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Rates, characteristics and circumstances of methamphetamine-related death in Australia: a national 7-year study

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ABSTRACT

Aims To (1) assess trends in the number and mortality rates of methamphetamine-related death in Australia, 2009–15; (2) assess the characteristics and the cause, manner and circumstances of death; and (3) assess the blood methamphetamine concentrations and the presence of other drugs in methamphetamine-related death. **Design** Analysis of cases of methamphetamine-related death retrieved from the National Coronial Information System (NCIS). **Setting** Australia. **Cases** All cases in which methamphetamine was coded in the NCIS database as a mechanism contributing to death (n = 1649). **Measurements** Information was collected on cause and manner of death, demographics, location, circumstances of death and toxicology. **Findings** The mean age of cases was 36.9 years, and 78.4% were male. The crude mortality rate was 1.03 per 100 000. The rate increased significantly over time ($P < 0.001$), and at 2015 the mortality rate was 1.8 [confidence interval (CI) = 1.2–2.4] times that of 2009. Deaths were due to accidental drug toxicity (43.2%), natural disease (22.3%), suicide (18.2%), other accident (14.9%) and homicide (1.5%). In 40.8% of cases, death occurred outside the major capital cities. The median blood methamphetamine concentration was 0.17 mg/l, and cases in which only methamphetamine was detected had higher concentrations than other cases (0.30 versus 0.15 mg/l, $P < 0.001$). The median blood methamphetamine concentration varied within a narrow range (0.15–0.20 mg/l) across manner of death. In the majority (82.8%) of cases, substances other than methamphetamine were detected, most frequently opioids (43.1%) and hypnosedatives (38.0%). **Conclusions** Methamphetamine death rates doubled in Australia from 2009 to 2015. While toxicity was the most frequent cause, natural disease, suicide and accident comprised more than half of deaths.

Keywords Circumstances, disease, epidemiology, methamphetamine, mortality, toxicity.

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INTRODUCTION

The use of methamphetamine, and crystal methamphetamine in particular, is a major public health problem, particularly in countries around the Pacific rim (North America, East/Southeast Asia, Oceania) [1–3]. It is estimated that there are some 35 million stimulant users world-wide, predominantly of methamphetamine, and there have been large increases in production, seizures and use in recent years [3]. Crystal methamphetamine first appeared in significant quantities in Australia in the early 2000s [4]. Its use appears to have increased substantially since 2009 [5,6], and the drug is frequently injected [6–9]. It should be noted that the increased use of potent crystal methamphetamine has implications for harm, as this form has a higher dependence liability [6,10].

Methamphetamine dependence is associated with an array of serious societal, psychiatric and physical health problems. It was estimated in the most recent Global Burden of Disease that there were 2.6 million disability-adjusted life years lost in 2010 attributable to amphetamine class dependence [3]. The physical health of dependent users is poorer than that of the general population [11,12], the predominant concern being cardiovascular disease. Methamphetamine is associated with a range of pathology involving the cardiovascular system, including accelerated atherosclerosis, ischaemic heart disease, hypertensive heart disease, various cardiomyopathies,

arrhythmias, cardiomegaly and aortic dissection [13–19]. There is also an increased risk of haemorrhagic stroke and rupture of intracranial aneurysms [15,20,21].

Methamphetamine use is also associated with a substantial burden of psychopathology, including mood and anxiety disorders, suicide and violent behaviours [13,22–26]. There is also an increased risk of developing a schizophreniform paranoid psychosis, a risk exacerbated by crystal methamphetamine use [23–25]. Finally, regular methamphetamine use is associated with increased risk of violent assault upon others and the self [7,9,13,26–29].

Given the above, it is not surprising that mortality rates are elevated among methamphetamine users, estimated at three to six times that of non-users [2,30–34]. Despite this risk, few studies have examined the toxicology of methamphetamine-related death, the manner and circumstances in which death occurs, or temporal trends in mortality [7,9,27,35]. In particular, the toxicity of methamphetamine, and what constitutes fatal blood concentrations, are poorly understood. Multiple drugs appear common, and may influence the toxicity of methamphetamine [7,9,13,27,35]. For example, the use of alcohol with methamphetamine increases heart rate and blood pressure beyond that seen for methamphetamine use alone [13,36]. The concomitant use of other serotonergic drugs (such as antidepressants and the opioid analgesic tramadol) in conjunction with methamphetamine increase the risk of seizures, serotonin syndrome and arrhythmias [37–39]. From the limited data on fatalities, there does not appear to be a clear dose response, such as seen with drugs such as alcohol or the opioids, and very low doses may be lethal [7,9,13,27,35]. The few clinical studies of methamphetamine-related death also indicate that cardiovascular disease is prominent in fatalities, as is suicide and, to a lesser extent, homicide [7,9,27,34,35].

