

## SUPPLEMENTARY APPENDIX

**Table S1. Opioid poisoning codes**

ICD-10 codes indicating opioid poisoning, by category:[2]

Description	ICD-10 codes
Poisoning by opium	T40.0
Poisoning by heroin	T40.1
Poisoning by other opioids*	T40.2
Poisoning by methadone	T40.3
Poisoning by synthetic opioid†	T40.4
Poisoning by unspecified/other opioids	T40.6

\*includes codeine, hydromorphone, morphine and oxycodone †includes buprenorphine, fentanyl, pethidine and tramadol

Accidental opioid poisoning was defined by meeting both of the following criteria.

- A hospital admission record is coded with an ICD-10 code opioid poisoning (**T40.0, T40.1, T40.2, T40.3, T40.4, or T40.6**). For hospital admissions related to accidental opioid poisoning, the hospital diagnosis type must also be coded as M (most responsible diagnosis); 1 (pre-admit comorbidity); W, X or Y (service transfer diagnoses); or 6 (proxy most responsible diagnosis).
- The hospital admission record is also coded with an external cause ICD-10 code corresponding to accidental opioid poisoning (**X42, Accidental poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified**). Note: This is distinguished from codes corresponding to intentional self-harm (X62), harm from therapeutic use (Y45.0), or unknown intent (Y12).

**Table S2. Diagnostic codes for exclusions**

Description	ICD-9	ICD-10
Encephalopathy (anoxic brain damage, toxic encephalopathy or unspecified encephalopathy)	348.1, 349.82	G93.1, G92, G93.4
Acute respiratory distress syndrome (ARDS)	518.82	J80
Respiratory failure	518.81	J96.0, J96.9
Pulmonary hemorrhage	770.3	R04.8

Aspiration pneumonia	507.0	J69.0
Cardiac arrest	427.5	I46
Ventricular arrhythmia	427.1, 427.4	I47.0, I47.2, I49.0
Heart failure	428	I50
Rhabdomyolysis	728.88	M62.8, T79.6
Paraplegia or tetraplegia	344.0, 344.1	G82
Acute renal failure	584	N17
Intentional self-harm	n/a†	X60 – X84

†Only hospital diagnoses were used for identifying intentional self-harm, because E-codes which could be used are only supplementary codes and MSP data are typically coded with only one diagnostic code.

**Table S3. Diagnostic codes for outcomes**

Type of outcome	Diagnosis	ICD-10 Codes
Neurological	Encephalopathy (anoxic brain damage, toxic encephalopathy or unspecified encephalopathy)	G93.1, G92, G93.4
Pulmonary	Adult respiratory distress syndrome (ARDS)	J80
	Respiratory failure	J96.0, J96.9
	Pulmonary hemorrhage	R04.8
	Aspiration pneumonia	J69.0
Cardiac	Cardiac arrest	I46
	Ventricular arrhythmia	I47.0, I47.2, I49.0
	Heart failure	I50
Other	Rhabdomyolysis	M62.8, T79.6
	Paraplegia or tetraplegia	G82
	Acute renal failure	N17

