

# Methamphetamine-related fatalities in Australia: demographics, circumstances, toxicology and major organ pathology

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## ABSTRACT

**Aim** To examine the demographic characteristics, circumstances of death, toxicological results and major organ pathology of methamphetamine-related deaths in Australia. **Design** Retrospective review of coronial files. **Setting** Australia. **Methods** Cases in which methamphetamine was listed as a cause of death were identified from the National Coronial Information System (NCIS). **Findings** A total of 371 cases were identified. The mean age of decedents was 32.7 years; 77% were male and 35% were employed. Route of administration was predominantly by injection (89%). Drugs other than methamphetamine were detected in 89% of cases, most commonly benzodiazepines (41%) and morphine (36%). The median blood methamphetamine concentration was 0.2 mg/l (range 0.02–15.0 mg/l). Deaths were overwhelmingly accidental, with 14% determined to be suicides, and occurred in a private home (71%). Cardiovascular pathology, typically coronary artery atherosclerosis, was detected in 54% of decedents. Cerebrovascular pathology, most commonly cerebral haemorrhage and hypoxia, was present in 20% of cases. **Conclusions** Methamphetamine has contributed to a substantial number of deaths in Australia. Users need to be informed of the potential harms of methamphetamine use, particularly those associated with the cardiotoxicity of methamphetamine and the use of methamphetamine in conjunction with other drugs.

**Keywords** Autopsy, cardiovascular, methamphetamine, mortality, pathology, toxicology.

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## INTRODUCTION

The illicit use of methamphetamine in Australia is widespread. According to the 2004 National Drug Strategy Household Survey, 21% of 20–29-year-olds had used methamphetamine in their life-time and 11% had used the drug in the preceding 12 months [1]. Following a shift in the mid-1990s from the production and supply of amphetamine to the more potent methamphetamine, as well as increases in the availability and use of high purity crystalline methamphetamine, there has been a marked increase in methamphetamine-related problems [2].

Much research into the harms associated with methamphetamine use has focused on psychological morbidity [3,4]. While adverse effects on physical health are often reported [5–7], they have received comparatively

little research attention. The most serious adverse effects of methamphetamine use are potential cardiovascular and cerebrovascular complications. Chest pain, hypertension, tachycardia and other cardiac arrhythmias are the most commonly observed acute cardiovascular effects of methamphetamine [8–11]. Other, less common, complications include myocardial infarction, coronary vasospasm, aortic dissection and sudden cardiac death [9,11–15].

Methamphetamine has also been associated with chronic cardiovascular pathology [8,9,16–19]. Methamphetamine use, and chronic use in particular, has been associated with the premature and accelerated development of coronary artery disease (CAD), with underlying cardiovascular disease found in a significant proportion of methamphetamine-related deaths [16,20–22]. CAD

has also been observed among emergency department patients presenting with acute coronary syndrome following methamphetamine use [10,17]. Clinical and experimental evidence suggests that the use of methamphetamine, particularly long-term use, can also induce cardiomyopathy [17–19,23–27]. Cerebrovascular accidents (i.e. strokes) are another well-recognized complication of methamphetamine use, with users at a significantly elevated risk of stroke, in particular haemorrhagic stroke [28,29].

While the use of methamphetamine has been associated with the aforementioned harms, little is known about the nature and extent of methamphetamine-related mortality [30]. Previous autopsy studies of methamphetamine-related fatalities have been based on deaths occurring in the United States [20,21,31] and Asia [32,33]. With the exception of Karch *et al.*'s [20] study of 413 methamphetamine-related deaths, which reviewed toxicological and autopsy findings, these studies have been based on small case series [31,33] or have focused primarily on the demographics and toxicology of cases [21,31,32]. There have been no investigations anywhere of the circumstances of these deaths, such as the location in which they occurred and the route of methamphetamine administration employed.

The current study aimed to extend upon previous research and investigate the circumstances, toxicology and associated organ pathology of methamphetamine-related deaths in Australia across a 5-year period. Specifically, the study aimed:

- to determine the number of methamphetamine-related fatalities that occurred in Australia between 1 July 2000 and 30 June 2005;
- to describe the demographic characteristics of decedents and the circumstances of death;
- to examine toxicological findings from methamphetamine-related fatalities; and
- to describe the major autopsy findings from methamphetamine-related fatalities.