The current study aimed to extend existing work on methamphetamine-related death by providing national data mortality, trends in mortality and the circumstances of death during a period of escalating methamphetamine use. Specifically, the study aimed to:

1 assess trends in the number and mortality rates of methamphetamine-related death in Australia, 2009–15;
2 assess the characteristics and the cause, manner and circumstances of death; and
3 assess the blood methamphetamine concentrations and presence of other drugs in methamphetamine-related death.

METHODS

National Coronial Information System

Ethical approval for the study was received from the National Coronial Information System (NCIS) and University of New South Wales Ethics Committees. The NCIS is a database provided by the coroners' courts in each Australian jurisdiction. A complete NCIS case file includes demographic information, a police narrative of circumstances, autopsy reports, toxicology reports and the coronial finding (which provides information as to whether death was natural disease, accidental, suicide or homicide, and confirms the cause of death). All coroners are judicial officers, generally of lower courts, and have legal but not medical training. Cause of death is ascertained by a forensic pathologist and noted on the autopsy and coroner's report. The forensic pathologist may report on: (i) the direct cause of death, (ii) the antecedent cause and (iii) other significant conditions associated with the death. The majority of autopsies in Australia are conducted by specialist forensic pathologists, with lesser numbers by anatomical pathologists. Each NCIS case has codes for 'Mechanism of Injury' and 'Object or Substance'. Cases in which the Coronial investigation has been completed are designated 'closed', while those in which the process is incomplete are designated 'open'.

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. Of pertinence to methamphetamine-related death, all jurisdictions require the reporting of violent or unnatural death, which comprise all the deaths reported in this study.

Case identification

All cases of methamphetamine-related death occurring between 1 January 2009 and 31 December 2015 were identified and inspected by the authors. Searches were conducted methamphetamine in codes for 'Cause of Death' and by 'Object or Substance Producing Injury'. For the purposes of this study a methamphetamine-related death was one in which methamphetamine was considered a contributing factor to the death of the individual, and includes drug toxicity, natural disease, accident, suicide and homicide. Cases were restricted to those in which the person's own methamphetamine use was contributory to their death. Cases of non-users whose death was due to another's methamphetamine use (e.g. passenger in a motor vehicle accident) were excluded. Due to the fact that methamphetamine may be present in the urine for up to 24 hours after consumption [15], and thus may not reflect

recent use, cases in which methamphetamine, or its primary metabolite amphetamine, was detected only in urine were excluded, as were cases where the presence of amphetamine was attributable solely to prescribed dexamphetamine.

Measures

Information was collected on age, marital status, employment, drug use history, treatment status, setting of the death and suicidal intent. For the purposes of analysis, the manner of death was classified as: (i) accidental drug toxicity, (ii) natural disease with contributing methamphetamine effect, (iii) accident, (iv) suicide (NCIS code for 'Intentional Self-harm') and (v) homicide. The geographical location of the fatal incident and death were recorded, as was the setting (e.g. home environment, public setting).

The majority of cases undergo a standardized forensic autopsy, with examination of all major organs and quantitative toxicological analysis. Toxicological data were reported for methamphetamine, other psychostimulants, hypnosedatives, alcohol, opioids, cannabis [Δ-9-tetrahydrocannabinol (THC)], antidepressants and antipsychotics. In cases of hospitalization prior to death, antemortem blood samples taken on or near admission to hospital were reported, and drugs administered by hospital and medical staff excluded.

Statistical analyses

For normally distributed variables, means, standard deviations (SD) and ranges were presented, otherwise medians, interquartile range (IQR) and range were presented. The Mann–Whitney *U*-test was used for bivariate comparison of methamphetamine concentrations. Crude mortality rates and 95% confidence intervals (CI) were calculated for each year of the study period, using annual population estimates from the Australian Bureau of Statistics [40]. In order to examine mortality rates over time, a Poisson regression was conducted. For each case, years of potential life lost (YPLL) were calculated by subtracting age at time of death from the average life expectancy of the Australian population, specified for gender and the year in which the death occurred [41]. All analyses were conducted using IBM SPSS statistics version 23.0 [42] and R [43].

