

# Risk of discharge against medical advice among hospital inpatients with a history of opioid agonist therapy in New South Wales, Australia: a cohort study and nested crossover-cohort analysis

## Authors

Dan Lewer (1, 2), Nicola Jones (1), Matthew Hickman (3), Sarah Larney (1, 4), Nadine Ezard (1, 5), Suzanne Nielsen (6), Louisa Degenhardt (1)

## Affiliations

1. National Drug and Alcohol Research Centre, 22-32 King St, Randwick NSW 2031, Australia
2. Department of Epidemiology and Public Health, University College London, 1-19 Torrington Place, London WC1E 7HB, UK
3. Population Health Sciences, Bristol Medical School, University of Bristol, Bristol BS2 8DZ, UK
4. University of Montreal, 2900 Edouard Montpetit Blvd, Montreal, Quebec H3T 1J4, Canada
5. Alcohol and Drug Service, St Vincent's Hospital, Sydney, NSW, Australia
6. Monash Addiction Research Centre and Eastern Health Clinical School, Monash University, Melbourne, Australia

## Corresponding author contact details

Dan Lewer, [d.lewer@ucl.ac.uk](mailto:d.lewer@ucl.ac.uk), +44 (0) 7766 395 792

Department of Epidemiology and Public Health, University College London, 1-19 Torrington Place, London WC1E 7HB, UK

## Word count

3,191

# Abstract

## Background

People who use illicit opioids have high rates of hospital admission. We aimed to measure the risk of discharge against medical advice among inpatients with a history of opioid agonist therapy (OAT), and test whether OAT is associated with lower risk of discharge against medical advice.

## Methods

We conducted a cohort study including all emergency hospital admissions between 1 August 2001 and 30 April 2018 in New South Wales, Australia, among patients with a previous episode of OAT in the community. The main outcome was discharge against medical advice, and the main exposure was whether patients had an active OAT permit at the time of admission.

## Results

14,035/116,957 (12.0%) admissions ended in discharge against medical advice. Admissions during periods of OAT had 0.79 (0.76-0.83;  $p < 0.001$ ) times the risk of discharge against medical advice, corresponding to an absolute risk reduction of 3.3 percentage points. Risk of discharge against medical advice was higher among patients who were younger, male, identified as Aboriginal and/or Torres Strait Islanders, admitted for accidents, drug-related reasons, or injecting-related injuries (such as cutaneous abscesses), and those discharged at the weekend. In a subsample of 7,793 patients included in a crossover-cohort analysis, OAT was associated with 0.84 (95% CI 0.76-0.93;  $p < 0.001$ ) times the risk of discharge against medical advice.

## **Conclusions**

Among patients with a history of OAT, one in eight emergency hospital admissions ends in discharge against medical advice. OAT enrolment at the time of admission is associated with a reduction of this risk.

## Keywords

Substance-Related Disorders; Opioid-related disorders; Health Services; Hospitalization; Continuity of Patient Care; Patient Discharge

# 1 Introduction

Hospitals usually plan patient discharge to optimise ongoing care. 'Discharge against medical advice' or 'self-discharge' occurs when a patient chooses to leave before a planned discharge date, and is an important marker that some of a patient's needs have not been met. It is consistently associated with poor health outcomes and readmission (Hwang et al., 2003). For example, patients who self-discharged from hospitals in New York had double the risk of death or readmission in the next 30 days, when compared to patients who follow recommended discharge plans (Southern et al., 2012). In general, self-discharge is not common, at 0.6% of hospital discharges in Australia, 1.4% in the US, and 1.3% in Canada (Australian Institute of Health and Welfare, 2019; Canadian Institute for Health Information, 2013; Ibrahim et al., 2007) but the risk is higher for some patient groups. For example, an international literature review found an average of 17% of psychiatric admissions end in self-discharge (Brook et al., 2006), and a hospital in Vancouver that serves an area with a high prevalence of homelessness and illicit drug use reported that 16% of admissions end in self-discharge (Choi et al., 2011).