## METHODS

### National Coroners Information System

The National Coroners Information System (NCIS) is a database of coronial information as provided by the coroners' courts in each Australian jurisdiction. The NCIS contains information on deaths occurring from 1 July 2000 which have been reported to an Australian coroner. A complete NCIS case file includes demographic information, a police narrative of circumstances, autopsy and toxicology reports and the coronial finding, which provides information as to whether death was accidental, suicide or homicide, and confirms the cause of death.

NCIS data, in the form of free text and coded data, is based on information contained within the coronial file. Cause of death, as determined by a forensic pathologist and noted on the autopsy and coroner's reports, is entered verbatim. Findings from police, autopsy and toxicology reports, as well as coronial findings, can also be obtained from attachments of the original reports where available.

In Australia, the criteria for reporting a death vary between jurisdictions. In general, a death is reportable to a coroner where: the person died unexpectedly and the cause of death is unknown; the person died in a violent and unnatural manner; the person died during or as a result of an anaesthetic; the person was 'held in care' or in custody immediately before they died; a medical practitioner has been unable to issue a death certificate stating the cause of death; or the identity of the decedent is unknown.

### Case selection

Methamphetamine-related deaths occurring between 1 July 2000 and 30 June 2005 were identified from the NCIS. Cause of death is determined by a forensic pathologist on the basis of the circumstances of death, a comprehensive autopsy and toxicological analyses. Methamphetamine-related deaths were defined as those in which methamphetamine was determined by the pathologist to have been a direct cause of death (i.e. leading directly to death), an antecedent cause of death (i.e. gave rise to the direct cause of death) or a significant contributing factor (i.e. contributed to death but not related to the disease/condition causing death).

### Demographics and circumstances of death

Demographic information was extracted from each case file. The circumstances surrounding death were obtained from accompanying police reports including, where available, the location of the fatal incident, evidence of drug use and route of drug administration, evidence of suicidal intent, drug treatment status and recent prison history.

### Toxicological results

Quantitative toxicological analysis is conducted routinely in all cases of unnatural or unexpected death (i.e. deaths reportable to the coroner), providing information on the blood concentrations of alcohol and other drugs. Toxicological analysis entails screening for, and quantifying concentrations of, a range of licit and illicit substances. Recent use of methamphetamine was determined by the presence of methamphetamine or amphetamine (the primary metabolite of methamphetamine).

**Table 1** Demographic characteristics of decedents.

	Males (n = 285)	Females (n = 86)	All (n = 371)
Age (years) (range)	32.7 (17–59)	32.5 (15–61)	32.7 (15–61)
Employment (%)			
Employed	38	24*	35
Home duties	0	15	4
Retired/pensioner	7	14	9
Student	1	1	1
Unemployed	42	37	41
Unknown	11	8	10
Marital status (% married/ <i>de facto</i> )	21	28	23
Body mass index (mean) (range)	24.5 (16.3–49.2)	22.7* (16.5–37.5)	24.1 (16.3–49.2)
Treatment status (%)†			
In treatment	10	11	10
Methadone	8	8	8
Buprenorphine	0	2	0.5
Naltrexone	2	2	2
Drug-free rehabilitation	0.5	0	0.5
Released from prison in last week (%)†	2	2	2

\* $P < 0.05$ ; † $n = 285$ .

### Autopsy reports

In cases of deaths reportable to the coroner a standardized forensic autopsy is conducted, entailing a comprehensive examination of all major organs, including microscopy of representative tissue samples. This is a retrospective study. As such, the autopsies reported were not collected prospectively for the study, but were standard forensic autopsies performed as part of the medico-legal responsibilities of the forensic medicine departments in each jurisdiction.

Information on the height and weight of the decedent, from which body mass index (BMI) was calculated, findings of major organ pathology, hepatitis C virus (HCV) and human immunodeficiency virus (HIV) serostatus and other clinically significant pathology was extracted from autopsy reports. Findings of particular relevance related to: cardiovascular pathology, cerebrovascular pathology, pulmonary pathology, hepatic pathology and renal pathology. Coronary atherosclerosis was classified as mild, moderate or severe on the basis of direct comment by the forensic pathologist in the post-mortem report or as indicated by arterial stenosis ranges of 10–50% (mild), 51–75% (moderate) and >75% (severe).

