Characteristics and outcomes of critically ill patients with drug overdose in Australia and New Zealand

Luca Cioccari, Nora Luethi, Michael Bailey, David Pilcher and Rinaldo Bellomo

ABSTRACT

Objective: The epidemiology of patients admitted to the intensive care unit after a drug overdose (OD) is poorly defined. We aimed to study the incidence, characteristics and outcomes of patients admitted to the ICU because of OD in Australia and New Zealand.

Design, setting and patients: Retrospective study of data from the Australian and New Zealand Intensive Care Society Adult Patient Database, including all patients admitted to an ICU with OD from 2005 to 2013.

Results: Overall, of 883 618 patients treated in the ICU during the study period, 18 050 (2.04%) were admitted because of OD. Over nearly a decade, the proportion of ICU admissions secondary to OD increased significantly from 1.3% in 2005 to 2.4% in 2013 ($P < 0.0001$). The annual incidence of OD-related admissions increased from 63 per million people in 2005 to 166 per million in 2013 ($P < 0.0001$). The largest increase was noted among Indigenous Australians, from 31 per million in 2005 to 436 per million in 2013, with a peak incidence in 2012 of 553 per million ($P = 0.0006$). Most patients were female (56.4%) and the mean age was 40.2 years (SD, 15.4 years). Overall, ICU and hospital mortality rates were low, at 1.3% and 1.7%, respectively, and did not change over time. Non-survivors were significantly older than survivors and had higher rates of organ failure, intubation and cardiac arrest at presentation, more chronic comorbidities and higher illness severity scores.

Conclusions: Drug OD accounts for an increasing proportion of ICU admissions in Australia and New Zealand. Its population incidence is increasing overall, particularly in Indigenous Australians.

Crit Care Resusc 2017; 19: 14-22

Accidental or intentional drug overdose (OD) is a major cause of morbidity and mortality[1-3] and relatively frequently leads to admission to an intensive care unit.[4,5] Most patients with OD are young and previously healthy[6] and therefore in the economically productive age group.[7-10] Consequently, any loss of life-years due to OD-associated injury is substantial and likely to have important socioeconomic implications. Retrospective studies suggest that preventive measures might be possible in many cases.[7] Therefore, understanding the characteristics and outcomes of patients with OD requiring ICU admission is the first and necessary step to establish a scientific basis for further interventional public health studies in the field. Our aim was to report trends in incidence and mortality in a large cohort of patients with OD requiring ICU admission in Australia and New Zealand from 2005 to 2013.

Methods

Study design

We performed a retrospective study of data from the Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database (APD), a high-quality database of almost all admissions to Australian and New Zealand ICUs.[11] The Alfred Hospital Human Research Ethics Committee (Melbourne, Australia) approved the study, with a waiver for informed consent. Population data were obtained from the Australian Bureau of Statistics and Statistics New Zealand.

All patients admitted to an ICU with the admission diagnosis of drug OD from 2005 to 2013 were included. We analysed the following outcomes: hospital mortality, discharge home, discharge to other hospital and discharge to rehabilitation. Patients were analysed in the following categories:

- age group (≤ 44 years, 45–64 years, 65–84 years and ≥ 85 years)
- comorbidities (defined by the Acute Physiology and Chronic Health Evaluation [APACHE] II or APACHE III classification)
- cardiovascular, respiratory or renal failure (a score of ≥ 3 on the Sequential Organ Failure Assessment [SOFA] scale was used to define organ failure on admission).

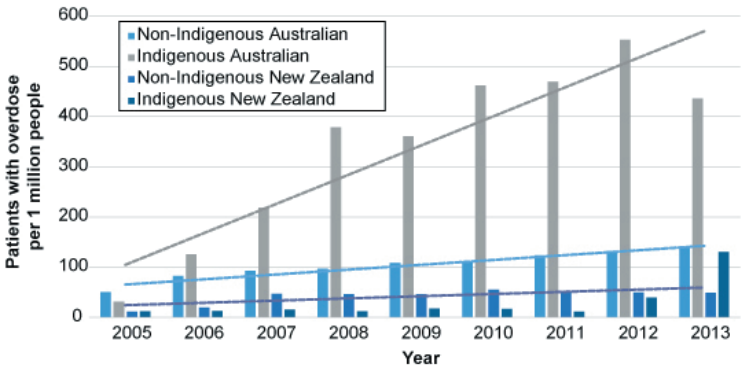
Statistical analysis

Data are shown as frequencies with percentages, means with standard deviations (SDs), or medians with interquartile ranges (IQRs). We used the χ^2 test for data of equal proportions, the Student *t* test for normally distributed data and the Wilcoxon rank-sum test otherwise, to assess differences. Changes in mortality and hospital outcomes over time were determined using logistic regression,

adjusting for illness severity and site, with the year of admission treated as a categorical variable, and as a continuous variable once linearity was established. Illness severity was determined in accordance with the Australian and New Zealand calibrated Risk of Death (ANZROD) model.[12]

