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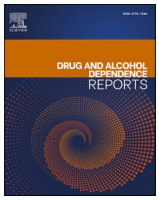

Differences in heroin overdose deaths in Australia by age, 2020-2022: Disease and estimated survival times

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HIGHLIGHTS

- Older cases were more likely die due to combined drug toxicity/disease.
- Older cases were more likely to have chronic pain.
- Older cases were more likely to have evidence of a sudden collapse.
- Older cases appared to have shorter survival times.
- Older cases had more extensive heart, lung, and liver disease.

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ABSTRACT

Background: The age of people who use illicit opioids has increased, with a clinical picture of accelerated ageing. The study aimed to determine, stratified by age: 1. The circumstances and characteristics of heroin-related toxicity deaths in Australia, 2020–2022; 2. The toxicological profile and autopsy findings; 3. The proportion of cases in which blood 6-acetyl morphine (6AM) was detected, as a measure of survival time.
Methods: Retrospective study of 610 cases of fatal heroin-related drug toxicity in Australia, 2020–2022. Cases were stratified as: <30 years, 30–39 years, 40–49 years, ≥50 years.
Results: Compared to the youngest group, those aged ≥50 years were more likely to have a history of chronic pain (12.4 v 3.3 %), to have their death attributed to combined drug toxicity/disease (20.1 v 3.3 %), and to have evidence of a sudden collapse (21.3 v 11.1 %). There were no differences in free morphine concentrations or glucuronide concentrations. Compared to the youngest group, however, the two older groups were significantly more likely to have 6AM present in blood, a proxy measure of a shorter survival time (52.0, 55.2 v 34.5 %). Compared to the youngest group, cases aged ≥50 years were more likely to be diagnosed with cardiomegaly (44.0 v 16.7 %), coronary artery disease (46.0 v 15.0 %), emphysema (35.0 v 5.1 %), hepatic steatosis (15.4 v 3.4 %), hepatic fibrosis (17.6 v 3.4 %), and cirrhosis (19.8 v 0.0 %).
Conclusions: Older cases of heroin overdose had more extensive heart, lung, and liver disease, and appeared more likely to have shorter survival times.

1. Introduction

Mortality among people who use heroin is 15 times the rate of the general population, which is reflected in an estimated 40 years of potential life lost (Darke et al., 2016; Degenhardt et al., 2019; Larney et al., 2020; Santo et al., 2021). The leading causes of this excess mortality are overdose and disease (Darke et al., 2016; Degenhardt et al., 2019; Larney et al., 2020; Santo et al., 2021). It is well established that people who use heroin are in poorer health than the general population (Clausen et al., 2009; Darke et al., 2009; Han et al., 2022; Hser et al., 2004; Lofwall et al., 2005; Reece, 2007, 2012; Reece and Hulse, 2014; Torres et al., 2011; Van Santen et al., 2018). Moreover, older people who use heroin are in poorer health than their younger counterparts, and the gap with the general population appears to widen with age. Pulmonary,

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cardiovascular, hepatic and renal disease are particularly notable, and the general pattern appears to be one of accelerated ageing (Bachi et al., 2017; Reece, 2012). In relation to this, it should be noted that more than 90 % of people who use heroin smoke tobacco (Guydish et al., 2016). Accelerated ageing is of particular relevance, since a defining characteristic of opioid dependence is its chronicity (Hser et al., 2007; Marel et al., 2023), and because the average age of people who use illicit opioids has increased across the past few decades (Bird and Robertson, 2020; Lewer et al., 2022b; Lynch et al., 2021).

There are reasons to suspect that systemic disease may play a significant role in overdose, particularly in older people who use heroin. Opioids are central nervous system depressants, and the mechanism of overdose is respiratory depression (Baselt, 2020). Death is usually due to respiratory failure, although cardiac arrest may occur secondary to myocardial oxygen deprivation (Baselt, 2020; Karch, 2015). Opioids are also emetics and cough suppressants, and aspiration pneumonia is frequently seen in overdose (Karch, 2015; Darke & Duflou, 2016). Pulmonary diseases, such as emphysema, may reduce the respiratory reserve in the presence of drugs such as heroin which depress respiration. Cardiac damage may increase susceptibility to the effects of opioid-induced hypoxia. Impaired opioid metabolism from liver diseases, such as cirrhosis, may also increase overdose risk. Finally, impaired kidney functioning may be relevant, as electrolyte imbalance and increased blood pressure may place strain upon the cardiovascular system and increase the risk of pulmonary oedema (Brunton and Knollmann, 2023).