### Statistical analyses

For continuous variables, *t*-tests were employed. Where distributions were highly skewed, medians were reported. For dichotomous categorical variables, odds ratios (OR)

and 95% confidence intervals (95% CI) were reported. In order to determine the variables that were associated independently with major organ pathology, simultaneous logistic regressions were conducted. All findings were examined for gender differences, and these are reported only where significant. All analyses were conducted using SPSS for Windows, version 14.0 [34].

## RESULTS

### Demographic characteristics

A total of 371 cases were identified. Methamphetamine use or toxicity was implicated in the direct cause of death in 73% of cases, as an antecedent cause in 11% of cases and as a significant contributing condition in 16% of cases. The mean age of decedents was 32.7 years [standard deviation (SD) 8.7, range 15–61 years] (Table 1). Almost half (46%) were between the ages of 25 and 34 years, and 4% were aged 50 years and over. The BMI of males was significantly higher than that of females ( $t_{208} = 2.39$ ,  $P < 0.05$ ) (Table 1).

The majority of decedents were male (77%) and more than a third were employed, with males significantly more likely to be employed (OR 1.92, 95% CI 1.11–3.31) (Table 1). Twenty-three per cent of decedents were in a married/*de facto* relationship and 10% were in treatment for drug dependence at the time of their death, predominantly methadone maintenance. Two per cent of decedents had been released from prison during the previous week (Table 1).

**Table 2** Direct cause of death.

Cause of death (%)	Male (n = 285)	Female (n = 86)	All (n = 371)
Methamphetamine toxicity	17	16	17
Combined drug toxicity	51	53	51
Cardiovascular	15	11	14
Cerebrovascular	4	13*	6
Injury	9	8	9
Pulmonary	5	4	5
Hanging	5	4	5
Other	7	6	7

\**P* < 0.05.

### Direct cause of death

In 68% of cases the forensic pathologist attributed the direct cause of death to methamphetamine toxicity (Table 2) and, in a further 5% of cases, the 'use' or 'effect' of methamphetamine directly contributed to death. Toxicity due to methamphetamine alone was a direct cause of death in 17% of cases and combined drug (i.e. methamphetamine in combination with other drugs) toxicity was a direct cause of death in 51% of cases. The most common drugs present with methamphetamine in cases where death was due to combined toxicity were opiates (82%), benzodiazepines (42%) and antidepressants (24%).

In 14% of cases, the forensic pathologist concluded that cardiovascular complications or disease arising from or complicated by methamphetamine use was the direct cause of death. Cardiovascular events and pathology causing death included coronary artery atherosclerosis/disease (22 cases), cardiac arrhythmia (five cases), cardiomegaly (five cases), ischaemic heart disease (six cases), myocardial infarction (four cases) myocardial ischaemia (two cases), cardiomyopathy (two cases), left ventricular hypertrophy (one case), aortic rupture (one case) and endocarditis (one case).

In 6% of cases, cerebrovascular complications were a direct cause of death, with the occurrence of such events significantly higher in females (OR 3.65, 95% CI 1.53–8.75). In the majority of these cases, death was caused by cerebral haemorrhage (17 cases), with the remaining deaths due to seizure (two cases) and hypoxic brain damage in association with methamphetamine toxicity (three cases).

Injuries such as those sustained in motor vehicle accidents, falls and, in a single case, gunshot wounds, were the direct cause of 9% of deaths. Pulmonary complications, typically bronchopneumonia, were a cause of death in 5% of cases and in a further 5% of cases, death was due to hanging. Other causes of death included

**Table 3** Circumstances of death.

	Males (n = 285)	Females (n = 86)	All (n = 371)
Location of fatal incident (%)			
Home	68	84*	71
Road	12	9	11
Public area	13	4*	11
Hospital	2	3	2
Other	6	0*	5
Suicide (%)†	14	12	14
Route of administration (%)‡			
Intravenous	90	84	89
Intranasal	2	0	2
Oral	7	16	9
Smoked	1	0	0.5

\**P* < 0.05; †*n* = 354; ‡*n* = 218.

carbon monoxide poisoning (five cases), drowning (six cases), aspiration of gastric contents (five cases) and hyperthermia (one case).