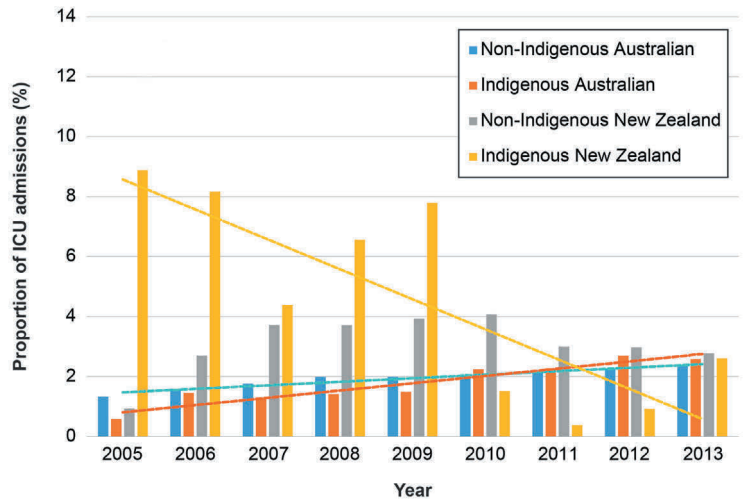
To identify independent predictors of presenting with OD and of mortality among patients with OD, we developed multivariate logistic regression models and validated them using stepwise selection and backwards elimination procedures, respectively. We developed mortality models for presentation to ICU and for after 24 hours in the ICU, to appropriately account for condition severity. All logistic regression results are shown as odds ratios (ORs) with 95% confidence intervals (CIs). We determined changes in length of stay (LOS) over time through log transformation and analysis using mixed linear modelling. We adjusted for site and illness severity, and report results as geometric means with 95% CIs. To calculate the population prevalence, we used end-of-year population estimates from the Australian Bureau of Statistics and Statistics New Zealand for Australian and New Zealand citizens aged ≥ 16 years, adjusting for the APD coverage of Australian and New Zealand ICU admissions for each year. We analysed data using SAS, version 9.4 (SAS Institute). Given the size of the database, we used a two-sided $P < 0.001$ to define the threshold for statistical significance, to more closely align clinical and statistical significance.

Figure 1. Population incidence of overdose in Australia and New Zealand, 2005–2013*



* Pearson correlation for trend per specific population subgroup: non-Indigenous Australians, $P < 0.0001$; Indigenous Australians (Aboriginal and Torres Strait Islander people), $P < 0.0006$; non-indigenous New Zealanders, $P < 0.01$; indigenous New Zealanders (Māori people), $P < 0.06$.

Figure 2. Proportion of intensive care unit admissions due to overdose*



* For significant trend: non-indigenous Australians, $P < 0.0001$; Indigenous Australians (Aboriginal and Torres Strait Islander people), $P < 0.0001$; non-Indigenous New Zealanders, $P < 0.37$; Indigenous New Zealanders (Māori people), $P < 0.007$.

Results

Of 883 618 patients treated in ICUs during the study period, 18 050 (2.04%) were admitted to the ICU because of a drug OD. The incidence of OD-related admissions increased from 63 per million people in 2005 to 166 per million in 2013 (Pearson correlation for trend, $P < 0.0001$). The largest increase was noted among Indigenous Australians (Aboriginal and Torres Strait Islander people), from 31 per million in 2005 to 436 per million in 2013, with a peak incidence in 2012 of 553 per million ($P = 0.0006$). The population incidence of indigenous New Zealanders (Māori people) remained fairly constant at 11 to 18 per million until 2011, and peaked in 2013 at 130 per million (Pearson correlation for trend, $P = 0.06$) (Figure 1).

Overall, the percentage of ICU admissions due to drug OD increased from 1.3% (1000/76 799) in 2005 to 2.4% (2916/11 9797) in 2013 ($P < 0.0001$). Again, we observed the largest increase among Indigenous Australians, from 0.58% to 2.58% ($P < 0.0001$) over this time. Interestingly, in Māori people, the proportion admitted to the ICU with OD decreased from 8.9% in 2005 to 2.6% in 2013 ($P = 0.007$) (Figure 2).

Baseline characteristics and outcomes of patients with OD are shown in Table 1. Most patients were female (56.4%),

Table 1. Characteristics of patients admitted to the ICU with overdose in Australia and New Zealand, 2005–2013

Characteristic	Data	Data available
Mean age, years (SD)	40.2 (15.4)	18 050
Men, *n* (%)	7869 (43.6%)	18 050
Current smoker, *n* (%)	1543 (8.5%)	18 050
Ex-smoker, *n* (%)	272 (1.5%)	18 050
Median time in hospital before ICU admission, hours (IQR)	2.83 (0.6–5.15)	18 050
Cardiac arrest in previous 24 h, *n* (%)	199 (1.2%)	16 406
Respiratory arrest, *n* (%)	303 (1.9%)	16 016
Mean APACHE II score (SD)	13.3 (7.34)	17 822
Mean APACHE III score (SD)	43.1 (26.1)	17 788
Mean SAPS II score (SD)	28.6 (15)	17 518
Chronic comorbidities, *n* (%)	894 (5.0%)	18 050
Chronic respiratory disease	363 (2.0%)	18 050
Chronic cardiovascular disease	258 (1.4%)	18 050
Chronic liver disease	136 (0.8%)	18 050
Chronic renal failure	58 (0.3%)	18 050
Immune disease	46 (0.3%)	18 050
AIDS	3 (< 0.1%)	18 050
Hepatic failure	22 (0.1%)	18 050
Lymphoma	15 (0.1%)	18 050
Metastases	48 (0.3%)	18 050
Leukaemia or myeloma	17 (0.1%)	18 050
Immunosuppression	73 (0.4%)	18 050
Cirrhosis	132 (0.7%)	18 050
Acute organ dysfunction, *n* (%)		
Acute failure of ≥ 1 organ	11 920 (66.0%)	18 050
Hypotension*	5282 (29.3%)	18 050
Ventilated or intubated	9499 (52.6%)	18 050
Hyperbilirubinaemia†	28 (0.2%)	18 050
Acute renal failure‡	778 (4.3%)	18 050
Thrombocytopenia§	134 (0.7%)	18 050
Median risk of death (IQR)		
ANZROD	0.017 (0.01–0.032)	17 781
Estimated ROD (APACHE II)	0.007 (0.003–0.014)	17 636
Estimated ROD (APACHE III)	0.008 (0.003–0.028)	17 746
Estimated ROD (SAPS II)	0.072 (0.026–0.230)	17 518
Hospital type, *n* (%)		
Rural	3935 (21.8%)	18 050
Metropolitan	6404 (35.5%)	18 050
Tertiary	7394 (41.0%)	18 050
Private	317 (1.8%)	18 050
Hospital admission source, *n* (%)		
Home	12 719 (70.5%)	18 050
Other hospital	3314 (18.4%)	18 050
Chronic care facility	216 (1.2%)	18 050
Other ICU	116 (0.6%)	18 050
ICU admission source, *n* (%)		
Operating theatre	69 (0.4%)	18 050
Emergency department	14 746 (81.7%)	18 050
Hospital ward	436 (2.4%)	18 050
Other ICU	2788 (15.4%)	18 050
Hospital outcome, *n* (%)		
Death	312 (1.7%)	18 050
Discharged home	14 582 (80.8%)	18 050
Discharged to rehabilitation	1147 (6.4%)	18 050
Discharged to other hospital	2009 (11.1%)	18 050
Median hospital LOS, days (IQR)	2.76 (1.54–6.11)	17 966
Median ICU LOS, hours (IQR)	33.7 (19.0–55.0)	18 046
ICU mortality, *n* (%)	243 (1.3%)	18 050
Patients with all data missing, n (%)	*228 (1.3%)*	