To date, few studies have reported on major autopsy findings in heroin overdose cases (Darke & Duflou., 2016; Darke et al., 2006, 2010; Fugelstad et al., 2003), and to our knowledge only one has stratified by age (Darke et al., 2006). In that paper, which examined 841 cases from 1998–2002 seen at the Institute of Forensic Medicine in central Sydney, we reported age-related differences in pre-existing disease across a range of pathologies that included emphysema, coronary artery disease, cirrhosis and nephrosclerosis (Darke et al., 2006). In the period since those fatalities occurred to the present there have been major changes in case demographics, drug use patterns and toxicological investigations. Consistent with international trends (Bird and Robertson, 2020; Lewer et al., 2022b; Lynch et al., 2021), the mean age of cases in the 2006 study was 33 years, but was 42 years in our most recent case series covering 2020–2022 (Darke et al., 2023). There have also been major increases globally in the use of psychostimulants (Darke et al., 2022; Man et al., 2021, 2022; United Nations Office on Drugs and Crime, 2022), that have been reflected in heroin overdose deaths. Whereas in the 2006 study fewer than 10 % of cases had a psychostimulant present in their blood (Darke et al., 2006), the figure was 45 % among the 610 cases of death due to heroin toxicity that occurred across Australia between 2020 and 2022 (Darke et al., 2023). Psychostimulants are pro-arrhythmic, increase myocardial oxygen demand and engender accelerated cardiovascular disease (Duflou, 2020). Their use in tandem with heroin (a drug that reduces oxygenation) may well increase the risk of cardiac failure, particularly in a person with a damaged heart.

Changes in routine toxicological screening across Australian jurisdictions since 2006 to include 6-acetyl morphine (6AM) has enabled the use of a proxy measure of survival times (Darke & Duflou, 2016, Darke et al., 2023). Heroin (diacetylmorphine) is a synthetic pro-drug that is rapidly deacetylated to 6AM. The conversion time for 6AM to be metabolised to morphine is estimated at 20–30 min (Baselt, 2020; Karch, 2015). During secondary phase metabolism, morphine is converted to its principal metabolite, morphine-3-glucuronide (M3G) and, more slowly and in smaller amounts, to morphine-6-glucuronide (M6G). The presence of 6AM in the blood suggests a more rapid death, while its absence suggests a more prolonged survival time. How survival times relate to age is currently unknown, but may have significant clinical implications.

The current study aimed to extend our work on fatal heroin overdose cases in Australia in the early 2020s by examining age and its relation to disease and survival times. Specifically, the study aimed to determine, stratified by age:

1. The circumstances of death and case characteristics of heroin-related toxicity deaths in Australia, 2020–2022;
2. The toxicological profile and major autopsy findings of cases; and
3. The proportion of cases in which blood 6AM was detected, as a proxy measure of survival times.

2. Methods

2.1. National coronial information system (NCIS)

The NCIS 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 NCIS case file includes demographic information, a police narrative of circumstances, autopsy reports and toxicology reports (where these processes were conducted), and the coronial finding. Cause of death is ascertained by a forensic pathologist and documented 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. This advice is provided to the coroner, who makes a formal determination of cause of death on the basis of medical and other information.

2.2. Case identification

All closed cases (i.e. the Coronial investigation had been completed and a cause of death issued) that occurred between 1 January 2020 and 31 December 2022 in which 'heroin and its metabolites', or 'morphine' was coded in the NCIS Drug Coding fields set as contributory to death were identified, and inspected by the authors (final search 9 March, 2023). We did not have access to ongoing cases, or their characteristics. As a study of heroin overdose, cases of death due to suicide by physical means, homicide, or natural causes in which heroin was deemed incidental in the coronial process, were excluded. Cases of drug toxicity in which morphine detected in blood was attributable to morphine administration, rather than heroin, were also excluded. Recent heroin use was confirmed by the presence of 6AM in blood or urine, specific attribution to heroin in the cause of death, or attribution in forensic pathology/coroners and/or, police reports.