RESULTS

Cases and population rates

A total of 1649 closed cases were identified (Fig. 1) and there were an additional 49 open cases suspected to be methamphetamine-related that were not included (2010: one; 2011: two; 2012: four; 2013: three; 2014: seven; 2015: 32). The figures for 2015 are conservative, due to the number of open cases, with the maximum possible number being 312.

The all-cause crude mortality rate across all study years was significantly higher among males than females (Table 1).

There was a significant rise in all-cause mortality over time (Wald $\chi^2_6 = 122.3$, $P < 0.001$). As may be seen from the confidence intervals presented in Fig. 2, rates between 2012 and 2015 were significantly higher than those from 2009 to 2011. The crude mortality rate was

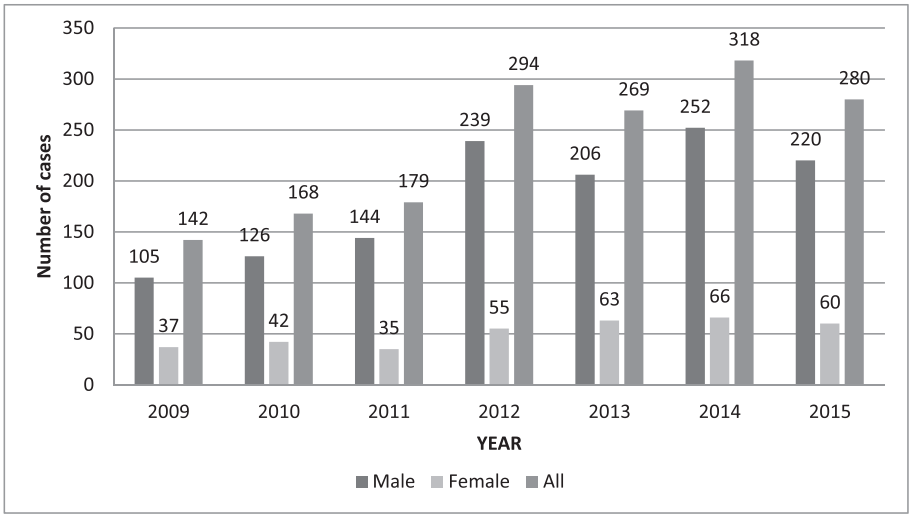

Figure 1 Number of methamphetamine-related deaths in Australia by gender, 2009–15. In 2015 there were a further 32 open cases coded in the National Coronial Information System (NCIS) as suspected methamphetamine-related

Table 1 Characteristics of methamphetamine-related fatalities in Australia, 2009–15.

	Males (n = 1292)	*Females (n = 357)*	*All cases (n = 1649)*
Crude mortality rate per 100 000 (CI)	1.62 (1.53–1.71)	0.44 (0.40–0.49)	1.03 (0.98–1.08)
Characteristics			
Age mean years	37.1	36.3	36.9
(SD, range)	(9.7,15–69)	(9.7, 14–65 years)	(9.7, 14–69 years)
Years of potential life lost (mean years)	42.9	47.7	43.9
(SD, range)	(9.7, 11–65 years)	(9.7, 19–70)	(9.9, 11–70 years)
Employment (%, *n*)			
Employed	35.6 (460)	26.3 (94)	33.6 (554)
Not employed	59.0 (762)	69.2 (247)	61.2 (1009)
Unknown	5.4 (70)	4.5 (16)	5.2 (86)
Married/*de-facto* relationship (%, *n*)			
Yes	26.6 (344)	37.3 (133)	28.9 (477)
No	68.3 (882)	60.2 (215)	66.5 (1097)
Unknown	5.1 (66)	2.5 (9)	4.5 (75)
History of injecting drug use (%, *n*)			
Yes	54.7 (707)	59.7 (213)	55.8 (920)
No	44.0 (568)	39.8 (142)	43.1 (710)
Unknown	1.3 (17)	0.6 (2)	1.2 (19)
Treatment status at death (%, *n*)			
Enrolled in treatment	7.6 (98)	10.7 (38)	8.2 (136)
Not enrolled	91.6 (1184)	88.8 (317)	91.0 (1501)
Unknown	0.8 (10)	0.6 (2)	0.7 (12)

