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Characteristics and circumstances of volatile solvent misuse-related death in Australia, 2000–2021

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ABSTRACT

Introduction: Volatile solvent misuse-related death is associated with neuropsychiatric, cardiovascular, respiratory and renal pathology, as well as sudden death. The study aimed to determine: (1) the circumstances of death and case characteristics of volatile solvent misuse-related death in Australia, 2000–2021; (2) the toxicological profile of cases; and (3) the major autopsy findings.

Methods: Retrospective study of volatile solvent misuse-related death in Australia, 2000–2021 retrieved from the National Coronial Information System.

Findings: One hundred and sixty-four cases were identified, 79.9% male, mean age 26.5 years (8.5% aged 40 years or older). Circumstances of death were unintentional toxicity (61.0%), unintentional asphyxia (20.1%), intentional self-harm (12.2%) and traumatic accident (6.7%). The most commonly reported acute presentation prior to death was sudden collapse (22 of 47 witnessed events). The most frequently used solvents at the fatal incident were gas fuels (35.4%), gasoline (petrol) (19.5%) adhesives/paints (19.5%), aerosol propellants (12.8%), and volatile anaesthetics (12.8%). The most commonly detected volatile substances were butane (40.7%), toluene (29.6%), and propane (25.9%). Cannabis was present in 27.6% and alcohol in 24.6%. The prevalence of acute pneumonia amongst autopsied cases was low (5.8%) which, together with reports of sudden collapse, suggests that in many cases, death was extremely rapid. There were low levels of major organ pathology.

Conclusions: While the average age of volatile solvent misuse-related death was in the mid-twenties, a substantial proportion occurred amongst people aged 40 years or older. Reflecting availability, gas fuels predominated. In many cases, death appeared to have been rapid.

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Introduction

Volatile solvent misuse is a frequently observed form of substance use, with a recognised diagnosis of Inhalant Use Disorder [1]. The term covers the inhalation of substances that vaporise at room temperature for the purpose of intoxication or sexual experience enhancement [1,2]. While there is a wide range of such solvents, they may be broadly categorised as gas fuels (e.g., cigarette lighter cannisters, gas bottles), gasoline (petrol), aerosol propellants (e.g., air fresheners, deodorant spray), solvents from adhesives and paints (e.g., glue, spray paints), volatile anaesthetics (e.g., nitrous oxide), and nitrites (e.g., amyl nitrite) [2]. These solvents have industrial and domestic uses independent of their psychotropic properties. They may be inhaled directly from gas cannisters, from plastic bags or balloons in which a volatile solvent has been inserted, and from cans into which volatiles such as gasoline have been poured. In the case of nitrous oxide, two-gram cannisters used in whipped cream dispensers are frequently inhaled [3,4]. Recently, there has been concern about the increasing availability of large cannisters (e.g., 1–3 kilograms) of nitrous oxide, and the concomitant increased risk involved [4].

The misuse of volatile substances is associated with a wide range of harms. Neuropsychiatric harms across the range of volatile solvents include cerebral and cerebellar white matter atrophy, cerebral oedema, in addition to intense agitation and an acute psychosis that may increase the acute risk of self-harm or traumatic injury [2,5,6]. Unlike other volatile solvents, nitrous oxide is causally associated with myeloneuropathy and spinal cord degeneration due to interference in the metabolism of vitamin B₁₂ [2,4,5,7,8]. Cardiovascular harms include cardiac dysrhythmias and cardiomyopathy [9–12]. Acute respiratory arrest has been documented [13,14], as well as kidney disease and kidney failure [2,15]. Hydrocarbons have also been associated with “sudden sniffing death”, a syndrome characterised by sudden collapse shortly after inhalation, due to cardiac and/or respiratory arrest [2,16,17]. Methaemoglobinaemia has rarely been implicated in deaths where amyl nitrite and similar volatiles have been consumed [18].