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.

2.3. Measures

Data on clinical characteristics, circumstances of death and toxicology were retrieved from police narratives, autopsy reports, toxicology reports and coronial findings. Information was collected on demographics, mention of a history of substance use problems, current drug treatment enrolment, a history of injecting drug use, mental health history (mention of a history of problems and/or treatment), and suicidal intent. Manner of death was classified as: i. Accidental drug toxicity or ii. Intentional self-harm by drug toxicity (determined by the NCIS intent designation code "Intentional self-harm").

Toxicological testing was conducted according to local protocols. In all cases of suspected drug toxicity, both drug identification and quantitation were performed. In 43 cases of hospitalisation prior to death, antemortem blood samples taken on or near admission to hospital were reported, and drugs administered by medical staff excluded. Results from blood toxicology samples were reported for 6AM, free morphine, morphine glucuronides (M3G, M6G), which comprised part of the

Table 1
Case characteristics and circumstances of death stratified by age among cases of fatal heroin toxicity in Australia, 2020–2022.

	Age range (years)				
	<30 years (n=90)	30-39 years (n=132)	40-49 years (n=219)	≥50 years (n=169)	
% (n)					
Male	84.4 (76)	79.5 (105)	81.7 (179)	77.5 (131)	X^2_3=2.2, p=.5
	OR 1.0	OR 0.7 CI 0.4-1.5	OR 0.8 CI 0.4-1.6	OR 0.6 CI 0.3-1.2	
Enrolled in treatment	3.3 (3)	3.8 (5)	8.7 (19)	11.2 (19)	X^2_3=9.4, p<.05
	OR 1.0	OR 1.1 CI 0.3-4.9	OR 2.8 CI 0.8-9.6	OR 3.6 CI 1.1-12.8	
Documented history of: Substance use problems	96.7 (87)	97.7 (129)	98.2 (215)	96.4 (163)	X^2_3=1.4, p=.7
	OR 1.0	OR 1.5 CI 0.3-7.5	OR 1.9 CI 0.4-8.5	OR 0.9 CI 0.2-3.8	
Mental health problems	46.7 (42)	47.7 (93)	42.5 (93)	33.7 (57)	X^2_3=7.4, p=.06
	OR 1.0	OR 1.0 CI 0.6-1.8	OR 0.8 CI 0.5-1.4	OR 0.6 CI 0.3-0.9	
Chronic pain	3.3 (3)	4.5 (6)	6.8 (15)	12.4 (21)	X^2_3=9.8, p<.05
	OR 1.0	OR 1.4 CI 0.4-5.7	OR 2.1 CI 0.6-7.6	OR 4.1 CI 1.2-14.2	
Circumstance of death Unintentional drug toxicity	94.4 (85)	92.4 (122)	85.8 (188)	77.5 (34)	X^2_3=20.7, p<.001
	OR 1.0	OR 0.7 CI 0.2-2.2	OR 0.4 CI 0.1-0.9	OR 0.2 CI 0.1-0.5	
Combined unintentional drug toxicity and disease	3.3 (3)	4.5 (6)	11.9 (26)	20.1 (34)	X^2_3=26.2, p<.001
	OR 1.0	OR 1.4 CI 0.4-5.7	OR 3.9 CI 1.2-13.3	OR 7.3 CI 2.2-24.5	
Intentional drug toxicity	2.2 (2)	3.0 (4)	2.3 (5)	2.4 (4)	X^2_3=0.2, p=.9
	OR 1.0	OR 1.4 CI 0.2-7.7	OR 1.0 CI 0.2-5.4	OR 1.1 CI 0.2-5.9	
Evidence of an apparent sudden collapse	11.1 (10)	12.9 (17)	15.1 (33)	21.3 (36)	X^2_3=
	OR 1.0	OR 1.2 CI 0.5-2.7	OR 1.4 CI 0.7-3.0	OR 2.2 CI 1.1-4.6	