CI = confidence interval; SD = standard deviation.

significantly higher among males in all study years (Fig. 2). At 2015, the rate was 1.8 (CI = 1.2–2.4) times that of 2009 (Fig. 2). Again, the 2015 rate is conservative, and the maximum estimate based upon closed and open cases is 1.30 per 100 000 (CI = 1.17–1.45) (males: 2.07 per 100 000, CI = 1.82–2.34; females: 0.55 per 100 000, CI = 0.43–0.69), 2.0 (CI = 1.4–2.6) times the 2009 rate.

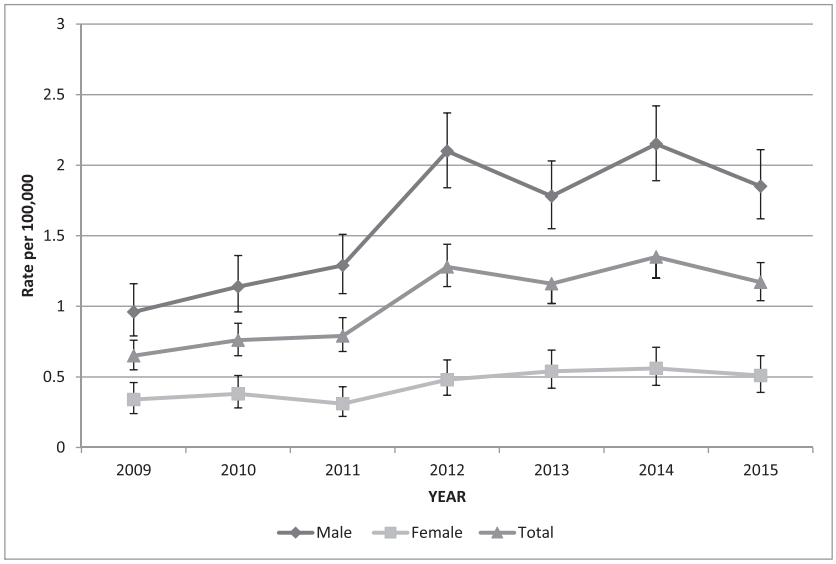

Figure 2 All cause methamphetamine-related population mortality rates per 100 000, by year (2009–15). In 2015 there were a further 32 open cases coded in the National Coronial Information System (NCIS) as suspected methamphetamine-related

Table 2 Manner and circumstances of death of methamphetamine-related fatalities in Australia, 2009–15.