IQR = interquartile range. APACHE = Acute Physiology and Chronic Health Evaluation. SAPS = Simplified Acute Physiology Score. ANZROD = Australian and New Zealand calibrated Risk of Death. AIDS = acquired immune deficiency syndrome. ROD = risk of death. ICU = intensive care unit. LOS = length of stay. * Mean arterial pressure < 65 mmHg, or systolic blood pressure < 90 mmHg. † Bilirubin level † 102 µmol/L. ‡ Creatinine level > 300 µmol/L or < 500 mL urine/24 h without known chronic renal impairment. § Platelet count ≤ 50 x 109/L.

and their mean age was 40.2 years (SD, 15.4 years). Only 5% of patients had chronic comorbidities, and these were more common in non-survivors than survivors. Most patients were admitted to a tertiary (41%) or metropolitan (35.5%) hospital. However, about one-fifth of all patients (21.8%) were admitted to a rural hospital. The OR for ICU admission due to OD was significantly higher for younger people, females, and patients who were admitted from home, after-hours, to a rural hospital or during the summer months (Table 2).

Outcomes

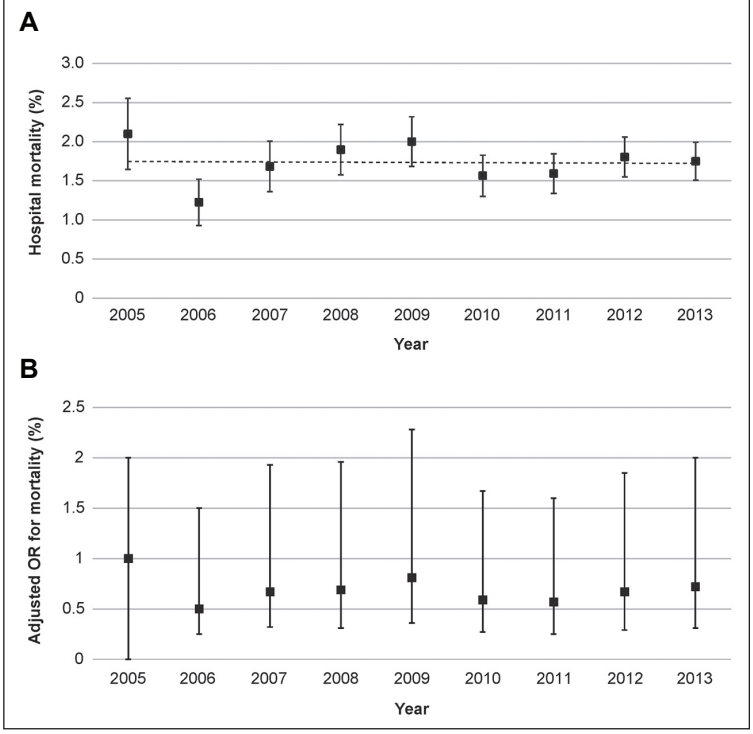
Overall, ICU and hospital mortality rates were low (1.3% and 1.7%, respectively) and remained constant over time, even after adjustment (Figures 3A and 3B). A total of 11 920 patients (66%) presented with signs of organ failure (Table 1). Apart from the need for intubation (52.6%), the most frequently observed evidence of organ dysfunction related to hypotension (29.3%) and acute renal failure (4.3%). Median hospital LOS was 2.76 days (IQR, 1.54–6.11 days) and most patients (80.8%) were discharged home. Non-

Table 2. Propensity scores: risk of being admitted to the ICU with drug overdose in Australia and New Zealand, 2005–2013

