatitis has been reported in cases of sudden death of chronic methamphetamine users.[60]

Because of the increased likelihood of high-risk sexual behaviours discussed in section 8.10.2, methamphetamine users are more likely to be diagnosed with a sexually transmitted infection than non-users.[135,138] Methamphetamine users are also at greater risk of viral hepatitis, especially where the drug is injected, but even among methamphetamine smokers and insufflators, hepatitis C is more common than it is in the general population.[209–211]

8.12.3.5. Oral/dental health

Methamphetamine use is associated with 'meth mouth', which is a constellation of symptoms, but it has been suggested that lifestyle factors, rather than the drug, may also be at play,[212] including poor personal hygiene and malnutrition.[213] Symptoms includes severe tooth decay and loss of teeth, advanced tooth wear, tooth fracture, and oral soft-tissue inflammation and breakdown.[214,215] A study of 301 adults dependent on methamphetamine found that 41.3% had oral or dental disease. They also had significantly more missing teeth than controls. The injecting of methamphetamine was significantly more likely to be associated with missing teeth than smoking the drug.[212]

8.12.3.6. Dermatological

Methamphetamine users may suffer from skin lesions resulting from compulsive scratching (due to formication – a sense of having ants under the skin). These lesions can result in bacterial cellulitis and, in some cases, bacteraemia and sepsis. In a case series of methamphetamine users presenting to an emergency department, skin infection accounted for 6% of the initial presentations and 54% of subsequent admissions to hospital.[61]

8.12.3.7. Pott puffy tumour

There is a case report of Pott puffy tumour (PPT) associated with the intranasal use of methamphetamine. This is an anterior extension of a frontal sinus infection that results in frontal bone osteomyelitis and subperiosteal abscess.[216]

8.12.3.8. Ophthalmological harms

Acute unilateral vision loss has been reported following a single dose of intranasal methamphetamine use and is believed to be due to ischaemic optic neuropathy secondary to methamphetamine-induced vasospasm and methamphetamine-associated vasculitis.[217,218]

8.12.3.9. Psychological and psychiatric effects

The frequent and prolonged use of methamphetamine has a number of adverse effects. There are direct physiological effects, but the cognitive and behavioural changes associated with its use may be secondary to neurotoxicity.[219]

There is a well established association between methamphetamine use and mental health problems.[76,220] Studies have found elevated rates of mood disorders, anxiety disorders and antisocial personality even after treatment.[221] Depressive disorders and symptoms are frequently associated with methamphetamine use.[170,172,173,222–225] The high prevalence of substance misuse among people with bipolar disorders or major depressive disorders has been established for a number of years.[226] It is also well established that substance misuse can exacerbate mental health problems.[227] There is some evidence that serious psychiatric disorders may emerge or worsen as a result of methamphetamine use,[48,56,153,228,229] including increased risk of suicide.[230]

The state of catechlolamine and serotonin depletion after several days of methamphetamine use can manifest itself as exhaustion, depression, lethargy and anhedonia. Psychological symptoms include persistent anxiety, paranoia, insomnia, auditory hallucinations, delusion, psychotic or violent behaviour and suicidal or homicidal thinking,[8] although violent behaviour is not an inevitable outcome of even heavy long-term use.[231] Some of the symptoms can resemble those of paranoid schizophrenia.[22]

Methamphetamine-induced psychotic disorder has been associated with the chronic, high-dose and continuous use of methamphetamine.[232] Symptoms may include paranoid delusions, persecutory delusions and other delusions, and auditory, visual and tactile hallucinations. The disorder is often associated with mood disturbances.[233] While sustained and high doses of methamphetamine can cause symptoms that resemble those of psychosis, relatively few studies have observed this in people using only methamphetamine who have no history of mental illness.[2] Nonetheless, a US study of 43 methamphetamine-dependent users and 42 cocaine-dependent users reported psychotic symptoms in at least 60% of both groups.[167] An Australian study of 27 treatment-seeking methamphetamine users with no prior diagnosis of schizophrenia, or other psychotic disorder, found that 18% had what was referred to by the authors as 'clinically significant' psychotic symptoms.[39]