### Circumstances of death

Information from the coroner's finding as to whether death was accidental or suicide was available for 354 cases. Death was determined to be suicide in 14% of cases (Table 3). Deliberate drug overdose was the method of suicide in 21 cases, hanging in 17 cases, carbon monoxide poisoning in five cases and self-inflicted injury in six cases.

The majority of fatal incidents occurred in a private home (Table 3). While females were significantly more likely than males to die in a private home (OR 2.45, 95% CI 1.31–4.58), males were more likely to die in a public place (OR 4.13, 95% CI 1.24–13.74).

Of the 58% of cases where the route of drug administration was evident, injecting was by far the most common route (Table 3) and there was clear evidence for the injection of methamphetamine specifically in 40% of these cases.

### Toxicology

Toxicology results indicating the presence or absence of methamphetamine in the blood were available for 260 cases, with methamphetamine and/or amphetamine detected in 249 cases (Table 4). In the remaining cases, recent use was determined by urinalysis or confirmed in the police report. The median concentrations of methamphetamine and amphetamine were 0.2 mg/l (range 0.02–15.0 mg/l) and 0.07 mg/l (range 0.01–2.0 mg/L), respectively.

Toxicological results indicating the presence or absence of other drugs in the decedents' blood were

**Table 4** Toxicological findings.

<i>Drug detected</i>	<i>Males (n = 194)</i>	<i>Females (n = 55)</i>	<i>All (n = 249)</i>
<b>Methamphetamine concentrations (median)</b>			
Methamphetamine (mg/l) (range)	0.2 (0.02–15.0)	0.2 (0.02–6.8)	0.2 (0.02–15.0)
Amphetamine (mg/l) (range)	0.06 (0.01–2.0)	0.07 (0.01–0.8)	0.07 (0.01–2.0)
<b>Presence of other drugs (%)†</b>			
Benzodiazepines	37	54*	41
Morphine	35	39	36
THC	28	28	28
Codeine	22	39*	26
Antidepressants	25	28	25
Alcohol	24	12	21
Methadone	19	21	19
MDMA	12	11	11
MDA	6	2	5
Antipsychotics	5	5	5
Cocaine/benzoyllecgonine	5	2	4
Ketamine	2	0	1
Miscellaneous other drugs	25	39	28

\* $P < 0.05$ ; † $n = 263$ . THC:  $\Delta 9$ -tetrahydrocannabinol; MDMA: 3,4-methylenedioxyamphetamine; MDA: 3,4-methylenedioxyamphetamine.

available in 263 cases (Table 4). Other drugs were detected in 89% of these cases, the most common being benzodiazepines, morphine,  $\Delta 9$ -tetrahydrocannabinol (THC), codeine and antidepressants. Females were more likely to test positive for benzodiazepines (OR 2.05, 95% CI 1.12–3.75) and codeine (OR 2.25, 95% CI 1.18–4.28).

### Major organ pathology

Complete autopsy reports were available for 205 cases, although there were a further 29 cases where major organ pathology was noted in the coroner's report or forensic pathologist's summary. Of the 220 cases where information on cardiac pathology was available, pathology was noted in 54% of cases (Table 5). Age, gender and BMI were entered as independent variables in logistic regression analyses conducted in order to determine the predictors of cardiac pathology. Older age (OR 1.10, 95% CI 1.06–1.14) and a greater BMI (OR 1.12, 95% CI 1.03–1.21) were significant independent predictors of the presence of cardiac pathology.

The most common type of cardiac pathology was coronary artery atherosclerosis (Table 5). Older age (OR 1.13, 95% CI 1.08–1.18), being male (OR 3.50, 95% CI 1.30–9.38) and a higher BMI (OR 1.14, 95% CI 1.05–1.23) were significant predictors of such pathology. Atherosclerosis was located typically in the coronary arteries (35%), with involvement of the aorta in 14% of cases. Atherosclerosis was moderate or severe in 18% of cases. Cardiomegaly and cardiac hypertrophy were the most prevalent types of cardiac pathology after atherosclerosis,