People who are dependent on illicit opioids have high rates of hospitalisation (Lewer et al., 2019) and high risk of self-discharge (Smith et al., 2015; Ti and Ti, 2015). Qualitative research with people who use illicit opioids has found that possible reasons include poor pain relief, delayed or low-dose opioid substitution, and stigmatising attitudes among some hospital staff (McNeil et al., 2014; Simon et al., 2019; Summers et al., 2018; van Boekel et al., 2013). Patients who use opioids may need higher doses of analgesia, while provision may be conservative due to concerns about safety and 'drug-seeking' (Hines et al., 2008). Lack of opioid substitution can cause patients to experience withdrawal and leave hospital to obtain opioids elsewhere.

Opioid agonist therapy (OAT) is usually prescribed in community settings to prevent withdrawal and the need to use illicit opioids. A large proportion of people who use illicit opioids in Australia have been prescribed opioid agonists either currently or historically, even if only for a short period (Larance et al., 2020). OAT is consistently associated with reduced mortality (Sordo et al., 2017) hospital admission (Lewer et al., 2019) and healthcare costs (Tkacz et al., 2014). There is some evidence that OAT is associated with lower risk of discharge against medical advice, but existing studies draw on small and selected patients groups from single centres (Chan et al., 2004; Suzuki et al., 2020; Ti et al., 2015). This study aims to measure the risk of self-discharge in a complete sample of people who have ever had an OAT permit in New South Wales, Australia, and test whether risk is lower for admissions that happen in periods when patients have an active permit for OAT (i.e. are likely to be currently taking methadone or buprenorphine).

## 2 Methods

### 2.1 Data source and study population

In Australia OAT is dispensed in settings including public and private general practice, community pharmacies, and prisons. The data for this study were drawn from the Opioid Agonist Treatment Safety (OATS) Study, a resource of electronic healthcare databases that includes all opioid agonist permits across these settings between 1 August 2001 and 19 September 2018. A 'permit' is an authority for a clinician to provide opioid agonist drugs to their patient. Patients are linked probabilistically to other datasets including the New South Wales database of admitted patient care. A detailed description of the OATS Study has been published elsewhere (Larney et al., 2018).

The study population was all hospital admissions occurring between 1 August 2001 and 30 April 2018 among patients with a previous OAT permit. Hospital admissions data were available for the full duration of follow-up regardless patients' OAT status (i.e. data were available during periods with no active OAT permit).

We excluded: (1) admissions that occurred before the first OAT permit (as these may have occurred before the individual was dependent on opioids); (2) those that did not end in discharge to the community, including patients who died during the admission and those who were transferred to other hospitals (though subsequent contiguous admissions were included); and (3) those not designated as 'emergency medical admissions' (such routine or planned admissions, or those relating to pregnancy and childbirth). We excluded planned admissions because they are usually short episodes of routine care such as physical rehabilitation or dental treatment, with discharge on the same day as admission, and discharge against medical advice is often unlikely. In this dataset, the most common reason

for planned admission was dialysis (18% of planned admissions) and the median duration of planned admissions was 1 day (IQR 1-4 days).

Figure 1 shows the derivation of the study population.

<< Figure 1: Derivation of the study population >>

## **2.2 Outcome**

Follow-up began at admission to hospital and ended at discharge. The outcome was a binary variable of whether or not admission ended with a discharge against medical advice, defined as 'Discharge Own Risk' recorded under the 'separation mode'. Admission dates, discharge dates, and separation mode were taken from linked hospital admission data.

## **2.3 Exposure**

The main exposure was whether the patient had an OAT permit at the time of admission ('on-OAT' vs. 'off-OAT'). Although we were able to distinguish permits for provision of methadone and buprenorphine, we did not separate these drugs because we had no hypothesis that they would have different effects.

Potential confounders were (a) age at admission; (b) sex; (c) whether the patient identifies as Aboriginal and/or Torres Strait Islander; (d) the primary cause of admission according to ICD-10 code, summarised into: 'drug-related', including withdrawal, intoxication and overdose (Degenhardt et al., 2014); injecting-related injuries & diseases, using a list of presentations relating to bacterial infections that are often related to drug injection: cutaneous abscess, cellulitis, phlebitis, septicaemia, osteomyelitis, endocarditis, necrotising fasciitis (Lewer et al., 2017); other bacterial and viral infections; accidents other than drug-related accidents, including self-harm; mental and behavioural disorders; 'signs and