Variable	Odds ratio (95% CI)	*P*
Patient age group, years		< 0.0001
≤ 44	15.18 (12.84–17.95)	
45–64	7.1 (6.0–8.4)	
65–84	1.41 (1.18–1.68)	
≥ 85	Reference	
Sex		< 0.0001
Female	1.86 (1.79–1.92)	
Male	Reference	
Smoking status		< 0.0001
Current smoker	1.22 (1.14–1.31)	
Ex-smoker	0.57 (0.5–0.65)	
Non-smoker	Reference	
Hospital level		< 0.0001
Rural	2.14 (1.02–4.52)	
Metropolitan	1.90 (1.52–2.37)	
Private	0.54 (0.25–1.17)	
Tertiary	Reference	
Hospital admission source		< 0.0001
Home	Reference	
Chronic care facility	0.68 (0.58–0.80)	
Other hospital	0.59 (0.55–0.62)	
Unknown	0.52 (0.46–0.59)	
Hospital admission time	< 0.0001	
12 am – 8 am	1.22 (1.17–1.28)	
4 pm – 12 am	1.13 (1.08–1.17)	
8 am – 4 pm	Reference	
State, territory or country		0.2167
ACT	7.35 (0.59–91.84)	
New South Wales	1.50 (0.39–5.72)	
Northern Territory	1.63 (0.10–27.66)	
New Zealand	3.53 (0.72–17.32)	
Queensland	3.49 (0.9–13.55)	
South Australia	Reference	
Tasmania	9.11 (1.19–69.88)	
Victoria	1.95 (0.49–7.68)	
Western Australia	2.99 (0.5–17.72)	
Month		< 0.0001
January	1.28 (1.17–1.39)	
February	1.35 (1.24–1.47)	
March	1.30 (1.20–1.41)	
April	1.18 (1.08–1.28)	
May	1.15 (1.06–1.26)	
June	1.06 (0.98–1.16)	
July	Reference	
August	1.06 (0.97–1.15)	
September	1.21 (1.12–1.32)	
October	1.32 (1.22–1.43)	
November	1.34 (1.23–1.46)	
December	1.36 (1.25–1.47)	

ICU = intensive care unit. * Patients nested within sites, and sites, treated as a random effect.

Figure 3. A: Overall hospital mortality (mean and SEM), 2005–2013. B: Odds ratio (OR) for mortality (with 95% CI), adjusted for severity and hospital site, 2005–2013 (*P* = 0.74)



survivors were significantly older than survivors and had higher rates of organ failure, intubation and cardiac arrest at presentation, more chronic comorbidities and higher illness severity scores (Table 3). The OR for death at admission increased with age, chronic cardiovascular disease, immunosuppression, insulin-dependent diabetes mellitus, liver failure and cardiac arrest in the first 24 hours (Table 4). After 24 hours, the OR for death was still elevated with higher illness severity (OR, 7.21 [95% CI, 6.22–8.36]; $P < 0.001$) and previous cardiac arrest (OR, 8.71 [95% CI, 5.52–13.73]; $P < 0.001$).

Indigenous versus non-indigenous patients

The proportion of indigenous people admitted with OD (average, 7.3% of the population admitted with OD) increased markedly over time, from 1.9% in 2005 to 8.5% in 2013 ($P < 0.0001$). Comparing indigenous and non-indigenous patients, we found no difference in sex, incidence of acute organ failure, illness severity, LOS or mortality (Figure 4). Indigenous patients from both countries, however, were more frequently admitted from home or a chronic care facility and to a rural hospital, and more likely to be discharged home after a shorter ICU stay (Table 5).

Discussion

Key findings

Over nearly a decade, the proportion of ICU admissions related to drug OD in Australia and New Zealand almost doubled, rising from 1.3% in 2005 to 2.4% in 2013, as has the incidence of OD-related admissions. The largest increase occurred among Indigenous