standard toxicology screen in all jurisdictions across the study period. Results were also reported for alcohol, antidepressants, antihistamines, antipsychotics, cannabis (Δ-9-THC), gabapentinoids, gamma hydroxybutyrate (GHB), hallucinogens, hypnosedatives, ketamine, other 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 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 examination of major organs. Major pathology was reported for the following systems: cardiovascular (cardiomegaly, coronary artery disease, replacement fibrosis), pulmonary (emphysema, aspiration of vomitus, bronchopneumonia), hepatic (steatosis, fibrosis, cirrhosis) and renal (nephrosclerosis, fibrosis). Cardiomegaly was diagnosed by heart weight exceeding the 95th percentile of normal weight ranges relative to body weight, with reference to the standard anatomical norms used by forensic pathologists (Kitzman et al., 1988; Scholz et al., 1988). Moderate to severe coronary artery atherosclerosis was defined as ≥50 % cross-sectional area stenosis or if recorded as present by the autopsy pathologist.

2.4. Statistics

For the purposes of analysis, cases were categorised into four age brackets: <30 years, 30–39 years, 40–49 years, ≥50 years. Medians, interquartile ranges (IQR) and ranges were calculated for skewed distributions. Group comparisons of continuous variables were analysed using the Kruskal-Wallace H test. For dichotomous variables, logistic regressions were conducted and Odds Ratios (OR) with 95 % Confidence Intervals (CI) calculated, using the <30 years group as the referent. All such analyses were conducted using IBM SPSS Statistics v.27.0 (IBM Inc., 2021).

3. Results

3.1. Case characteristics

The series comprised 610 cases: <30 years ($n = 90$), 30–39 years ($n = 132$), 40–49 years ($n = 219$), ≥50 years ($n = 169$). Recent heroin use was confirmed by 6AM in blood or urine (486 cases), or attribution in the cause of death and/or accompanying coronial investigations (124 cases). The characteristics of this series have been described in detail elsewhere (Darke et al., 2023). Briefly, the mean age was 42.6 years (range 18–73 years), 80.5 % were male, and 7.5 % were enrolled in a drug treatment programme. Documented histories were noted of substance use problems (97.4 %), injecting drug use (98.2 %), mental health problems (41.8 %) and chronic pain (7.4 %). The circumstances of death were unintentional drug toxicity (86.2 %), combined unintentional drug toxicity/disease (11.3 %), and intentional drug toxicity (2.5 %).

There were no group differences in sex or having a documented history of substance use problems. Compared to the youngest group, those aged ≥50 years were less likely to have documented mental health problems, but more likely to have a history of chronic pain and to be enrolled in a treatment programme. In almost all cases death was due to unintentional drug toxicity. Compared to the youngest group, both the two older groups were less likely to have death attributed solely to unintentional drug toxicity, and more likely for it to be attributed to the combined effects of unintentional drug toxicity and pre-existing disease. In comparison to the youngest group, the oldest group was twice as likely to show evidence of a sudden collapse (Table 1).

3.2. Toxicological profile

Toxicological findings were available for 560 cases. There were no significant group differences in free morphine concentrations, glucuronide concentrations, or the ratio of glucuronides to free morphine. Compared to the youngest group, however, the two older groups were significantly more likely to have 6AM present in blood. While 6AM was present in a third of young cases, it was present in over half of cases in each of the two oldest groups, suggesting a smaller proportion of the older groups may have survived for longer than 20–30 min.

Almost all cases had psychoactive drugs other than heroin metabolites in their blood. Compared to the youngest group, the two older groups were more likely to have opioids other than heroin metabolites present. There were no group differences in the presence of psychostimulants or other depressant drugs (Table 2).

3.3. Major autopsy findings

Autopsy data were available in 61.0 % of cases (Table 3). Compared to the youngest group, cases aged ≥50 years were more likely to be diagnosed with cardiomegaly and moderate-severe coronary artery disease. They were also more likely to have a diagnosis of emphysema, but less likely to have aspirated vomitus or to have been diagnosed with

Table 2
Blood toxicology stratified by age among cases of fatal heroin toxicity in Australia, 2020–2022.