	Males (n = 1292)	*Females (n = 357)*	*All cases (n = 1649)*
Circumstances of death (%, n)			
Accidental drug toxicity	40.7 (526)	52.1 (186)	43.2 (712)
Methamphetamine only	6.1 (79)	3.4 (12)	5.5 (91)
Multiple drugs	34.6 (447)	48.7(174)	37.7 (621)
Natural disease[a]	23.0 (297)	19.6 (70)	22.3 (367)
Coronary disease	18.0 (233)	11.8 (42)	16.7 (275)
Ichaemic heart disease	11.6 (150)	5.0 (18)	10.2 (168)
Cardiomegaly	2.7 (35)	1.4 (5)	2.4 (40)
Cardiomyopathy	1.9 (24)	1.4 (5)	1.8 (29)
Sudden cardiac arrythmia	1.2 (15)	2.5 (9)	1.5 (24)
Hypertensive heart disease	1.0 (13)	0.8 (3)	0.9 (16)
Other coronary disease	0.9 (11)	1.4 (5)	0.9 (16)
Intracranial haemorrhage	1.7 (22)	4.2 (15)	2.2 (37)
Ischaemic stroke	0.01 (1)	0.0 (0)	0.1 (1)
Kidney disease	0.6 (8)	0.6 (2)	0.6 (10)
Liver disease	0.5 (6)	1.1 (4)	0.6 (10)
Pulmonary thromboembolism	0.3 (4)	0.6 (2)	0.4 (6)
Other pulmonary disease	1.2 (16)	0.8 (3)	1.2 (19)
Other	1.6 (21)	1.1 (4)	1.5 (25)
Suicide	17.9 (231)	19.3 (69)	18.2 (300)
Violent means	15.6 (201)	15.4 (55)	15.5 (256)
Hanging	12.5 (162)	13.7 (49)	12.8 (211)
Exsanguination	1.0 (13)	0.6 (2)	0.9 (15)
Firearms	0.9 (11)	0.0 (0)	0.7 (11)
Other	1.2 (15)	1.2 (4)	1.2 (19)
Poisoning	2.3 (30)	3.9 (14)	2.7 (44)
Drug overdose	1.1 (14)	3.4 (12)	1.6 (26)
Carbon monoxide	1.2 (16)	0.6 (2)	1.1 (18)
Accident	16.8 (217)	7.8 (28)	14.9 (245)
MVA[b] (single vehicle)	6.3 (81)	2.5 (9)	5.5 (90)
MVA (multiple vehicles)	4.6 (60)	1.7 (6)	4.0 (66)
Drowning	1.4 (18)	2.5 (9)	1.6 (27)
Fall	1.1 (14)	0.6 (2)	1.0 (16)
Pedestrian	0.7 (9)	0.3 (1)	0.6 (10)
Other	2.7 (35)	0.3 (1)	2.2 (36)
Homicide	1.6 (21)	1.1 (4)	1.5 (25)
Stabbing	0.7 (9)	0.6 (2)	0.7 (11)
Firearms	0.7 (9)	0.0 (0)	0.5 (9)
Blunt force injury	0.2 (3)	0.6 (2)	0.3 (5)
Location and setting (%)			
Geographic location			
Metropolitan	59.0 (762)	60.2 (215)	59.2 (977)
Rural and regional	41.0 (530)	39.8 (142)	40.8 (672)
Setting			
Home environment	62.3 (805)	71.4 (255)	64.3 (1060)
Public location	26.4 (341)	12.6 (45)	23.4 (386)
Hospital	11.3 (146)	16.0 (57)	12.3 (203)

[a]Multiple diseases may be given in cause of death; [b]motor vehicle accident (MVA).

Demographic characteristics

The mean age of cases was in the mid-30s, and 78.4% were male (Table 1). A third were employed and a third were in married/*de-facto* relationships. Just over half had histories, or the cutaneous stigmata, of injecting drug use. Few were known to be enrolled in a drug treatment programme at the time of death.

Manner and circumstances of death

The most common manner of death was accidental drug toxicity (Table 2), which was attributed solely to methamphetamine toxicity in a minority of cases. Close to half of deaths occurred in locations outside major metropolitan regions, and the majority occurred in a home setting.

Death due primarily to natural disease in conjunction with methamphetamine toxicity was attributed in a fifth of cases. The most frequent natural disease was cardiac and/or cardiovascular disease, and ischaemic heart disease in particular. Among cases of death due to stroke, almost all were due to intracranial haemorrhage.

Almost a fifth died due to suicide, predominantly by violent means (most prominently hanging). The predominance of violent methods was seen among both genders. One in seven cases were due to accident, most commonly driver motor vehicle accident. Homicide, in which the person's consumption of methamphetamine was considered a mechanism relevant to their death, was the least frequent circumstance.

Toxicology

Full quantitative toxicology was available for 97.5% of cases (Table 3). Methamphetamine and/or its primary metabolite amphetamine was detected in all cases. Cases in which only methamphetamine was detected had a significantly higher blood methamphetamine concentration than other cases ($U = 136451.5$, $P < 0.001$). The median blood methamphetamine concentrations of groups varied within a narrow range, as did amphetamine concentrations.

In the majority of cases (82.8%), and across all groups, substances other than methamphetamine or amphetamine were detected, most frequently opioids and hypnosedatives. Psychostimulants other than methamphetamine were present in small proportions. Psychiatric medications were prominent, with a fifth having antidepressants detected, and an eighth antipsychotic medications.