Symptoms usually remit after acute intoxication but some individuals may develop psychosis weeks or months after stopping methamphetamine,[233,234] and may prove to be refractory to antipsychotic medication.[235]

Stress can precipitate spontaneous psychosis in former methamphetamine users who are abstinent.[236]

Much of the literature on persistent methamphetamine psychosis comes from Japan, where methamphetamine has been illicitly used for over 50 years, which suggests that persistent methamphetamine psychosis is not uncommon.[235] Japanese studies also reported that psychotic symptoms may recur where there is new exposure to the drug.[235,237–241] Japanese research has also reported discouraging results with standard antipsychotic drugs, as many patients remain clinically psychotic after many months of treatment.[234,242]

8.12.3.10. Cognitive effects

Neuroimaging in chronic users has shown significant neural damage in patients and evidence of cognitive impairment, but it is not established whether the link is causal.[40,243]

8.12.4. Co-morbidities of methamphetamine use disorders and HIV

Methamphetamine has been shown to interfere with the efficacy of HIV medication and treatment.[244]. Its use has been linked to non-adherence to medication regimens[245] and there is a suggestion that it may be associated with increased viral loads, even among those taking antiretroviral medication.[246]

Both methamphetamine use and HIV may be associated with impaired cognitive function, and in combination may result in greater impairment than each condition alone.[244] There is evidence that hepatitis C increases these cognitive deficits.[247]

8.13. Management of harms of chronic and dependent use of methamphetamine

8.13.1. Identification and assessment of dependence

The identification and assessment of chronic use of methamphetamine and ensuing harms are similar to those for ATS in general (see Chapter 7), but with particular vigilance to the issues pertaining to MSM, who are currently the group in the UK who mostly use methamphetamine.

8.13.2. Psychosocial interventions for dependence

Studies have shown that some people dependent on drugs may achieve abstinence without the need for treatment.[248]

At present, the most effective treatments for methamphetamine addiction are psychosocial interventions and behavioural therapies. Historically, treatment for stimulant dependence has relied on cognitive-behavioural therapy (CBT), with efforts to integrate contingency management (CM) (for more information see Chapter 7).

Overall, the evidence suggests that psychosocial interventions, such as CBT and CM, are moderately effective in achieving methamphetamine abstinence.[249] A Cochrane review of psychosocial interventions for cocaine and psychostimulant amphetamine disorders reported that comparisons between different types of behavioural interventions showed results in favour of treatments with some form of contingency management with respect to both reducing drop-outs and lowering use. However, the review also reports there are few significant behavioural changes even after reductions in drug consumption following an intervention. The authors conclude that there are no data supporting a single-treatment approach that is able to tackle the

multidimensional facets of addiction and to resolve the chronic, relapsing nature of addiction, with all its correlates and consequences.[250]

A number of US studies have reported the effectiveness of CM within specific research and drug treatment settings,[251] as well as outside those settings.[252] CM in combination with other interventions, such as CBT, has proved to be modestly effective at reducing methamphetamine dependence.[252–255] CM was also shown to have superior efficacy to CBT during drug treatment.[251,256]

Similarly, there is some evidence that behavioural-based treatment for methamphetamine misuse can be effective in reducing HIV infections, in terms not only of injecting behaviours but also of unsafe sexual practices.[102] Studies have shown the effectiveness of CM with methamphetamine users in changing other risk behaviours. For example, a pilot study of 35 MSM (not in drug treatment) who were given post-exposure prophylaxis (PEP) and CM showed that this may be useful as a combination HIV prevention strategy.[257]

Although psychosocial and behavioural interventions have been the most effective treatment for methamphetamine use, some argue that their role is still in question. CM, in particular, has shown benefit but a key limitation o includes its failure to address adequately mental health needs or develop relapse prevention plans for after the intervention.[89] There is also some evidence that CM is not likely to have a sustained and large effect on methamphetamine use.[258] One randomised controlled trial of CM to reduce methamphetamine use and sexual risk studied 217 non-treatment-seekers over 12 weeks and found that CM was potentially associated with an increase in methamphetamine use and decreases in sexual risk, but these were not statistically significant.[258]