symptoms', which relates to admissions that have recorded symptoms such as abdominal pain or convulsions, but no formal diagnosis; cancers; and other non-communicable diseases; (e) co-morbidity, measured using the count of unique ICD-10 chapters recorded in any diagnostic position for the admission; and (f) the era of the admission, defined as 2001-2006, 2007-2011 and 2012-2018. The data also allowed us to calculate the length of hospital admissions, but we did not use this as a measure of disease severity because it would introduce overadjustment (because the length of stay is shorter where patients self-discharge). For each of these variables, we also reported the univariable association with discharge against medical advice, and an estimate adjusted for a subset of the other variables. We also reported the association between discharge on a weekend and discharge against medical advice, following evidence that discharge against medical advice may be more common at weekends (Chan et al., 2004), but did not include this variable as a confounder.

## **2.4 Statistical analysis**

We described admissions according to the outcome and independent variables, and plotted the cumulative incidence of discharge against medical advice by the day of admission, using the Kaplan-Meier method and censoring patients at planned discharge. We then used two approaches to estimate the association between OAT and discharge against medical advice. First, we fit a mixed generalised linear model with a binary outcome of whether the admission ended in self-discharge, fixed effects for the exposures, random effects for the patient identifier (to account for individuals contributing multiple admissions), with a Poisson distribution and an offset for the duration of admission (in days). We included a single term for age, standardised so that the coefficient represents the risk ratio associated with an increase of one standard deviation in age.

Second, we conducted a crossover-cohort analysis (Maclure and Mittleman, 2000). This analysis is self-controlled and designed to control time-invariant confounders, such as personality, health, or the degree of drug dependence, which may be difficult to control using measured variables in the main analysis. Patients were eligible for inclusion in this analysis if they had at least one admission during periods both on-OAT and off-OAT (i.e. they 'cross-over' between exposure statuses). We used conditional Poisson regression (Armstrong et al., 2014) to estimate a risk ratio for discharge against medical advice, controlling for potential time-varying confounders: age at admission and the primary cause of admission. Some patients had multiple admissions either on-OAT or off-OAT. We therefore used within-subject pairwise resampling (Luo and Sorock, 2008). This involves random sampling of a single pair of admissions for each patient, one on-OAT and the other off-OAT, and calculating the risk ratio as described above. We repeated this process 10,000 times and calculated the point estimate and standard error by pooling the results.

The only variable used in analysis with missing data was the primary cause of admission. Admissions where this was missing were excluded from analysis (0.3% of admissions). Analysis was conducted using R version 4.0.2.

### 3 Results

The study population was 116,957 hospital admissions from 26,082 individuals. The median age at admission was 39.0; 36% of admissions were among female patients; and 29% among patients identifying as Aboriginal and/or Torres Strait Islander. The derivation of the study population is shown in Fig. 1. The median number of admissions per patient was 2 (IQR 1-5), with a prominent right skew. Patients spent a total of 849,212 days admitted to hospital, with a median duration of 2 days (IQR 3-7). The duration was shorter for patients who self-discharged (median 2 days; IQR 2-4) than other patients (median 3 days; IQR 2-8). 59% (72,008/116,957) of hospital admissions occurred when the patient was in OAT (Table 1).

Table 1: Characteristics of emergency hospital admissions among people with a history of opioid agonist therapy in New South Wales, 2001-2018