Deaths due to volatile solvent misuse have been documented for butane [16,19–28], isobutane [17], propane [20,21,24–26,28], toluene [14,29–33], 1,1 – difluoroethane [33–37], gasoline [27,33], nitrous oxide [5,38–40] and nitrites

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[40]. The major causes of death in these cases have been asphyxia, respiratory arrest, cardiac arrest, suicide, and traumatic injury. Cases predominantly involved males in their twenties [20,40–42]. There are, however, a notable proportion of cases involving individuals aged 40 years or older. Indeed, in the UK, the mean age at death has risen from 28 to 46 years over the past two decades [40].

To date, the vast majority of the literature on volatile substance misuse-related death consists of case reports or epidemiological data. The current study aims to characterise volatile solvent misuse-related deaths in a national case series covering two decades. Specifically, the study aimed to determine:

1. The circumstances of death and case characteristics of volatile solvent misuse-related death in Australia, 2000–2021
2. The toxicological profile of cases, and
3. The major autopsy findings concerning neurological, cardiovascular, respiratory and renal pathology.

Methods

National coronial information system

The National Coronial Information System is a database of medicolegal death investigation records provided by the coroners' courts in each Australian and New Zealand jurisdiction, commencing in July 2000 for Australia (January 2001 for Queensland) and July 2007 for New Zealand. Only Australian cases were accessed in this study. A complete National Coronial Information System case file includes demographic information, a police narrative of circumstances, autopsy reports, toxicology reports and the coronial finding. Autopsy and toxicology reports are included where these procedures were undertaken. Cause of death is ascertained by a forensic pathologist and documented on the autopsy and coroner's report. The forensic pathologist may report on: (1) the direct cause of death, (2) the antecedent cause, and (3) other significant conditions associated with the death. This advice is provided to the coroner, who makes a formal determination of cause of death based on the medical and other information.

Case identification

All closed cases (i.e., the coronial investigation had been completed) of volatile solvent misuse-related death aged ≥ 15 years at the time of death occurring between 1 July 2000 and 31 December 2021 were retrieved and inspected by the authors. Searches were conducted using the National Coronial Information System "Other non-pharmaceutical chemical substance" coding fields set contributory to death for "Fuel or solvent", "Glue or adhesive", "Paint, coating or stripping agents", and "Cleaning agents". In addition, the National Coronial Information System Drug coding fields set of "Pharmaceutical substance for human use" contributory to death were searched for "Nitrous oxide". Text searches for amyl nitrite and alkyl nitrite were also conducted. Final searches were conducted in October 2022. Intentional self-

harm was determined by the National Coronial Information System "Intentional self-harm" intent designation code. The identification of the incriminating volatile substances was determined by the coroner from toxicology and/or crime scene evidence.

Data on clinical characteristics, circumstances of death and toxicology were retrieved from police narratives, autopsy reports, toxicology reports, and coronial findings. All National Coronial Information System cases record the findings concerning the direct cause of death, the antecedent cause, and other significant conditions associated with the death. Ethical approval for the study was received from the Justice Human Research Ethics Committee, Western Australia Coronial Ethics Committee and University of New South Wales Human Research Ethics Committee.

Measures

Information was collected on demographics (age, sex, employment, marital status), mental health history (mention of a history of problems and/or treatment), drug use history (mention of a history of substance use problems, drug treatment enrolment, previous medical intervention for volatile solvent misuse-related incident), history of injection drug use (mention of a history and/or stigmata of injection observed at autopsy), circumstances of volatile substance misuse (using solvents alone or with others, used for sexual enhancement), suicidal intent, location (private enclosed setting/public setting) and medical intervention (ambulance attendance and/or hospitalisation). Manner of death was classified as: (1) unintentional drug toxicity, (2) unintentional asphyxia, (3) intentional self-harm, and (4) traumatic accident.