Table 3. Characteristics of survivors of drug overdose versus non-survivors

Parameter	Data available	All patients	Survivors	Non–survivors	*P*
Mean age, years (SD)	18 050	40.2 (15.4)	40 (15.23)	50.21 (18.71)	< 0.0001
Male, *n* (%)	18 050	7869 (43.6%)	7711 (43%)	158 (51%)	0.011
Mean weight, kg (SD)	2220	78.9 (21)	78.85 (20.89)	80.84 (26.15)	0.55
Mean height, cm (SD)	1651	164 (31.1)	164.22 (31.31)	170.92 (8.66)	0.28
Current smoker, *n* (%)	18 050	1543 (8.5%)	1524 (9%)	19 (6%)	0.12
Ex-smoker, *n* (%)	18 050	272 (1.5%)	265 (1%)	7 (2%)	0.28
Indigenous, *n* (%)	14 846	1082 (7.3%)	1070 (7%)	12 (5%)	0.11
Median time in hospital before ICU admission, h (IQR)	18 050	2.83 (0.6–5.15)	2.83 (0.62–5.17)	2.24 (0.24–4.45)	0.003
Cardiac arrest in previous 24 hours, *n* (%)	16 406	199 (1.2%)	151 (1%)	48 (16%)	< 0.0001
Respiratory arrest, *n* (%)	16 016	303 (1.9%)	252 (2%)	51 (18%)	< 0.0001
Mean APACHE II score (SD)	17 822	13.3 (7.34)	13.06 (7.11)	26.16 (8.74)	< 0.0001
Mean APACHE III score (SD)	17 788	43.1 (26.1)	42.24 (25.05)	93.8 (35.06)	< 0.0001
Mean SAPS II score (SD)	17 518	28.6 (15)	28.2 (14.54)	54.01 (18.44)	< 0.0001
Chronic comorbidity, *n* (%)	18 050	894 (5%)	843 (5%)	51 (16%)	< 0.0001
Respiratory disease	18 050	363 (2%)	352 (2%)	11 (4%)	0.05
Cardiovascular disease	18 050	258 (1.4%)	240 (1%)	18 (6%)	< 0.0001
Liver disease	18 050	136 (0.75%)	128 (1%)	8 (3%)	0.0002
Renal failure	18 050	58 (0.32%)	52 (< 1%)	6 (2%)	< 0.0001
Immune disease	18 050	46 (0.26%)	42 (< 1%)	4 (1%)	0.0003
AIDS	18 050	3 (0.02%)	3 (< 1%)	0	1
Hepatic failure	18 050	22 (0.12%)	18 (< 1%)	4 (1%)	< 0.0001
Lymphoma	18 050	15 (0.08%)	14 (< 1%)	1 (< 1%)	0.14
Metastases	18 050	48 (0.27%)	44 (< 1%)	4 (1%)	0.0004
Leukaemia or myeloma	18 050	17 (0.09%)	17 (< 1%)	0	1
Immunosuppression	18 050	73 (0.41%)	64 (< 1%)	9 (3%)	< 0.0001
Cirrhosis	18 050	132 (0.73%)	124 (1%)	8 (3%)	0.0001
Acute organ dysfunction, *n* (%)					
Acute failure of ≥ 1 organ	18 050	11920 (66%)	11639 (66%)	281 (90%)	< 0.0001
Hypotension	18 050	5282 (29.3%)	5104 (29%)	178 (57%)	< 0.0001
Ventilated or intubated	18 050	9499 (52.6%)	9251 (52%)	248 (79%)	< 0.0001
Hyperbilirubinemia	18 050	28 (0.16%)	25 (0%)	3 (1%)	0.0003
Acute renal failure	18 050	778 (4.3%)	672 (4%)	106 (34%)	< 0.0001
Thrombocytopenia	18 050	134 (0.74%)	120 (1%)	14 (4%)	< 0.0001
Median ANZROD (IQR)	17 781	0.017 (0.01–0.032)	0.02 (0.01–0.03)	0.11 (0.05–0.2)	< 0.0001
Median est. prob. of death (APACHE II) (IQR)	17 636	0.0069 (0.0029–0.014)	0.01 (0–0.01)	0.05 (0.02–0.11)	< 0.0001
Median est. prob. of death (APACHE III) (IQR)	17 746	0.0083 (0.0028–0.028)	0.01 (0–0.03)	0.13 (0.04–0.28)	< 0.0001
Median est. prob. of death (SAPS II) (IQR)	17 518	0.072 (0.026–0.23)	0.07 (0.03–0.23)	0.55 (0.31–0.8)	< 0.0001
Rural hospital, *n* (%)	18 050	3935 (21.8%)	3882 (22%)	53 (17%)	0.038
Metropolitan hospital, *n* (%)	18 050	6404 (35.5%)	6296 (35%)	108 (35%)	0.75
Tertiary hospital, *n* (%)	18 050	7394 (41%)	7249 (41%)	145 (46%)	0.046
Private hospital, *n* (%)	18 050	317 (1.8%)	311 (2%)	6 (2%)	0.82
Admitted from home, *n* (%)	18 050	12719 (70.5%)	12521 (71%)	198 (63%)	0.006
Admitted from other hospital, *n* (%)	18 050	3314 (18.4%)	3236 (18%)	78 (25%)	0.002
Admitted from chronic care facility, *n* (%)	18 050	216 (1.2%)	215 (1%)	1 (< 1%)	0.15
Admitted from other ICU, *n* (%)	18 050	116 (0.64%)	109 (1%)	7 (2%)	0.0004
Admitted to ICU from operating theatre, *n* (%)	18 050	69 (0.38%)	68 (< 1%)	1 (< 1%)	0.86
Admitted to ICU from emergency department, *n* (%)	18 050	14746 (81.7%)	14509 (82%)	237 (76%)	0.008
Admitted to ICU from hospital ward, *n* (%)	18 050	436 (2.4%)	427 (2%)	9 (3%)	0.59
Admitted to ICU from other ICU, *n* (%)	18 050	2788 (15.4%)	2723 (15%)	65 (21%)	0.008
All data missing, *n* (%)		228 (1.3%)	226 (1%)	2 (1%)	0.32

ICU = intensive care unit. IQR = interquartile range. APACHE = Acute Physiology and Chronic Health Evaluation. SAPS = Simplified Acute Physiology Score. AIDS = acquired immune deficiency syndrome. ANZROD = Australian and New Zealand calibrated Risk of Death. est. prob. = estimated probability.

Table 4. Odds ratios for death, at admission

Variable	Odds ratio (95% CI)	*P*
Age group, years		
45–64 v ≤ 44	1.55 (1.19–2.04)	< 0.0001
65–84 v ≤ 44	3.74 (2.66–5.26)	< 0.0001
≥ 85 v ≤ 44	6.66 (3.53–12.59)	< 0.0001
Chronic cardiovascular disease	2.24 (1.27–3.96)	0.0056
Cardiac arrest in previous 24 h	22.61 (15.52–32.96)	< 0.0001
Care type, ICU v HDU	5.02 (3.05–8.26)	< 0.0001
Liver failure	10.33 (3.10–34.38)	0.0001
Insulin-dependent diabetes mellitus	2.67 (1.50–4.75)	0.0008
Immunosuppression	4.53 (1.99–10.35)	0.0003
ICU admission time		
12 am to 8 am v 8 am to 4 pm	0.51 (0.37–0.70)	0.0002
4 pm to 12 am v 8 am to 4 pm	0.79 (0.61–1.04)	0.0002

ICU = intensive care unit. HDU = high dependency unit.

Australians (but not in Māori people), with more than a 10-fold increase over this period. Most patients with OD are young, female and free of comorbidities, but two-thirds present with signs of organ failure. Hospital mortality is low and has not significantly changed over time, but drug OD in Indigenous Australians is clearly a rapidly growing problem.