As relapse rates are high,[259] there have been calls for more work in improving methamphetamine treatment. Further research into cognitive-behavioural and behavioural treatments for methamphetamine users is required, with a focus on increasing the duration of the effect of intervention and improving its effectiveness among patients with more complex presentations.[260]

8.13.2.1. Implementation of CM

Some studies have looked in greater detail at the impact of CM and at variations in CM models used and which specific factors were most effective in producing positive treatment outcomes. Roll et al. found that there were significant differences in terms of a CM schedule's ability to initiate and maintain abstinence. The schedule based on an escalating programme of reinforcement with a reset contingency (developed by Higgings[261]) showed the best results for a successful treatment episode.[262]

Ling Murtaugh et al. found, in their study of 162 MSM methamphetamine-dependent users, that it was the act of voucher redemption, rather than the receipt or size of payment, that affected subsequent abstinence from methamphetamine. Participants who delayed spending the vouchers, and those who saved the vouchers, had worse outcomes once they did finally redeem them. The authors recommend that frequent

purchases in incentive-based programmes should be promoted to improve abstinence outcomes.[263]

8.13.3. Pharmacological interventions for methamphetamine dependence and withdrawal

The need to develop safe and effective medication for methamphetamine dependence continues to be a global strategic aim. According to the US National Institute on Drug Abuse (NIDA), one approach currently tried is to target the activity of glial cells with a drug called AV411 (ibudilast). This has been shown to inhibit methamphetamine self-administration in rats; it is now being studied in clinical trials to establish its safety and effectiveness in humans. Other approaches currently under study use the body's immune system to neutralise the drug in the bloodstream before it reaches the brain. These approaches involve injecting a user with (anti)methamphetamine antibodies or with vaccines that stimulate the body to produce its own antibodies.[264] A clinical study is currently being conducted to establish the safety of an anti-methamphetamine monoclonal antibody, known as mAb7F9, in human methamphetamine users.[264]

As well as new compounds, a number of medications approved for other conditions have been tested for their efficacy and safety in treating methamphetamine dependence. These have included serotonergic agonists, dopaminergic agonists, monoamine agonists and mixed monoamine agonists/antagonists.[57,82,265–280]

For the moment, however, psychosocial therapies continue to be the cornerstone of treatment, with drug therapy regarded as an adjunct rather than a replacement for psychosocial approaches.[8] There is currently no approved pharmacotherapy for methamphetamine dependence[259] and no specific medication to counteract the effects of methamphetamine, or prolong abstinence.

A recent Cochrane review[281] of the efficacy and safety of psychostimulant medications for amphetamine dependence (dexamphetamine, bupropion, methylphenidate and modafinil), in addition to psychosocial interventions, reported that no significant differences were found between psychostimulants and placebo for any of the studied outcomes. Overall retention in studies was low (50.4%). Psychostimulants did not reduce amphetamine use, or amphetamine craving, and did not increase sustained abstinence. The proportion of dropouts due to adverse events was similar for psychostimulants and placebo. The review concluded that the evidence does not support the prescribing of psychostimulants (at the tested doses) as replacement therapy, although further research may change this conclusion.[281]

A small double-blind placebo-controlled study on the use of N-acetyl cysteine plus naltrexone found no significant difference with placebo on treatment outcomes.[276]

Other trials conducted with methamphetamine users have tested selegeline, ondansetron, paroxetine,[267] fluoxetine[282,283] and sertraline,[253,269] usually accompanied by a psychosocial structured therapy. A placebo-controlled trial studying the selective serotonin reuptake inhibitor sertraline, for the treatment of methamphetamine use showed that subjects receiving sertraline did not show improvements in depressive

symptoms or craving compared with those who did not receive it.[269] It has been argued that, overall, results suggest that sertraline, and possibly *all* selective serotonin reuptake inhibitors, are ineffective and may even be contraindicated for methamphetamine dependence.[269]