DISCUSSION

The current study presents, to our knowledge, the largest case series of methamphetamine-related death reported to date. Consistent with estimates of use [5,6], there were large and significant increases in mortality rates, which doubled during the study period. This increase is consistent with increases of a similar magnitude observed in psychostimulant-related death in the United States in the first decade of the current century [44]. Cases were predominantly male and aged in their late 30s, with a significant proportion of older fatalities. The human cost of these deaths is illustrated by average of 44 years of potential life lost for each death, a figure similar to that reported for heroin [45]. Importantly, and again consistent with prior epidemiological findings, methamphetamine-related death was not restricted to major cities, with nearly half occurring in rural and regional locations. To place this in context, a third of the Australian population live outside the major capital cities [40]. Unlike fatalities related to drugs such as heroin, in which injecting drug use predominates overwhelmingly [46], half these cases had no evidence of drug injecting.

Consistent with earlier studies [7,9,27,32,35,44], the most common manner of death was accidental drug toxicity, most frequently involving multiple drugs. Polydrug use appeared to be associated with toxicity, with the blood methamphetamine concentration of methamphetamine-only cases twice that of other cases, a finding noted in one previous study [27]. The fact that there was little difference in methamphetamine concentrations across different manners of death is consistent with studies suggesting there is no obvious dose response [7,9,27,35]. As has been noted elsewhere [27], even modest amounts of methamphetamine may engender cardiac arrhythmia, and other drugs may influence this. In the case of polydrug toxicity, the effects of methamphetamine may increase the likelihood of death. Multiple stimulants will increase the overall burden upon the cardiovascular system. In the case of central nervous system depressants, such as the opioids and hypnosedatives, there is depressed respiration in the presence of a contiguous increase in myocardial oxygen demand associated with methamphetamine. In such a circumstance, the likelihood of cardiac arrhythmia is increased.

The prevalence of psychiatric medications is worthy of note. One in eight cases had antipsychotics in their blood at the time of death. Methamphetamine is associated with both the development and exacerbation of psychosis [23–25]. It would appear that there was a substantial level of psychosis among these cases, who continued to use methamphetamine to the point of death. Importantly, a fifth of cases had antidepressants in their blood, whose use with methamphetamine is contraindicated due to the risk of seizures and arrhythmias [37,38].

Cardiac and cardiovascular disease were prominent. There is a reflexive causality here. The hypertensive effect of methamphetamine places strain upon the cardiovascular system, and is a causal factor in the progressive and accelerated development of cardiac disease, coronary atherosclerosis and other vascular disease [13,15,17]. The use of methamphetamine in people with a compromised cardiovascular system then increases the likelihood of arrhythmia, myocardial infarction and death. In addition, the cases of intracranial haemorrhage are worthy of note. This may reflect a number of causes.

Table 3 Psychoactive blood toxicology of methamphetamine-related deaths in Australia 2009–15, by circumstance of death.