	Age range (years)				
	<30 years (n=87)	30-39 years (n=128)	40-49 years (n=200)	≥50 years (n=145)	
Free morphine concentration median mg/L (IQR, range)	0.15 (0.19, 0.00-1.20)	0.15 (0.16, 0.00-2.80)	0.20 (0.20, 0.00-4.20)	0.18 (0.21, 0.00-2.60)	H=7.8, p=.05
Glucuronide concentration mg/L (IQR, range)	0.20 (0.40, 0.00-2.40)	0.25 (0.44, 0.00-16.00)	0.22 (0.38, 0.00-3.70)	0.20 (0.43, 0.00-2.93)	H=1.9, p=.6
Ratio Glucuronides /Free morphine (IQR, range)	1.38 (3.59, 0.00-27.5)	1.52 (3.88, 0.00-38.00)	0.91 (2.15, 0.00-42.00)	0.87 (2.18, 0.00-41.86)	H=6.2, p=.1
6AM present % (n)	34.5 (30)	38.3 (49)	52.0 (104)	55.2 (80)	X^2_3=8.6, p<.05
	OR 1.0	OR 1.2 CI 0.7-2.1	OR 2.1 CI 1.2-3.5	OR 2.3 CI 1.4-4.1	
Psychoactive drugs other than heroin*	95.4 (83)	94.5 (128)	96.0 (192)	94.5 (145)	X^2_3=0.6, p=.9
	OR 1.0	OR 1.21 CI 0.4-4.2	OR 1.0 CI 0.4-2.9	OR 1.4 CI 0.5-3.8	
Other opioids % (n)	9.2 (8)	14.8 (19)	27.0 (54)	24.1 (35)	X^2_3=16.8, p<.001
Other opioids*	OR 1.0	OR 1.7 CI 0.7-4.1	OR 3.6 CI 1.7-8.1	OR 3.1 CI 1.4-7.1	
Other drugs	46.0 (40)	53.1 (68)	47.5 (95)	33.1 (48)	X^2_3=12.4, p<.01
Psychostimulants	OR 1.0	OR 1.3 CI 0.8-2.3	OR 1.1 CI 0.6-1.8	OR 0.5 CI 0.3-1.0	
Other depressants (alcohol, hypnosedatives, gabapentinoids)	81.6 (71)	77.3 (99)	77.5 (155)	74.5 (108)	X^2_3=1.6, p=.7
	OR 1.0	OR 0.8 CI 0.4-1.5	OR 0.8 CI 0.4-1.5	OR 0.7 CI 0.3-1.3	

* Excluding codeine Referent= <30 years; 6AM= 6-acetyl morphine; Glucuronides: morphine-3-glucuronide, morphine-6-glucuronide.

acute bronchopneumonia. All three older groups were more likely to have a diagnosis of moderate to severe hepatic steatosis than the youngest group. In addition, cases aged ≥50 years were also more likely than the youngest group to have hepatic fibrosis (not yet advanced to cirrhosis), and end stage cirrhosis. Much of the may be due to hepatitis C, but serology was not routinely conducted. There were no significant group differences in diagnoses involving the kidneys.

4. Discussion

The current study presents new data on the relationship between age, disease, and survival times in fatal heroin overdose. An outstanding feature of the case series was their age, with close to two thirds aged forty or older. By comparison, in our 2006 case series, cases older than 44 years comprised fewer than 10 %. The older age demographic was reflected in higher rates of chronic pain amongst those aged fifty years or older, and in death being a combination of drug toxicity and disease in the two older age groups. Indeed, one in five older cases were attributed to this combination. Physical health problems were not reflected in more frequent mental health problems, which were less common in the oldest group.

Autopsy findings presented a clinical picture of extensive disease amongst older cases. Close to half of the oldest group were diagnosed with coronary artery disease, a third with emphysema, and a fifth with hepatic cirrhosis. These findings demonstrate the burden of disease amongst older people who use heroin more generally. This clinical picture is consistent with the significant proportions of heroin-using cohorts who die due to systemic disease (Gao et al., 2019; Larney et al., 2023), as well as what has been posited as accelerated ageing (Bachi et al., 2017). Indeed, a recent study on causes of death amongst people who use illicit opioids found that deaths due to non-communicable diseases increased more rapidly with age (Lewer et al., 2022a). By accelerated ageing we mean that the levels of systemic disease seen in many cases are more typical of people some decades older than the people in question. Moreover, the overall degree of disease appears to have increased from Australian case series conducted earlier in this century (Darke et al., 2006, 2010), which may reflect the age of cases and, in the case of cardiovascular disease, the widespread use of methamphetamine. As noted earlier, the high rates of disease, most prominent amongst older cases, may have increased the vulnerability to overdose.