Relationship to previous studies

The percentage of OD-related ICU admissions has been variably reported in the literature. In an Australian single-centre study of 732 patients from 25 years ago, patients with OD admitted to an ICU represented 13.8% of all hospital admissions, and used 6% of available ICU bed-days.[4] Similarly, in an Irish single-centre survey of 80 patients, OD accounted for 3.8% of ICU admissions.[13] Prospectively collected data from a Finnish registry including 28 ICUs showed that 4.5% of all ICU admissions were due to OD.[14] However, a prospective observational study including patients admitted to an intermediate care unit (or high

Table 5. Characteristics of indigenous versus non-indigenous patients admitted to the ICU with drug overdose in Australia and New Zealand, 2005–2013

	All patients		Non-indigenous		Indigenous		
Patient characteristic	*n*	Result	*n*	Result	*n*	Result	*P**
Mean age, years (SD)	14 846	40.2 (15.5)	13 764	40.35 (15.5)	1082	38.8 (14.76)	0.002
Male, % (*n*)	14 846	43.7% (6494)	13 764	44% (5995)	1082	46% (499)	0.1
Current smoker, % (*n*)	14 846	9.5% (1406)	13 764	9% (1220)	1082	17% (186)	< 0.0001
Chronic comorbidities, % (*n*)	14 846	5.2% (776)	13 764	5% (730)	1082	4% (46)	0.13
Ex-smoker, % (*n*)	14 846	1.7% (248)	13 764	2% (222)	1082	2% (26)	0.05
Cardiac arrest previous 24 h, % (*n*)	14 018	1.2% (171)	13 001	1% (165)	1017	1% (6)	0.06
Respiratory arrest, % (*n*)	14 004	2% (275)	12 985	2% (258)	1019	2% (17)	0.48
Mean APACHE II score (SD)	14 679	13.3 (7.35)	13 604	13.3 (7.35)	1075	12.8 (7.25)	0.029
Mean APACHE III score (SD)	14 645	42.8 (26.1)	13 571	42.94 (26.17)	1074	41.23 (24.86)	0.038
Mean SAPS II score (SD)	14 545	28.6 (15)	13 475	28.7 (15.06)	1070	26.93 (14.53)	0.0002
Acute organ dysfunction, % (*n*)†							
Acute failure of ≥ 1 organ	14 846	65.8% (9772)	13 764	66% (9109)	1082	61% (663)	0.001
Hypotension	14 846	30% (4450)	13 764	30% (4134)	1082	29% (316)	0.57
Ventilated or intubated	14 846	51.9% (7712)	13 764	52% (7202)	1082	47% (510)	0.001
Hyperbilirubinaemia	14 846	0.141% (21)	13 764	0% (19)	1082	0% (2)	0.69
Acute renal failure	14 846	4.1% (615)	13 764	4% (578)	1082	3% (37)	0.22
Thrombocytopenia	14 846	0.727% (108)	13 764	1% (98)	1082	1% (10)	0.43
Median ANZROD (IQR)	14 639	0.017 (0.01–0.032)	13 565	0.02 (0.01–0.03)	1074	0.02 (0.01–0.03)	0.05
Median APACHE II est. prob. of death (IQR)	14 671	0.0069 (0.0029–0.014)	13 597	0.01 (0–0.01)	1074	0.01 (0–0.01)	0.038
Median APACHE III est. prob. of death (IQR)	14 641	0.0081 (0.0027–0.028)	13 567	0.01 (0–0.03)	1074	0.01 (0–0.02)	0.045
Median SAPS II est. prob. of death (IQR)	14 545	0.072 (0.026–0.23)	13 475	0.07 (0.03–0.23)	1070	0.06 (0.02–0.2)	0.0003
Rural hospital, % (*n*)	14 846	21.9% (3245)	13 764	21% (2922)	1082	30% (323)	< 0.0001
Metropolitan hospital, % (*n*)	14 846	38.7% (5747)	13 764	40% (5467)	1082	26% (280)	< 0.0001

Table 5 (continued). Characteristics of indigenous versus non-indigenous patients admitted to the ICU with drug overdose in Australia and New Zealand, 2005–2013

	All patients		Non-indigenous		Indigenous		
Patient characteristic	*n*	Result	*n*	Result	*n*	Result	*P**
Tertiary hospital, % (*n*)	14 846	37.8% (5611)	13 764	38% (5162)	1082	41% (449)	0.009
Private hospital, % (*n*)	14 846	1.6% (243)	13 764	2% (213)	1082	3% (30)	0.002
Adm. fr. home, % (*n*)	14 846	70.5% (10461)	13 764	70% (9617)	1082	78% (844)	< 0.0001
Adm. fr. other hospital, % (*n*)	14 846	19.3% (2862)	13 764	19% (2670)	1082	18% (192)	0.18
Adm. fr. chronic care facility, % (*n*)	14 846	0.667% (99)	13 764	1% (73)	1082	2% (26)	< 0.0001
Adm. fr. other ICU, % (*n*)	14 846	0.626% (93)	13 764	1% (88)	1082	0% (5)	0.48
Died, % (*n*)	14 846	1.7% (254)	13 764	2% (242)	1082	1% (12)	0.11
Discharged home, % (*n*)	14 846	81.1% (12046)	13 764	81% (11120)	1082	86% (926)	0.0001
Discharged to rehabilitation, % (*n*)	14 846	6% (897)	13 764	6% (839)	1082	5% (58)	0.33
Discharged to other hospital, % (*n*)	14 846	11.1% (1649)	13 764	11% (1563)	1082	8% (86)	0.0006
Median hospital LOS, d (IQR)	14 776	2.8 (1.56–6.46)	13 698	2.81 (1.56–6.49)	1078	2.7 (1.47–5.81)	0.06
Median ICU LOS, h (IQR)	14 844	33.8 (19–55.2)	13 762	34.2 (19.1–56)	1082	29.1 (17.7–47.4)	< 0.0001
ICU mortality, % (*n*)	14 846	1.3% (194)	13 764	1% (187)	1082	1% (7)	0.047
All data missing, % (*n*)		1.1% (167)	13 764	1% (160)	1082	1% (7)	0.12