Toxicological testing was conducted according to local protocols. In all cases of suspected drug toxicity, toxicology was conducted for drug identification and quantitation. In seven cases of hospitalisation prior to death, antemortem blood samples taken on or near admission to the hospital were reported, and drugs administered by medical staff were excluded. Detection of volatile solvents were tested by their presence in blood, lung tissue, liver tissue, brain tissue or body fat. Results from blood toxicology samples were reported for, alcohol, antidepressants, antipsychotics, cannabis, cocaine, gabapentinoids, gamma hydroxybutyrate (GHB), hallucinogens, hypnotosedatives (benzodiazepines, z-class hypnotics, barbiturates), ketamine, opioids, psychostimulants and synthetic cannabinoid receptor agonists. All samples were tested using a range of methodologies specific to that laboratory, including immunoassay, gas chromatography, high-performance liquid chromatography (HPLC) and liquid chromatography-quadrupole time-of-flight mass spectrometry (LC-QTOF-MS) for common drugs of abuse and selected therapeutic substances. While the time between sampling and testing was not known, all specimens were preserved and stored at 4 °C prior to testing.

The majority of cases underwent a standardised forensic autopsy, with an examination of major organs and quantitative toxicological analysis. Cardiomegaly was diagnosed by heart weight exceeding the 95th percentile of normal weight

ranges relative to body weight [43,44]. Severe coronary artery atherosclerosis was defined as $\geq 75\%$ cross-sectional area stenosis or recorded as present by the autopsy pathologist.

Statistics

Means, standard deviations and ranges were presented, as medians for skewed distributions. For low-frequency cells where case identification may pose a risk, the frequency was reported as $n < 5$. All such analyses were conducted using IBM SPSS Statistics v.27.0 [45].

Results

Case characteristics

A total of 164 cases were identified, predominantly involving males (Table 1). While the mean age was 26.5 years (standard deviation 9.7, range 15–64 years), there was a notable proportion of cases (8.5%) aged 40 years or older. A majority (62.2%) were unemployed, and few were in a married/de facto relationship (9.1%) or enrolled in a drug treatment program (<5). A majority (60.4%) had a documented history of substance use problems, but a history of injection drug use was infrequent (12.8%). Mental health problems were noted

Table 1. Demographic characteristics and circumstances of death in 164 cases of volatile solvent misuse-related fatalities in Australia, 2000–2021.

	Number (%)
Sex	
Male	131 (79.9)
Female	33 (20.1)
Age ranges	
15–19 years	46 (28.0)
20–29 years	62 (37.8)
30–39 years	42 (25.6)
≥ 40 years	14 (8.5)
Employment status	
Unemployed	102 (62.2)
Employed	36 (22.0)
Student	20 (12.2)
Retired/pensioner	6 (3.7)
Married/de facto relationship	15 (9.1)
Enrolled in drug treatment program	<5
Documented history of:	
Substance use problems	99 (60.4)
Injection drug use	21 (12.8)
Mental health problems	45 (27.4)
Affective disorders	37 (22.6)
Psychotic illness	9 (5.5)
Previous medical intervention for volatile substance misuse-related incident	11 (6.7)
Circumstance of death	
Unintentional toxicity	100 (61.0)
Unintentional asphyxia	33 (20.1)
Intentional self-harm (all cases)	20 (12.2)
Drug toxicity	7 (4.3)
Physical means	13 (7.9)
Traumatic accident	11 (6.7)
Location of fatal incident	
Private enclosed setting (e.g., private home, private hotel room)	126 (76.8)
Public location (e.g., park, car on street)	38 (23.2)
Social setting of use	
Only person using solvents	129 (78.7)
Using solvents with others	35 (21.3)
Sexual enhancement	6 (3.7)
Medical intervention (e.g., ambulance)	27 (16.5)

in 45 cases (27.4%), mainly affective disorders (22.6%). In 11 cases (6.7%), there was documentation of a previous medical intervention for a volatile substance misuse-related incident.