**Table S4. Diagnostic codes for covariates**

Description	Subcategory (if applicable)	ICD codes
Mental or behavioural disorders due to psychoactive substance use	Opioids	ICD-9: 304.0, 304.7, 305.5 ICD-10: F11
	Sedatives and hypnotics	ICD-9: 304.1, 305.4 ICD-10: F13
	Stimulants	ICD-9: 304.2, 305.6, 304.4, 305.7 ICD-10: F14, F15
	Other (alcohol, cannabinoids, hallucinogens, volatile solvents, multiple drug use or use of other psychoactive substances)	ICD-9: 303, 304.3, 304.5, 304.6, 304.8, 304.9, 305.0, 305.2, 305.3, 305.8, 305.9 ICD-10: F10, F12, F16, F18, F19
Other psychiatric illness	Depression	ICD-9: 311, 296.2, 296.3 ICD-10: F32, F33
	Bipolar disorder/ mixed mania	ICD-9: 296.0, 296.1, 296.4, 296.9 ICD-10: F31
	Schizophrenia	ICD-9: 295 ICD-10: F20
	Personality disorders	ICD-9: 301 ICD-10: F60
	Other psychosis	ICD-9: 297 - 299 ICD-10: F21 – F29
	Pneumonia (excluding aspiration pneumonia)	ICD-9: 480-486, 487.0 ICD-10: J10.0, J11.0, J12-J18
	Other respiratory illness	COPD
Asthma		ICD-9: 493 ICD-10: J45
Sleep apnea		ICD-9: 327.23, 780.57 ICD-10: G47.3, P28.3
HIV disease		ICD-9: 042 ICD-10: B20-B24
Hepatitis B	ICD-9: 070.2, 070.3 ICD-10: B16, B18.0, B18.1	
Hepatitis C	ICD-9: 070.41, 070.44, 070.51, 070.54, 070.7 ICD-10: B17.1, B18.2	
Cancer	ICD-9: 140-208, 209.0-209.3 ICD-10: C00-C96	

**Table S5. Prescription opioids**

Opioids indicated for pain treatment	Opioid substitution medications
Buprenorphine (patch only)	Buprenorphine/ naloxone (trade name: Suboxone)
Codeine	Methadone
Fentanyl	
Hydromorphone	
Pethidine (also known as: meperidine)	
Morphine	
Oxycodone	
Tapentadol	
Tramadol	

**Table S6.** Influence of readmission for accidental opioid overdose and covariates on encephalopathy, compared to initial admission

Predictor variable		Adjusted OR (95% CI)	
<b>Exposure</b>			
Repeat admission (vs initial admission)		0.57 (0.13, 2.49)	
<b>Covariates</b>			
Sex	Female	0.46 (0.26, 0.81)	
	Male	1.00	
Age (years)	Under 25	1.02 (0.45, 2.28)	
	25 to 39	1.35 (0.72, 2.54)	
	40 to 49	1.00	
	50 to 59	0.55 (0.24, 1.24)	
	60 to 69	0.27 (0.07, 1.00)	
	70 or above	0.11 (0.02, 0.76)	
Cohort entry year	2006	1.00	
	2007	0.28 (0.05, 1.41)	
	2008	0.52 (0.15, 1.82)	
	2009	0.55 (0.15, 1.97)	
	2010	0.27 (0.05, 1.32)	
	2011	0.77 (0.27, 2.19)	
	2012	1.08 (0.41, 2.87)	
	2013	0.73 (0.27, 2.01)	
	2014	0.51 (0.17, 1.47)	
Income	2015	0.73 (0.28, 1.89)	
	Low income	0.44 (0.21, 0.92)	
	Mid to high income	1.00	
	Residence	Rural	0.47 (0.17, 1.32)
		Urban	1.00
Substance use disorders*	Opioids	0.76 (0.29, 2.03)	
	Sedatives and hypnotics	0.83 (0.44, 1.58)	
	Stimulants	0.77 (0.24, 2.53)	
Romano comorbidity score*	Zero	0.95 (0.51, 1.75)	
	1 to 2	1.00	
	3 or more	0.74 (0.20, 2.75)	
Other medical history*	Psychiatric illness	0.84 (0.48, 1.48)	
	Pneumonia	1.56 (0.60, 4.08)	
	Other respiratory illness	0.79 (0.35, 1.78)	
	Cancer	2.55 (0.66, 9.82)	
Opioid prescription history†	High dose opioid for pain	0.32 (0.10, 0.97)	
	Low to intermediate dose for pain	1.00	
	No use of opioids for pain	0.95 (0.55, 1.64)	
Other prescription history†	Sedatives and hypnotics	0.65 (0.30, 1.42)	

Readmissions are defined as additional accidental opioid overdose admissions within 365 days of prior admission. \*Based on diagnoses at a physician or hospital visit in the 365 days before opioid overdose. †Based on dispensings in the 180 days prior to opioid overdose. High dose opioid use is defined by a dispensing of opioid pain medication of >90 oral morphine equivalents per day.