ICU = intensive care unit. APACHE = Acute Physiology and Chronic Health Evaluation. SAPS = Simplified Acute Physiology Score. ANZROD = Australian and New Zealand calibrated Risk of Death. IQR = interquartile range. est. prob. = estimated probability. Adm. fr. = admitted from. LOS = length of stay. * Continuous data compared by Student t test or Wilcoxon rank-sum test, categorical data by χ^2 test or Fisher exact test. † Hypotension: mean arterial pressure < 65 mmHg or systolic blood pressure < 90 mmHg; hyperbilirubinemia: bilirubin level ≥ 102 μmol/L; thrombocytopenia: platelets ≤ 50 x 10^9/L; acute renal failure: creatinine level > 300 μmol/L or < 500 mL urine/24 h without known chronic renal impairment.

dependency unit) of a tertiary referral centre in Germany reported a percentage of OD-related admissions as high as 17.3%.[15] Finally, in a recent Dutch study of close to a quarter of a million ICU admissions, 3.7% were due to drug intoxication.[16] These findings suggest that the incidence of OD leading to ICU admission in Australia and New Zealand may be lower than in other countries. Despite the overall, apparently lower, incidence of OD admissions to the ICU in Australia and New Zealand, we observed a relative increase of 85% in the proportion of ICU admissions related to OD over the past decade, and a disproportionately increased incidence among Indigenous Australians (Aboriginal and Torres Strait Islander people) but not among Māori people in New Zealand.

A large, retrospective, single-centre study of 9116 non-ICU patients from the United Kingdom showed an overall increase in the number of self-poisoning episodes by 93% over the 13-year study period.[17] A similar retrospective review of Scottish data showed that, between 1990 and 1997, annual discharge rates for OD increased by 47.5% in women and 53% in men.[18] The prevalence of organ failure in our cohort was high, affecting two-thirds of patients. In our study, as well as in previous reports,[14] the OR for death was increased in the presence of organ failure.

Overall mortality in our study population was low (1.7%). This is similar to most studies from Western countries. Weilemann and colleagues studied 153 patients with suicidal or parasuicidal overdose, 65 of whom were treated in the ICU.[5] Fifty-three patients were male (35%) and 100 were female (65%); the mean age was 36 years. The authors found a mortality of 2%, as did the previously mentioned Australian study.[4] Another longitudinal, single-centre study of 674 ICU patients with OD reported a lower death rate, of 1.2%,[19] and in the Finnish multicentre study (255 admissions from 28 ICUs), hospital mortality was 2.3%.[14] Higher mortality rates are reported in cohorts from regions (developing countries) where poisoning by organophosphates and other agricultural products is frequently encountered.[20-24] Finally, a recent Dutch study showed a 2.1% hospital mortality after ICU admission following drug intoxication.[16]

Implications of study findings

Our findings imply that OD is a growing source of morbidity and mortality in a relatively young, healthy population. As this is associated with an increasing loss of person-years and productive years, drug OD has important human, psychosocial, socioeconomic and health economic implications.

Further, the rising incidence of OD in the Indigenous population of Australia is a matter of growing concern. The use of all types of illicit drugs among Indigenous Australians has been reported to be more than twice that among the non-Indigenous population.[25] Factors contributing to illicit

drug use among Indigenous people include education, employment, income, family and social factors, as well as the historical context of Indigenous disadvantage. Policies and strategies addressing illicit drug use among Indigenous people are urgently needed and have been proposed elsewhere.[25]

Strengths and weaknesses

To our knowledge, our study is the largest epidemiological study of patients with OD admitted to the ICU, and the only binational survey of the incidence and mortality of patients with OD admitted to an ICU. We retrieved the data from a database that includes more than 90% of all ICU admissions in Australia and New Zealand, which made it possible to derive reasonably accurate population estimates. The data were collected prospectively for quality surveillance purposes. Such data are therefore unlikely to be biased or affected by changing diagnostic criteria. The size of the study cohort enabled robust analysis of outcomes.

A major limitation of our study is its retrospective design based on analysis of registry data, but the large number of patients included reduces the risk of bias. We could not differentiate between different types of drug OD, or whether they were intentional or accidental. However, our study was aimed at describing the epidemiology and outcomes of OD, without focusing on specific agents. Moreover, the pattern of substances involved in self-poisoning varies geographically and temporally, reflecting availability of illicit drugs and trends in prescribing.[26,27] Last, we can only report hospital mortality, which can be used, however, as a surrogate for 30-day mortality in such patients.[28]

Conclusions

Drug overdose accounts for an increasing proportion of ICU admissions in Australia and New Zealand. The incidence of OD requiring ICU admission is increasing, and is a source of morbidity and mortality in a relatively young, healthy population. The increasing incidence of OD in the Indigenous population of Australia is a matter of growing concern. Although mortality rates after ICU admission are low, the loss of life-years is substantial. Interventions to prevent future fatalities from OD are urgently needed.

Acknowledgements

We received financial support from the Austin Hospital Intensive Care Trust Fund.

Competing interests

None declared.

Author details

Luca Cioccari, Research Fellow[1] and Intensivist[2]
Nora Luethi, Research Fellow[1]
Michael Bailey, Associate Professor and Biostatistician[3]
David Pilcher, Professor[3] and Adult Patient Database Director[4]
Rinaldo Bellomo, Professor and Director of Intensive Care Research[1] and Co-director[3]

1 Department of Intensive Care, Austin Hospital and University of Melbourne, Melbourne, VIC, Australia.
2 Department of Intensive Care Medicine, Lucerne Cantonal Hospital, Lucerne, Switzerland.
3 Australian and New Zealand Intensive Care Research Centre, School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia.
4 Centre for Outcome and Resource Evaluation, Australian and New Zealand Intensive Care Society, Melbourne, VIC, Australia.