There were no age-related differences in the morphine and glucuronide concentrations. There was, however, notable age-related difference in the presence of 6AM in the blood, a proxy marker for survival times. While 6AM was present in over half of the two older age groups, it was present in only a third of the younger groups. Using 6AM as a biomarker, it appears that death was rapid (under 20–30 min) in more than half of the older group cases, compared to a third of the younger cases. Thus, while older cases had no more morphine in their blood than younger cases, at least a subgroup appeared to die more quickly. Consistent with this profile, older cases were more likely to exhibit evidence of a sudden collapse following heroin administration, but less likely to have aspirated vomitus and be diagnosed with acute bronchopneumonia. Evidence of a sudden loss of consciousness and/or collapse might reasonably be taken to indicate a more rapid death. Also, given that pneumonia takes time to develop, and prolonged inertia increases risk, it is more likely to be associated with a longer survival time.

The current work has clinical implications. The reporting of 6AM and other heroin metabolites in post-mortem cases provides a clearer picture of heroin-related deaths, and would be a welcome addition to toxicology screens worldwide. Consistent with studies of the living (Darke et al., 2009; Han et al., 2022; Hser et al., 2004; Lofwall et al., 2005; Reece, 2007, 2012; Reece and Hulse, 2014; Van Santen et al., 2018), the health of cases in this series was particularly poor, with clinically significant disease common. Treating such health conditions appears to be crucial, particularly as many of these conditions may increase the risk of overdose and death. An obvious way to provide such management is enrolment in a drug treatment programme. Enrolment in a treatment programme substantially reduces the risk of overdose and death, and also improves the health of those enrolled, particularly older people (Chaillon et al., 2022; Fareed et al., 2009; Larney et al., 2023; Mannelli, 2021). Buprenorphine, in particular, has been demonstrated to reduce overdose mortality for older people enrolled in opioid substitution treatment, and for those with cardiovascular and respiratory disease (Larney et al., 2023). More active engagement in treatment and testing for causes of preventable morbidity in settings that provide services to people who use heroin, such as opioid substitution clinics, residential rehabilitation, and needle and syringe programmes, would appear appropriate. This is particularly relevant given that the stigma associated with heroin use, and the consequent barriers to treatment in the general medical settings. Given the levels of liver disease, regular hepatitis C testing would appear prudent. In terms of acute response, these data indicate that there is time to intervene for many cases, and for the majority of older cases. People who are older who use heroin should be advised of their risk for shorter survival times. The use of wearable technology ('mHealth') to detect, and initiate responses to overdose

Table 3
Major organ pathology stratified by age among cases of fatal heroin toxicity in Australia, 2020–2022.