Circumstances of death

The most frequent cause of death was unintentional toxicity (61.0%) (Table 1). In 33 cases (20.1%), death was due to unintentional asphyxia caused by volatile solvent administration. There were 20 cases of suicide, mostly using physical means. The most common traumatic accident was motor vehicle accidents ($n = 6$).

The fatal incidents mostly occurred in a private setting (76.8%) and the person was often the only one using solvents (78.7%). In six cases (3.7%), solvents were being used for sexual experience enhancement. In fewer than a fifth, there was medical intervention prior to death.

In 47 cases (28.7%), there were witnesses to the fatal incident. The most commonly reported acute presentations prior to death were sudden collapse ($n = 22$), intense agitation ($n = 15$), seizure ($n = 6$) and vomiting ($n = 4$).

Types of volatile solvents used in the fatal incident

By far the most frequently used volatile solvents at the fatal incident (Table 2) were gas fuels (35.4%), followed by liquid fuels (e.g. gasoline) (19.5%) and adhesives/paints (19.5%). Of the 21 cases where death was due to volatile anaesthetics, 20 (95.3%) involved nitrous oxide. There were no cases of death due to nitrites.

Toxicology

Toxicology was conducted in all cases but was available for inspection for 134 (81.7%) (Table 3). Of these cases, 128 had blood samples taken from peripheral sites and six from central sites. Toxicological analysis for volatile solvents was conducted and available for 108 cases, with no methods available to detect the solvent implicated in 26 cases. Reflecting the pre-eminence of gas fuels, butane was the most commonly detected volatile solvent (38.9%), with other gas fuels also being common. Toluene, most commonly from adhesives and paints, was the next most common (29.6%). Nitrous oxide was detected in blood samples in only five cases. The low incidence reflects the fact that, in 15 of the 20 nitrous oxide cases, the relevant laboratory at the time could not test for the drug.

Table 2. Types of volatile solvents involved among 164 cases of volatile solvent misuse-related fatalities in Australia, 2000–2021.

	Number (%)
Gas fuels (e.g., disposable cigarette lighter cannisters, gas bottles)	58 (35.4)
Liquid fuels (gasoline)	32 (19.5)
Adhesives and paints (e.g., glue, spray paints, paint thinners)	32 (19.5)
Aerosol propellants (e.g., air fresheners, deodorant spray, hair spray)	21 (12.8)
Volatile anaesthetics (nitrous oxide, isoflurane)	21 (12.8)
Nitrites (alkyl nitrite, amyl nitrite)	0 (0.0)

Table 3. Toxicology of volatile solvent misuse-related fatalities in Australia, 2000–2021.

	Number (%)
Volatile solvents (n = 108) [#]	
Butane	42 (38.9)
Toluene	32 (29.6)
Propane	27 (25.0)
Isobutane	20 (18.5)
Gasoline	16 (14.8)
Xylenes	10 (9.3)
Benzene	6 (5.6)
Nitrous oxide	5 (4.6)
Trichloroethylene	1 (0.9)
1,1 – difluoroethane	1 (0.9)
Drugs other than volatile solvents (n = 134)	
Any drugs detected	81 (60.4)
Cannabis	37 (27.6)
Alcohol	33 (24.6)
Opioids (any)	21 (15.7)
Methadone	10 (7.5)
Morphine	8 (6.0)
Codeine	4 (3.0)
Fentanyl	0 (0.0)
Other opioids (dextromethorphan, pethidine, pholcodine, propoxyphene, tramadol)	4 (3.0)
Hypnosedatives	19 (14.2)
Benzodiazepine	18 (13.4)
Barbiturates	1 (0.7)
Antidepressants	17 (12.7)
Psychostimulants (any)	13 (9.7)
Metamphetamine	9 (6.7)
3,4-Methylenedioxyamphetamine (MDMA)	4 (3.0)
Antipsychotics	88 (6.0)
Hallucinogens (psilocin*)	1 (0.7)

[#]Major ingredients detected by type of volatile solvent used at the fatal incident: Gas fuels (butane, benzene, isobutane, propane, toluene, xylene), Liquid fuels (benzene, isobutane, gasoline, toluene, xylene), Adhesives and paints (benzene, butane, toluene, trichloroethylene, xylene), Aerosol propellants (butane, 1,1 – difluoroethane, propane, toluene), Volatile anaesthetics (nitrous oxide). Ingredients may be present in cases across more than one volatile solvent.