A number of small studies have suggested that there may be a potential for the use of mirtazapine (a noradrenergic and specific serotonergic antidepressant).[8,82,284] Mirtazapine (in addition to counselling) was shown to reduce use among active methamphetamine users.[82] It was also shown to lessen the symptoms of methamphetamine withdrawal (including the subjective symptoms) over 10 days of abstinence, with reductions in agitation, anxiety, fatigue, irritability, paranoid ideation, anhedonia, vivid dreams and suicide ideation. It also increased the amount of sleep.[277]

The impact of mirtazapine, in addition to counselling, on sexual behaviours that were shown by one study is noteworthy. A 12-week double-blind trial of mirtazapine among 60 MSM found that most sexual risk behaviours decreased significantly in the mirtazapine arm of the study in comparison with the placebo arm, even though both arms received HIV risk-reduction counselling at baseline. The study also found that the reduction in sexual risks was associated with a reduction in negative test results for amphetamine use, perhaps suggesting a possible causal pathway between the two outcomes.[82]

Not all studies of mirtazapine have shown its effectiveness in the management of methamphetamine dependence.[278] One study which focused on patients with acute withdrawal symptoms showed that it does not facilitate retention or recruitment in outpatient methamphetamine withdrawal treatment.[278]

The use of anticonvulsants has also been investigated. A randomised controlled trial of 140 methamphetamine-dependent adults prescribed topiramate (at doses of up to 200 mg/day) suggested that this medication does not promote abstinence. However, there is some indication that it may reduce amounts ingested and can reduce relapse rates among those already abstinent.[265]

Similarly, a trial randomly assigning people to an active medication regimen – comprising flumazenil (2 mg infusions on days 1, 2, 3, 22, 23), gabapentin (1200 mg to day 40) and hydroxyzine (50 mg to day 10) – or placebo showed that the regimen was no more effective than placebo in reducing methamphetamine use, retaining patients in treatment or reducing craving.[285] These results were different from those of another study using the same protocol that found fewer positive urine tests for methamphetamine throughout the trial and decreased cravings.[275] Differences may be due to study conditions and different demographic characteristics of participants in a private medical setting.[285]

A double-blind study of 60 subjects with bipolar or major depressive disorder and methamphetamine dependence randomised them to placebo or citicolin, an over-the-counter nutritional supplement (2000 mg/day), for 12 weeks. A significant between-group difference in depressive symptoms was observed. The study also showed significantly higher completion rates among those on citicolin than those on placebo.[227]

8.13.4. Treatment effectiveness, impact, retention and completion

Some studies have shown that, when methamphetamine users seek treatment, there is a substantial likelihood of treatment drop-out and relapse,[36] although the treatment outcomes for methamphetamine users are not necessarily different from those of the users other drugs.[286,287] There is, though, a lack of treatment provision.[288]

Treatment for methamphetamine use/dependence can have a positive impact on other high-risk behaviours. A study on CM and CBT for MSM found that those who reported the greatest decrease in methamphetamine use also reported the greatest and quickest reduction in depressive symptoms and high-risk sexual behaviour.[289] The authors suggest that lowering methamphetamine use can have an effect on depression and sexual behaviour and that some users who respond well to treatment may show improvements in these co-occurring problems, without the need for more intensive targeted interventions.[289]

Similar findings were reported by other studies.[82] There is some evidence that interventions to reduce or eliminate methamphetamine use for MSM in drug treatment settings also produce reductions in high-risk sexual behaviours and resultant HIV transmission. Drug treatment may be an important part of an HIV/STI prevention strategy for MSM.[251] One study of methamphetamine users found that longer treatment retention and greater rates of treatment completion were significantly related to greater reductions in risky sexual and injecting behaviours and were associated with reductions in HIV risk three years after treatment.[290]