**Table 5** Major organ pathology.

<i>Type of pathology (%)</i>	<i>Males (n = 172)</i>	<i>Females (n = 48)</i>	<i>All (n = 220)</i>
Cardiovascular pathology	55	48	54
Atherosclerosis	43	26*	39
Mild	20	15	19
Moderate	3	2	3
Severe	17	7	15
Unspecified	1	2	1
Sites of atherosclerosis	40	17*	35
Coronary arteries	14	17	14
Aorta			
Cardiomegaly	18	6	16
Hypertrophy	13	11	12
Ischaemic heart disease	6	2	5
Cerebrovascular pathology†	19	26	20
Pulmonary pathology‡	42	42	42
Hepatic pathology§	61	60	61
Renal pathology¶	12	13	13

\* $P < 0.05$ ; † $n = 214$ ; ‡ $n = 217$ ; § $n = 208$ ; ¶ $n = 206$ .

and were associated independently with increased age (cardiomegaly: OR 1.08, 95% CI 1.03–1.14; hypertrophy: OR 1.08, 95% CI 1.02–1.14) and BMI (cardiomegaly: OR 1.20, 95% CI 1.09–1.32; hypertrophy: OR 1.23, 95% CI 1.11–1.37).

Cerebrovascular pathology was noted in 20% of cases (Table 5). Older age was the only independent predictor of cerebrovascular pathology (OR 1.05, 95% CI 1.01–1.09). The most common types of cerebrovascular

pathology were non-traumatic cerebral haemorrhage (9%) and hypoxic damage (8%). Being older (OR 1.08, 95% CI 1.01–1.15) and female (OR 4.60, 95% CI 1.40–15.05) were associated significantly with cerebral haemorrhage. Pulmonary pathology was reported in 42% of cases (Table 5). Pneumonia (19%) was the most commonly reported pulmonary pathology, followed by pulmonary fibrosis (9%). Hepatic pathology was reported in 61% of cases, with changes associated with HCV infection (31%) and steatosis (fatty liver) (28%) the most prevalent forms of pathology. Renal pathology was reported in 13% of cases. The most common types of renal pathology were nephrosclerosis (4%), fibrosis (3%) and inflammation (3%). Other organ pathology was noted in 9% of cases, and included pathology of the spleen (3%), stomach (3%), gallbladder (1%) and pancreas (1%).

## DISCUSSION

Methamphetamine contributed to a clinically significant number of deaths in Australia between 2000 and 2005. In contrast to previous studies in which methamphetamine-related deaths were due primarily to homicide and accidental trauma [21,31,33], methamphetamine toxicity was the predominant cause of death. Similarly, Karch *et al.* [20] reported that more than half of methamphetamine-related deaths were due directly to methamphetamine toxicity. Such findings illustrate that methamphetamine toxicity is itself a primary cause of death, and not merely a cause of behaviours which, in turn, increase the risk of death.

In almost one in five deaths, methamphetamine was the only drug contributing to death. Most commonly, death was due to combined drug toxicity. Combined drug toxicity is a common finding of studies of drug-related fatalities [21,31,35–37] and reflects the fact that poly-drug use is the norm among illicit drug users [7,38,39]. The finding that opiates were involved in the majority of deaths due to combined drug toxicity is consistent with other studies of methamphetamine- [20,21,31] and cocaine-related fatalities [31,35–37,40]. That opiate toxicity is a common feature of psychostimulant-related death suggests that the combination of psychostimulants and opiates may increase the risk of drug-related mortality. Indeed, previous research suggests that when methamphetamine is combined with alcohol, cocaine or opiates, toxicity is increased [8,30,41].

The majority of decedents were males in their early 30s, a profile consistent with other studies [20,21,31,33]. As was also seen in cases of cocaine fatalities [35–37], these are not typically cases of death among young, naive users. The higher proportion of male decedents may reflect the fact that males in the

general Australian population are more likely to have used methamphetamine [1]. It may also reflect the higher prevalence of CAD among the males in this study, CAD being more common among men than women in the general population.

Injection was the predominant administration route prior to death, a probable reflection of the high prevalence of injecting among regular, dependent methamphetamine users in Australia. While potentially fatal cardiovascular complications due to methamphetamine use are known to occur with all routes of administration [42], the risk of complications is likely to be higher with administration routes that deliver a higher dose of the drug and are associated with frequent use (e.g. injecting and smoking) [7,39,43].