*Metabolite of psilocybine.

Other than volatile solvents, cannabis, alcohol and other substances were present in 60.4% (Table 3). The most commonly observed drugs were cannabis (median 0.009 mg/L, range 0.001–0.211 mg/L) and alcohol (median 0.042 g/100 mL, range 0.008–0.234 g/100 mL). Opioids were the third most common group, with methadone (median 0.85 mg/L, range 0.09–4.40 mg/L) and morphine (median free 0.08 mg/L, range 0.00–0.50 mg/L, median total 0.10 mg/L, range 0.00–1.10 mg/L) being the most frequent. In two cases, the presence of morphine appeared to be due to the recent heroin administration. Psychostimulants, mainly metamfetamine, were present in 9.7% of cases (median 0.15 mg/L, range 0.02–0.15 mg/L).

Major autopsy findings

Autopsy findings were available for inspection in 104 cases. The diagnoses included pulmonary oedema (70.2%), aspiration of vomit (15.4%), cerebral oedema (10.6%), cardiomegaly (9.6%), acute pneumonia (5.8%), cerebral atrophy (2.9%), acute kidney failure (1.9%) and dilated cardiomyopathy (1.0%). Pneumonia due to aspiration was diagnosed in four deaths (8.7%) attributed to volatile solvent toxicity but was present in no case of death due to asphyxia. Other cardiovascular pathologies, renal pathologies and hepatic

pathologies were seen in fewer than five cases. In no case was spinal cord degeneration diagnosed.

Discussion

A number of major findings emerged from this case series. The first concerns the age of the decedents. While the mean age was in the mid-twenties, which is consistent with earlier reports [20,40–42], the proportion of cases involving older subjects was notable, extending into the fifties. Indeed as noted earlier, in the UK, the mean age at volatile substance misuse-related death has risen from the mid-twenties to the mid-forties [40]. It is not clear if cases involving older subjects had a history of use or if they had more recently initiated use.

Gas fuels predominated, but liquid fuels (e.g. gasoline) and adhesives/paints were common, and together constituted 74.4% of cases. The toxicology was consistent with these patterns, with butane, toluene, and propane being the solvents most commonly detected. Solvents such as butane, petroleum, and glue are all readily available, and these findings may reflect use patterns among people who misuse volatile solvents. While there has been legitimate concern about nitrous oxide [4], such cases constituted a relatively small proportion of this series. Why this is the case is unclear, but could be due to wider use of substances such as butane, or the relative recency of widespread nitrous oxide use. Similarly, nitrite inhalation, although capable of causing methaemoglobinaemia, was not identified as a cause of death. Other substances were present in just over half of the cases, mainly cannabis and alcohol.

The most common cause of death was unintentional toxicity (61.0%), most likely causing sudden cardiac and/or respiratory arrest, after solvent use. Unintentional asphyxia was the cause of death in 20.1% of cases, whether due to inhalation of non-respirable gas or plastic bag asphyxia (in which the decedent lost consciousness with a plastic bag used to inhale gas covering their mouth and nose). Consistent with previous reports [2,20,40–42], cases of suicide, traumatic injury, and neurological damage also occurred. Most suicides involved physical means, mainly hanging. In all deaths due to suicide or traumatic injury, there was evidence of solvent use immediately preceding the fatal incident.