There is a growing body of evidence on the factors that help predict methamphetamine treatment success, and most particularly failure, including retention in treatment and treatment completion.[36] There is consistent evidence that poorer outcomes are associated with:

- greater frequency of use prior to treatment;[36,270,291–294]
- more extensive history of previous treatment;[292,293,295]
- lower educational attainment,[36,292] although conflicting evidence on this has been reported.[291,294]

Other factors have also been associated with success or failure, but the evidence is either limited or inconsistent. These include greater craving for methamphetamine,[180] legal coercion of treatment,[36] residential versus outpatient treatment,[292] shorter treatment duration,[295] disability,[36] selling methamphetamine[295] and intravenous use.[36,293] Race, gender and ethnicity have also been associated with treatment success or failure, but the findings have differed between the studies.

Similar factors were identified as affecting health-related quality of life (HRQOL) for those completing treatment. A study of the HRQOL trajectories of 723 people dependent on methamphetamine, resulting from treatment completion and continued care over one year, found greater improvements in mental health. It described 'fairly static' trajectories in physical health status, in comparison with those who did not complete treatment or who continued to use services. The study showed differential

patterns of health improvement. Factors identified as negatively affecting HRQOL included unemployment, lifetime trauma, suicide history, interpersonal conflict, continued use of methamphetamine, poly-drug use and medical and psychiatric impairment.[296] The study also found that higher education was associated with a poorer health outcome, a finding that is not supported by the literature. The authors speculated that this might be because drug use among highly educated subjects can lead to a lower perceived health status, with the subjects not being able to maintain previous health standards and not able to fulfil goals they had set before drug use. The study also showed poorer health outcomes for women on methamphetamine.[296]

The frequency of use at entry to treatment and early treatment responsiveness have been identified as predictors of treatment success. One study of 60 individuals looked at whether cognitive performance can predict success in treating methamphetamine dependence, and considered whether cognitive performance is more or less predictive of treatment success than the established factors, such as frequency of use.[297]

The study found that, although a few neurocognitive and psychiatric variables were associated with treatment outcome, the frequency of methamphetamine use at the study outset was a much stronger predictor of outcomes. Participants who had two or fewer urine tests positive for methamphetamine during the first two weeks were much more likely to complete treatment and achieve abstinence in the majority of the treatment weeks,[297] a finding that was consistent with several other studies.[36,270,291–293,298]

The authors suggest that it is possible that this finding was partially due to study design. Nonetheless, the study did show that patterns of methamphetamine use during the initial stages of treatment were able to predict the outcomes in terms of continued use and treatment attendance. A few cognitive measures were related to treatment outcome, but these did not allow for prediction after adjustment for methamphetamine use at the beginning of the study. The authors concluded that clinicians who want to identify patients at risk of treatment failure should use multiple urine tests. They also suggest that it is more plausible to predict treatment failure than treatment success.[297]

Similarly, a study of bupropion found that early treatment responsiveness may be important for positive outcomes, a finding consistent with smoking cessation[273] and with some research in cocaine treatment.[273,274] Data analysis showed that the inability of users to provide at least three methamphetamine-free samples in the first two weeks of treatment was associated with a likelihood of treatment failure exceeding 90%. The authors suggest that clinicians prescribing bupropion can predict treatment failures confidently within two weeks when they carry out drug testing three times a week, with weekly testing yielding acceptable predictive power within three weeks. The ability to predict treatment failure was substantially more precise than the prediction of treatment success, which the authors attributed partially to the overall treatment failure rates. The absence of an early response predicts treatment failure better than the presence of an early good response predicts treatment success. The authors therefore suggest that this prediction of treatment failure is relevant to clinicians, as it signals the need to change treatment modality and intensity.[272]

8.13.5. Access to treatment

People dependent on methamphetamine may not access treatment services for many years and there is often a delay between first use, first recognising a problem with methamphetamine, and first treatment assessment. Different studies have shown a range for average length of time for the first treatment. An Australian study found that methamphetamine users can wait an average of five years from first experiencing problems to seeking treatment.[299] US studies have reported an average of eight[300] and nine years.[48]