Correspondence: rinaldo.bellomo@austin.org.au

References

1 Centers for Disease Control and Prevention. Vital signs: overdoses of prescription opioid pain relievers — United States, 1999–2008. *MMWR Morb Mortal Wkly Rep* 2011; 60: 1487-92.
2 Bronstein AC, Spyker DA, Cantilena LR Jr, et al. 2011 Annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 29th Annual Report. *Clin Toxicol (Phila)* 2012; 50: 911-1164.
3 Bentur Y, Lurie Y, Cahana A, et al. Poisoning in Israel: annual report of the Israel Poison Information Center, 2007. *Isr Med Assoc J* 2008; 10: 749-56.
4 Henderson A, Wright M, Pond SM. Experience with 732 acute overdose patients admitted to an intensive care unit over six years. *Med J Aust* 1993; 158: 28-30.
5 Weilemann LS, Hilgers HJ, Reckmann A. Current aspects of para-suicidal poisoning. *Med Klin* 1996; 91: 355-8.
6 Lam SM, Lau ACW, Yan WW. Over 8 years experience on severe acute poisoning requiring intensive care in Hong Kong, China. *Hum Exp Toxicol* 2010; 29: 757-65.
7 Gjersing L, Jonassen KV, Biong S, et al. Diversity in causes and characteristics of drug-induced deaths in an urban setting. *Scand J Public Health* 2013; 41: 119-25.
8 Sinyor M, Howlett A, Cheung AH, Schaffer A. Substances used in completed suicide by overdose in Toronto: an observational study of coroner's data. *Can J Psychiatry* 2012; 57: 184-91.
9 Susnjara IM, Smoljanovic A, Gojanovic MD. Drug related deaths in the Split–Dalmatia County 1997–2007. *Coll Antropol* 2011; 35: 823-8.
10 Burillo-Putze G, Munne P, Duenas A, et al. National multicentre study of acute intoxication in emergency departments of Spain. *Eur J Emerg Med* 2003; 10: 101-4.
11 Stow PJ, Hart GK, Higlett T, et al. Development and implementation of a high-quality clinical database: the

Australian and New Zealand Intensive Care Society Adult Patient Database. *J Crit Care* 2006; 21: 133-41.

12 Paul E, Bailey M, Pilcher D. Risk prediction of hospital mortality for adult patients admitted to Australian and New Zealand intensive care units: development and validation of the Australian and New Zealand Risk of Death model. *J Crit Care* 2013; 28: 935-41.

13 McMahon A, Brohan J, Donnelly M, Fitzpatrick GJ. Characteristics of patients admitted to the intensive care unit following self-poisoning and their impact on resource utilisation. *Ir J Med Sci* 2014; 183: 391-5.

14 Liisanantti JH, Ohtonen P, Kiviniemi O, et al. Risk factors for prolonged intensive care unit stay and hospital mortality in acute drug-poisoned patients: an evaluation of the physiologic and laboratory parameters on admission. *J Crit Care* 2011; 26: 160-5.

15 Schwake L, Wollenschlager I, Stremmel W, Encke J. Adverse drug reactions and deliberate self-poisoning as cause of admission to the intensive care unit: a 1-year prospective observational cohort study. *Intensive Care Med* 2009; 35: 266-74.

16 Brandenburg R, Brinkman S, de Keizer NF, et al. In-hospital mortality and long-term survival of patients with acute intoxication admitted to the ICU. *Crit Care Med* 2014; 42: 1471-9.

17 Townsend E, Hawton K, Harriss L, et al. Substances used in deliberate self-poisoning 1985–1997: trends and associations with age, gender, repetition and suicide intent. *Soc Psychiatry Psychiatr Epidemiol* 2001; 36: 228-34.

18 Bateman DN, Bain M, Gorman D, Murphy D. Changes in paracetamol, antidepressants and opioid poisoning in Scotland during the 1990s. *QJM* 2003; 96: 125-32.

19 Furst S, Habscheid W. [Acute poisoning in patients of a medical intensive care unit] [German]. *Dtsch Med Wochenschr* 1993; 118: 849-53.

20 Cengiz M, Baysal Z, Ganidagli S, Altindag A. Characteristics of poisoning cases in adult intensive care unit in Sanliurfa, Turkey. *Saudi Med J* 2006; 27: 497-502.

21 Jamil H, Khan A, Akhtar S, Sultana N. Patients with acute poisoning seen in the department of intensive care — Jinnah Postgraduate Medical Centre, Karachi. *J Pak Med Assoc* 1977; 27: 358-60.

22 Seydaoglu G, Satar S, Alparslan N. Frequency and mortality risk factors of acute adult poisoning in Adana, Turkey, 1997-2002. *Mt Sinai J Med* 2005; 72: 393-401.

23 Tay SY, Tai DY, Seow E, Wang YT. Patients admitted to an intensive care unit for poisoning. *Ann Acad Med Singapore* 1998; 27: 347-52.

24 Charra B, Hachimi A, Benslama A, Motaouakkil S. [Severe acute poisonings in adult in a medical ICU] [French]. *Ann Toxicol Anal* 2013; 25: 7-11.

25 Catto M, Thomson N. Review of illicit drug use among Indigenous peoples. *Aust Indig Health Bull* 2008; 8. http://healthbulletin.org.au/articles/review-of-illicit-drug-use-among-indigenous-peoples (accessed Nov 2017).

26 Nogue S, Marruecos L, Nolla J, et al. The profile evolution of acute severe poisoning in Spain. *Toxicol Lett* 1992; 64-65: 725-7.

27 Ajdacic-Gross V, Weiss MG, Ring M, et al. Methods of suicide: international suicide patterns derived from the WHO mortality database. *Bull World Health Organ* 2008; 86: 726-32.

28 Graham PL, Cook DA. Prediction of risk of death using 30-day outcome: a practical end point for quality auditing in intensive care. *Chest* 2004; 125: 1458-66. ❑