Methamphetamine-related deaths in the current study were associated with a wide range of methamphetamine concentrations. Previous autopsy studies have shown that methamphetamine-related death can be associated with low or high levels of methamphetamine in the blood [16,21,31,33,44]. There does not appear to be a clear dose–response for methamphetamine toxicity [30], and methamphetamine concentrations should not be interpreted in isolation from other factors. In cases of methamphetamine-related death, low levels of methamphetamine may be associated particularly with pre-existing cardiac and cerebrovascular pathology and the presence of other drugs [16,21].

Cardiovascular pathology was noted in over half of cases for which autopsy findings were available. Decedents who were older and had a greater BMI were more likely to have some type of cardiac pathology. The most common type of cardiac pathology was coronary artery atherosclerosis, with two in five autopsy reports noting the disease. Males were more than three times more likely than females to have coronary artery atherosclerosis. As mentioned above, methamphetamine has been associated with both acute and chronic cardiovascular pathology, and its cardiotoxicity has been well documented [42]. The high prevalence of cardiovascular pathology among decedents in the current study, particularly CAD, is consistent with the view that methamphetamine use may cause the premature and accelerated development of such disease and exacerbate pre-existing pathology [16,20,21].

The levels of cardiovascular pathology found among cases in the present study are similar to those found among cocaine-related fatalities [45]. In a study comparing major organ pathology among deaths due to cocaine toxicity, opioid toxicity and non-drug related causes, Darke *et al.* [45] found that 51% of cocaine-related fatalities had some form of cardiac pathology, a substantially higher prevalence than that among opioid- (29%) and non-drug-related fatalities (24%) [45]. Levels of coro-

nary artery atherosclerosis, hypertrophy and ischaemic heart disease among the cases in this study were also similar to those among cocaine fatalities and higher than those among opioid and control cases [45]. Cocaine is regarded as a more cardiotoxic drug than methamphetamine. Thus, the similar levels of pathology among methamphetamine and cocaine users may reflect the fact that, in Australia, methamphetamine is used more frequently, and is of a generally higher purity than cocaine.

Cerebrovascular pathology was found in one in five cases where autopsy findings were available, and non-traumatic cerebral haemorrhage was noted in almost half of these cases. As mentioned above, there is evidence to suggest that methamphetamine use can increase the risk of haemorrhagic stroke [28,29], and cerebral haemorrhage has been documented in previous studies [20,21,33,46]. While there were no significant gender differences with respect to cerebrovascular pathology overall, females were more than four times more likely to have suffered a cerebral haemorrhage. It is unclear why females were at greater risk of haemorrhage. A history of oral contraceptive use was unable to be ascertained, as such information was unavailable. Thus, the effect of oral contraceptive use could not be examined. While previous studies investigating an association between oral contraceptive medication and stroke have yielded conflicting findings [47], the effect of methamphetamine on any such relationship is unknown.

The major limitation of the current study is that case files in the NCIS were often incomplete. Autopsy reports were unavailable in 45% of cases and toxicological findings in 29% of cases. Information as to risk factors for cardiovascular and cerebrovascular pathology, such as smoking and a positive relevant family history, was also unavailable, as was the extent of past drug use by the decedent. Such information, however, is unlikely to be obtained from any retrospective study based on coronial files. Future prospective cohort studies may provide a better understanding of the interaction between methamphetamine use and other mortality risk factors.

The current study is the most comprehensive examination of methamphetamine-related mortality to date. This study indicates that in Australia, as in other countries, methamphetamine-related death is not a rare event and occurs among a demographically diverse group of users. The high prevalence of cardiovascular pathology, along with the evidence for the cardiotoxicity of methamphetamine, highlights the need to educate users, particularly dependent users, about the potential harms of methamphetamine use. Users should also be informed of the risks of using methamphetamine in conjunction with other stimulants, opiates and alcohol, which are known to increase toxicity. While injection was the predominant route of administration, non-injectors are also at risk of

toxicity related complications, particularly if they engage in frequent, long-term use. Given the widespread use of methamphetamine, an understanding of the associated risk of mortality is of major importance and should remain a primary research objective.

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