Pathology	Age range (years)				
	<30 years	30-39 years	40-49 years	≥50 years	
Cardiovascular % (n)	(n=60)	(n=75)	(n=137)	(n=100)	
Cardiomegaly	16.7 (10)	24.0 (18)	29.2 (40)	44.0 (44)	X^2_3=15.7, p<.001
	OR 1.0	OR 1.6 CI 0.7-3.7	OR 2.1 CI 0.9-4.5	OR 3.9 CI 1.8-8.6	
Coronary artery disease (Moderate-severe)	15.0 (9)	12.0 (9)	27.7 (38)	46.0 (46)	X^2_3=31.5, p>.001
	OR 1.0	OR 0.8 CI 0.3-2.1	OR 2.2 CI 0.9-4.8	OR 4.8 CI 2.1-10.9	
Replacement fibrosis	10.0 (6)	5.3 (4)	13.9 (19)	21.0 (21)	X^2_3=10.3, p<.05
	OR 1.0	OR 0.5 CI 0.1-1.9	OR 1.5 CI 0.5-3.8	OR 2.4 CI 0.9-6.3	
Pulmonary % (n)	(n=59)	(n=75)	(n=137)	(n=101)	
Emphysema	5.1 (3)	8.1 (6)	13.3 (18)	35.0 (36)	X^2_3=34.7, p<.001
	OR 1.0	OR 1.6 CI 0.4-6.9	OR 2.9 CI 0.8-10.2	OR 10.1 CI 2.9-34.5	
Acute presentation Aspiration of vomitus	33.9 (20)	21.6 (16)	14.1 (19)	15.0 (15)	X^2_3=11.0, p<.05
	OR 1.0	OR 0.5 CI 0.2-1.2	OR 0.3 CI 0.2-0.7	OR 0.3 CI 0.2-0.7	
Acute bronchopneumonia	27.1 (18)	17.6 (13)	10.4 (14)	11.0 (11)	X^2_3=9.4, p<.05
	OR 1.0	OR 0.6 CI 0.3-1.3	OR 0.3 CI 0.1-0.7	OR 0.3 CI 0.1-0.8	
Hepatic % (n)	(n=58)	(n=70)	(n=134)	(n=91)	
Steatosis (Moderate-severe)	3.4 (2)	18.6 (13)	20.1 (27)	15.4 (14)	X^2_3=11.4, p<.01
	OR 1.0	OR 6.4 CI 1.7-29.6	OR 7.1 CI 1.6-30.8	OR 5.1 CI 1.1-23.3	
Fibrosis	3.4 (2)	8.6 (6)	11.9 (16)	17.6 (16)	X^2_3=8.5, p<.05
	OR 1.0	OR 2.6 CI 0.5-13.5	OR 3.8 CI 0.8-17.1	OR 5.9 CI 1.3-27.0	
Cirrhosis	0.0 (0)	5.7 (4)	6.7 (9)	19.8 (18)	X^2_3=22.8, p<.001
	OR 1.0	OR 7.9 CI 0.4-150.2	OR 8.9 CI 0.5-154.8	OR 29.5 CI 1.7-499.0	
Renal % (n)	(n=58)	(n=69)	(n=133)	(n=90)	
Nephrosclerosis	6.9 (4)	5.8 (4)	8.3 (11)	17.8 (16)	X^2_3=7.8, p=.05
	OR 1	OR 0.8 CI 0.2-3.5	OR 1.2 CI 0.4-4.0	OR 2.9 CI 0.9-9.2	
Fibrosis (any)	10.3 (6)	5.8 (3)	6.8 (9)	20.0 (18)	X^2_3=12.7, p<.01
	OR 1.0	OR 0.4 CI 0.1-1.7	OR 0.6 CI 0.2-1.9	OR 2.2 CI 0.8-5.8	

Referent= <30 years

represents a potential new form of intervention that does not rely upon others being present (Tas et al., 2023). The provision of take-home naloxone is warranted for all people who use heroin, but is particularly salient those who are older, as take-home naloxone has been demonstrated to be an effective intervention (McDonald et al., 2017; Moustaqim-Barrette et al., 2021).

As in all studies, caveats must be borne in mind. The series comprised closed cases, and in recent years there will be open cases in which the coronial process was still underway. We did not have access to open cases, or their characteristics. Blood concentrations at the time of death, or at hospital admission, may also not be the peak concentration. It is also accepted that postmortem redistribution likely means the blood retrieved from the body at the time of postmortem examination may well have been different to that at the time of death (Maskell et al., 2019). Details of clinical histories were restricted to those documented in case files and may thus be conservative estimates. By necessity, autopsy data were restricted to those cases in which the procedure was conducted and available for inspection, although this was the case for the majority of cases. Finally, survival times can only be estimated as based upon on the metabolism of 6AM as a proxy measure, with more precise estimates not possible.

In summary, older heroin overdose cases had more extensive heart, lung, and liver pathology than younger cases. They also appeared more likely to have had shorter survival times than the youngest cases, a possible refection of the reduced respiratory of cardiovascular resilience due to disease.

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CRediT authorship contribution statement

Shane Darke: Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Johan Duflou:** Writing – original draft, Investigation, Conceptualization. **Amy Peacock:** Writing – original draft, Investigation, Conceptualization. **Michael Farrell:** Writing – original draft, Investigation, Conceptualization. **Julia Lappin:** Writing – original draft, Investigation, Conceptualization.

Declaration of competing interest

The author confirm that there is no financial, or personal interest or belief that could affect their objectivity in the conduct of this study.

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