There are many reasons why this may be the case. A US study reported a common belief among methamphetamine users that it is a 'functional drug', which may encourage frequent and prolonged daily use.[48,301] Similarly, Kenny et al. reported common reasons for not seeking methamphetamine treatment: users did not believe that they were dependent (despite meeting DSM-IV criteria for dependence); they did not feel that regular use of methamphetamine warranted formal treatment; they discounted their dependence; and they recognised their dependence but were not ready to do anything about it.[302]

There is also some non-UK evidence that treatment services may not be, or be perceived to be, accessible to methamphetamine users. An Australian study[303,304] suggested that the reasons for the under-representation of methamphetamine users in the treatment system include poor orientation of services for this group, lack of information about treatment options and little confidence in the effectiveness of programmes.

Barriers to treatment are not only constructed by service users but also by clinical staff. A study has also looked into barriers to methamphetamine treatment from the perspective of treatment providers, who saw barriers as extensive and wide-ranging. They included the particular personality characteristics of methamphetamine users, complexities associated with mental health co-morbidity, waiting periods resulting in loss to treatment, the binge nature of methamphetamine use, lack of pharmacological options and negative attitudes of staff towards this patient group.[305]

Improved understanding of the ways methamphetamine users access other treatment services could be used to facilitate effective referral pathways. Studies have looked at the factors, and user characteristics, that make individuals more likely to seek support.[306,307] GPs have been identified as a likely common starting point for patients seeking referral, for all drug-related problems.[308]

Quinn et al.'s study suggests that service utilisation for other problems, such as mental health or other drug problems, increases the likelihood of accessing treatment for methamphetamine use.[307] They suggest that contact with other services may increase the opportunity for treatment of methamphetamine misuse and break down barriers to professional support, such as ignorance of the services available and stigma associated with service utilisation.[309] People who use services for other issues are more receptive to seeking treatment for methamphetamine misuse.[307] The authors also note that these findings suggest a need to facilitate professional support pathways for treating methamphetamine users who engage in harmful use patterns.[307]

The availability of appropriate and relevant services has been identified as enhancing service uptake. Australian studies have suggested that methamphetamine injectors are more likely than those who smoke or snort the drug to seek and receive treatment from specialist services.[307,310,311] It has been suggested that there is greater availability of services for people who inject and fewer barriers to treatment (such as needle exchanges).

In comparison with other substances such as opiates, it may be important to make the treatment settings specific to methamphetamine users, to accommodate the different nature of methamphetamine dependence and withdrawals. Although this may be beyond the means of many drug treatment systems and services, services can undertake some small changes that could have a large impact on user perception, such as allocating some time each day for methamphetamine clients or allocating specific staff or rooms with specific methamphetamine resources.[302]

The cultural competence of services has also been identified as enhancing treatment uptake. A study of behavioural psychological interventions on depression, sexual risk behaviour and methamphetamine use among 162 MSM found that a gay-specific CBT intervention reported the greatest reduction in all three outcomes.[289]

Treatment readiness may also be key to accessing support for methamphetamine problems. Quinn et al. found that two key factors were associated with seeking help for methamphetamine problems: seeking help from family or peers in the year before entry into the study; and adoption of personal methods for the reduction or cessation of methamphetamine use.[307] It has been suggested that targeted interventions to identify and access individuals when they first experience readiness to change could be important. Motivational interviewing and stepped care could be beneficial.

One study found that only a small number of methamphetamine-using participants had reported access to more intensive drug treatment services (i.e. residential detoxification and/or rehabilitation), maybe suggesting a preference for low- rather than high-threshold treatment services,[307,312] or that many individuals feel that they are able to address harmful and/or dependent use without the need for intensive professional intervention.[248]

8.13.6. Aftercare and support

See section 7.10.5.

8.14. Harm reduction

The implications of driving under the influence of methamphetamine has been discussed.[313]

Harm reduction is covered in Chapter 7.

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