	Accidental drug toxicity (n = 697)	*Natural disease (n = 349)*	*Accident (n = 240)*	*Suicide (n = 297)*	*Homicide (n = 24)*	*All cases (n = 1607)*
Methamphetamine present (%, *n*)	96.7 (675)	98.0 (342)	97.5 (234)	97.3 (289)	95.8 (23)	97.2 (1653)
Methamphetamine concentration	0.15	0.20	0.20	0.15	0.17	0.17
Median (mg/l) (IQR, range)	(0.04–0.40, 0.00–22.00)	(0.07–0.44, 0.00–12.00)	(0.07–0.58, 0.00–5.70)	(0.05–0.38, 0.00–24.00)	(0.04–0.66, 0.00–8.7)	(0.05–0.43, 0.00–24.00)
Amphetamine present (%, *n*)	78.9 (551)	76.2 (266)	80.8 (194)	84.8 (252)	79.2 (19)	79.7 (1282)
Amphetamine concentration	0.03	0.02	0.03	0.03	0.03	0.03
Median (mg/l) (IQR, range)	(0.01–0.06,0.00–1.50)	(0.01–0.05,0.00–0.40)	(0.01–0.08,0.00–2.60)	(0.01–0.06,0.00–0.80)	(0.01–0.08,0.00–0.90)	(0.01–0.06, 0.00–2.60)
Methamphetamine only (%)	6.6 (47)	29.9 (104)	27.3 (65)	19.0 (57)	12.5 (3)	17.2 (276)
Methamphetamine concentration	0.30	0.28	0.36	0.26	0.40	0.30
Median (mg/l) (IQR, range)	(0.08–0.75,0.02–0.22)	(0.12–0.60,0.00–10.00)	(0.15–0.90,0.00–3.70)	(0.06–0.53,0.01–24.00)	(0.05–0.99)[a]	(0.11–0.70, 0.00–24.00)
Methamphetamine only	0.14	0.16	0.18	0.14	0.16	0.15
Other drugs present	(0.04–0.40, 0.00–20.00	(0.06–0.37, 0.00–12.00)	(0.05–0.44,0.00–5.70)	(0.05–0.34,0.00–6.00	(0.03-0.52,0.00–8.70)	(0.05–0.40, 0.00–20.00)
Other psychostimulants (%, *n*)	6.9 (48)	3.7 (13)	5.4 (13)	5.4 (16)	25.0 (6)	6.0 (96)
Cocaine	3.5 (25)	2.6 (9)	0.4 (1)	1.3 (4)	12.5 (3)	2.6 (42)
MDMA	4.0 (28)	1.4 (5)	5.0 (12)	4.7 (14)	12.5 (3)	3.9 (62)
MDA	2.6 (18)	0.9 (3)	2.5 (6)	0.7 (2)	0.0 (0)	1.8 (29)
Hypnosedatives (%, *n*)	56.2 (392)	25.2 (88)	21.7 (52)	23.6 (70)	37.5 (9)	38.0 (611)
Diazepam	45.9 (320)	19.5 (68)	13.8 (33)	18.2 (54)	33.3 (8)	30.1 (483)
Temazepam	16.1 (112)	6.3 (22)	5.8 (14)	8.1 (24)	8.3 (2)	10.8 (174)
Alprazolam	17.6 (123)	4.9 (17)	8.3 (20)	6.1 (18)	12.5 (3)	11.3 (181)
Oxazepam	15.9 (111)	5.4 (19)	4.6 (11)	6.1 (19)	4.2 (1)	10.0 (161)
Clonazepam	4.9 (34)	1.4 (5)	2.1 (5)	0.3 (1)	0.0 (0)	2.8 (45)
Nitrazepam	2.4 (17)	0.3 (1)	0.8 (2)	0.0 (0)	0.0 (0)	1.2 (20)
Flunitrazepam	0.6 (4)	0.0 (0)	0.0 (0)	0.3 (1)	0.0 (0)	0.3 (5)
Pregabalin	0.6 (4)	0.6 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (6)
Zolpidem	0.6 (4)	0.0 (0)	0.4 (1)	0.3 (1)	0.0 (0)	0.4 (6)
Alcohol (%, *n*)	20.7 (144)	13.5 (47)	33.8 (81)	38.0 (113)	37.5 (9)	24.5 (394)

(*Continues*)

Table 3. (Continued)

	Accidental drug toxicity (n = 697)	*Natural disease (n = 349)*	*Accident (n = 240)*	*Suicide (n = 297)*	*Homicide (n = 24)*	*All cases (n = 1607)*
Opioids (%, *n*)	72.6 (506)	30.7 (107)	16.7 (40)	12.1 (36)	16.7 (4)	43.1 (693)
Morphine	47.1 (321)	15.8 (55)	8.3 (20)	5.7 (17)	0.0 (0)	25.7 (413)
Methadone	18.4 (128)	9.5 (33)	5.8 (14)	3.7 (11)	8.3 (3)	11.8 (189)
Oxycodone	9.3 (65)	4.3 (15)	3.7 (9)	3.0 (9)	4.2 (1)	6.2 (99)
Fentanyl	8.2 (57)	2.9 (10)	0.4 (1)	0.0 (0)	0.0 (0)	4.2 (68)
Tramadol	5.0 (35)	3.4 (12)	1.2 (3)	1.7 (5)	0.0 (0)	3.4 (55)
Δ^9 THC (%, *n*)	20.8 (145)	28.1 (98)	33.8 (81)	28.6 (85)	41.7 (10)	26.1 (419)
Antidepressants (%, *n*)	28.1 (196)	15.2 (53)	5.1 (12)	19.5 (58)	29.2 (7)	20.3 (326)
SSRIs[b]	12.1 (84)	4.3 (15)	1.7 (4)	7.7 (23)	8.3 (2)	8.0 (128)
Tricyclics	8.8 (61)	4.3 (15)	1.3 (3)	2.7 (8)	8.3 (2)	5.5 (89)
Tetracyclics	5.3 (37)	4.0 (13)	2.1 (5)	4.3 (13)	12.5 (3)	4.4 (71)
SNRIs[b]	4.4 (31)	4.3 (15)	0.8 (2)	5.0 (15)	0.0 (0)	3.9 (63)
MAOIs[b]	0.0 (0)	0.0 (0)	0.0 (0)	1.0 (3)	0.0 (0)	1.9 (3)
Antipsychotics (%, *n*)	18.1 (126)	9.7 (34)	2.5 (6)	8.4 (25)	12.5 (3)	12.1 (194)