Reflecting the fact that in most instances the decedent was using solvents alone, witnesses were present in a minority of cases. There was evidence, however, to suggest that “sudden sniffing death” (characterised by sudden collapse) [2,16,17], occurred in a substantial proportion of cases. A sudden collapse of the decedent after use was the most common witness report. Moreover, there was a low prevalence of aspiration pneumonia and other forms of pneumonia amongst autopsied cases (5.8%). Given that pneumonia takes time to develop after aspiration of gastric contents, and prolonged inertia also increases risk, it is more likely to be seen in cases with a longer survival time. By comparison, amongst heroin overdose cases, a third of those who survived longer than 20 min were diagnosed with pneumonia, as were a fifth of rapid deaths [46]. The low incidence of

pneumonia in this series, together with reports of sudden collapse, suggests that in many cases, death was rapid.

There was little evidence of major disease processes among decedents. Notably, there was no report of spinal cord degeneration. The cases in which cerebral oedema or acute kidney failure were diagnosed are consistent with the known acute effects of volatile solvents [2,15]. The only cardiovascular pathology of note was that ten individuals had cardiomegaly, which may have increased the risk of a dysrhythmia in the presence of volatile solvents. Again, these findings stand in contrast to the high levels of major organ pathology seen amongst cases of death due to other drugs of abuse, including heroin, metamfetamine and cocaine [47].

Given their ubiquity, what can be done to reduce the morbidity and mortality associated with volatile substance misuse? Education on the harms that these products may cause appears essential. It is unlikely that many people who use volatile solvents are aware of risks such as spinal cord degeneration or “sudden sniffing death” [48,49]. An education campaign on the harms of household products for parents and teachers was associated with a sustained reduction in volatile solvent misuse-related deaths [41]. In relation to such an approach, the 20 cases involving students are noteworthy. Given the age range associated with these cases, ways must be found to address awareness among relatively older people (aged 40 years or older) of the dangers associated with using what might be seen as harmless commercial products. Moreover, there needs to be recognition that in cases of sudden collapse, medical attention is imperative. Working with retailers to restrict access, while difficult, should be considered, along with manufacturers on responsible product design and warning labels [49]. Given the harms associated with the misuse of larger canisters of nitrous oxide, the concerns expressed in Europe about the increased availability of two-kilogram tanks is a case in point. Attention to reducing the intoxication capacity of volatile solvents appears warranted, such as the development of low aromatic fuels [50]. Finally, in order to accurately diagnose cases, forensic laboratories need to have the capacity to test for volatile solvents.

As in all studies, caveats must be borne in mind. By necessity this series comprised closed cases, so cases in which investigations were still being undertaken were not available for inspection. In addition, cases were restricted to decedents aged 15 years or older. Also, volatile solvents are not routinely screened for in cases of sudden or unnatural death that come to the attention of a coroner, unless there is reason to suspect their use. As such, this series may be conservative, and other cases may not have been captured in the coronial process. Details of decedent histories, acute clinical characteristics and circumstances of death were by necessity restricted to those contained in case files. While toxicology was conducted in all cases, the report was unavailable for inspection in 30 cases. Postmortem blood samples were taken peripherally in 128 cases, and centrally in six. Peripheral sampling is known to minimise the effects of postmortem redistribution and is considered best practice

sampling in most medicolegal autopsy facilities in Australia. Detailed postmortem redistribution characteristics of the various volatile solvents detected in this series of cases are not known. Moreover, in some cases, there were no methods available to detect the solvent implicated at the death scene. As is typical of drug-related death, multiple substances were present in the majority of cases. It is thus not possible to determine the exact relative contributions of various substances to individual deaths. Finally, autopsies were not always conducted, or not all reports were available for inspection.

In summary, while the average age of volatile substance misuse-related death was in the mid-twenties, a substantial proportion occurred amongst people aged 40 years or older. Reflecting availability, gas fuels predominated. In many cases, death appears to have been rapid.

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