Interquartile range (IQR). [a]No IQR calculated, $n = 3$. [b]SSRIs = selective serotonin re-uptake inhibitors; SNRIs = serotonin and noradrenaline re-uptake inhibitors; MAOIs = monoamine oxidase inhibitors; MDA = 3,4-methylenedioxyamphetamine; MDMA = 3,4-methylenedioxymethamphetamine; THC = tetrahydrocannabinol.

Hypertension from methamphetamine use places strain upon the cerebrovascular system, increasing the likelihood of vessel wall damage and rupture. Moreover, if there is a pre-existing aneurysm, there is an existing weakness in the vessel wall. There is also evidence that methamphetamine directly affects the integrity of vasculature, predisposing to aneurysm and vessel rupture [47].

An outstanding feature of this study was the data on suicide. Studies among general populations, and indeed of drug users, show consistently that males predominately use violent means, and females self-poisoning [48,49]. In this series, however, violent means were the main methods used by both genders. The reason for this pattern is unclear, but the aggression and disinhibition associated with methamphetamine intoxication may be involved.

Deaths from accident were common, as has been reported previously [7,9,27,34,35], and were dominated by motor vehicle accidents. The majority of these were single-vehicle accidents. In cases where other cars were involved the decedent was typically driving erratically, and frequently on the wrong side of the road. Several factors may be involved here, including disinhibition and, possibly, falling asleep after a methamphetamine binge. In contrast, homicides represented a surprisingly small proportion of cases.

The study has clinical and public health implications. Few cases were in treatment at the time of their death. Increasing the number of users in treatment appears to be a priority. These cases were not a young, inexperienced group, and had an average age older than the average for treatment entrants to methamphetamine dependence [8]. While there are no proven pharmacotherapies for methamphetamine dependence [50], long-term residential rehabilitation has been shown to reduce methamphetamine use and harm [8]. Health professionals also need to be aware of the prominent role of suicide. For clinicians treating methamphetamine users, suicide histories should be taken, and regular risk monitoring for ideation and suicide planning appear prudent. While much public attention is focused upon violence, the role of disease is given less attention. Heart disease, in particular, is a major factor in methamphetamine death, and users may be unaware of this, or of the risk of intracranial haemorrhage. Moreover, such pathologies develop regardless of the route of administration. More focused attention on the role of methamphetamine in causing such pathology appears warranted. Finally, polydrug use was a prominent feature. Methamphetamine users, and medical practitioners, need to be aware of the risks of combining methamphetamine with other substances, including prescription drugs. While changing drug use patterns may be difficult, a knowledge of the dangers is imperative. Moreover, the risks of combining methamphetamine with substances that might appear to have no implications for toxicity, such as respiratory depressants, is crucial.

As in all studies, caveats must be borne in mind. Cases were restricted to those in which the person's own recent methamphetamine use was contributory to death. As such, the study does not measure the impact of methamphetamine use upon the deaths of others, such as fatalities caused by a methamphetamine-affected driver or assailant. Similarly, as a study of recent methamphetamine use and death, cases where historical methamphetamine use may have caused long-term health effects that eventually result in death (e.g. cardiovascular disease) are not included, and may not come to the attention of a coroner. Background data on cases was restricted to that provided in the cases files. It should also be noted that in all studies of mortality, suicidal intent is problematic. In this study, suicide intent was based upon the NCIS code for 'Intentional Self-harm', which derives from the case circumstances (e.g. note, verbal intent) and the conclusions of the coroner.

In summary, national methamphetamine mortality rates doubled during a period of 7 years. While toxicity was the most frequent cause, natural disease, suicide and accident together contributed to more than half of deaths. Methamphetamine is a major public health problem of increasing significance, of which death represents the most severe end.

Declaration of interests

None.

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