Variable	Level	Total N (%)	In OAT N (%)	Out of OAT N (%)
Total		116,957 (100)	72,008 (100)	44,949 (100)
Age	Median (IQR)	39.0 (31.9-46.9)	40.4 (33.2-48.5)	36.8 (30.4-44.3)
Female sex		42,290 (36.2)	26,900 (37.4)	15,390 (34.2)
Aboriginal and/or Torres Strait Islander		34,059 (29.1)	19,423 (27.0)	14,636 (32.6)
Primary cause of admission	Non-communicable diseases	31,125 (26.6)	21,663 (30.1)	9,462 (21.1)
	Drug-related	23,556 (20.1)	12,041 (16.7)	11,515 (25.6)
	Mental health	19,921 (17.0)	10,891 (15.1)	9,030 (20.1)
	Accidents	18,211 (15.6)	11,384 (15.8)	6,827 (15.2)
	Signs and symptoms	12,258 (10.5)	8,244 (11.4)	4,014 (8.9)
	Injecting-related diseases	9,363 (8.0)	6,052 (8.4)	3,311 (7.4)
	Infections	1,843 (1.6)	1,230 (1.7)	613 (1.4)
	Cancers	680 (0.6)	503 (0.7)	177 (0.4)
Comorbidities	0	19,356 (16.5)	10,816 (15.0)	8,540 (19.0)
	1	21,603 (18.5)	13,190 (18.3)	8,413 (18.7)
	2	21,058 (18.0)	12,772 (17.7)	8,286 (18.4)
	3	17,081 (14.6)	10,746 (14.9)	6,335 (14.1)
	4	12,835 (11.0)	8,098 (11.2)	4,737 (10.5)
	5+	25,024 (21.4)	16,386 (22.8)	8,638 (19.2)
Discharged at the weekend		20,453 (17.5)	12,341 (17.1)	8,112 (18.0)
Era	2001-2006	32,493 (27.8)	19,209 (26.7)	13,284 (29.6)
	2007-2011	33,113 (28.3)	19,697 (27.4)	13,416 (29.8)
	2012-2018	51,351 (43.9)	33,102 (46.0)	18,249 (40.6)
Discharged against medical advice		14,035 (12.0)	7,428 (10.3)	6,607 (14.7)

### 3.1 Main analysis

12.0% (14,035/116,957) of admissions ended in self-discharge, with a lower proportion for admissions occurring during periods on-OAT (10.3% vs. 14.7%;  $p < 0.001$ ) and an unadjusted risk ratio of 0.73 (95% CI 0.70-0.76;  $p < 0.001$ ). Risk of discharge against medical advice was greatest on second day of admission (Figure 2). Adjusting for potential confounders gave a risk ratio of 0.79 (0.76-0.83;  $p < 0.001$ ). This equates to an absolute risk reduction of 3.0%. Results of the Poisson regression are shown in Table 2. Self-discharge was associated with younger age at admission (see Supplementary Information for a

visualisation of the association between age and discharge against medical advice); male sex; identification as Aboriginal and/or Torres Strait Islander; admissions caused by accidents, drug-related problems, signs and symptoms, and injecting-related diseases (compared to non-communicable diseases); and being discharged at the weekend.

Admissions caused by mental health problems, infections, and cancers were associated with lower risk of self-discharge (compared to non-communicable diseases). There was a graded relationship between co-morbidity and discharge against medical advice, with lower risk for patients with greater comorbidity.

<< Figure 2: Cumulative incidence of discharge against medical advice among people with a history of opioid agonist therapy, stratified by treatment status at the time of hospital admission >>

Table 2: Risk ratios for discharge against medical advice among inpatients with a history of opioid agonist therapy (results of Poisson regression)

Variable	Level	Unadjusted risk ratio (95% CI)	Adjusted risk ratio <sup>1</sup> (95% CI)
In OAT		0.73 (0.70-0.76)	0.79 (0.76-0.83)
Age <sup>2</sup>		0.72 (0.70-0.74)	-
Female sex		0.78 (0.74-0.83)	-
Aboriginal and/or Torres Strait Islander		1.40 (1.32, 1.49)	-
Primary cause of admission	Non-communicable diseases (ref)	1	1
	Drug-related	1.55 (1.46-1.64)	1.39 (1.31-1.47)
	Mental health	0.37 (0.34-0.40)	0.31 (0.28-0.33)
	Accidents	1.40 (1.32-1.48)	1.78 (1.68-1.90)
	Signs and symptoms	2.30 (2.15-2.45)	1.88 (1.76-2.01)
	Injecting-related diseases	1.09 (1.01-1.17)	1.13 (1.05-1.21)
	Infections	0.83 (0.70-0.99)	0.80 (0.67-0.95)
	Cancers	0.29 (0.20-0.40)	0.43 (0.31-0.61)
Comorbidities	0 (ref)	1	1
	1	0.76 (0.72-0.81)	0.77 (0.72-0.82)
	2	0.72 (0.68-0.76)	0.73 (0.69-0.78)
	3	0.67 (0.62-0.71)	0.68 (0.64-0.73)
	4	0.63 (0.59-0.67)	0.65 (0.60-0.70)
	5+	0.34 (0.32-0.36)	0.36 (0.34-0.38)
Discharged at the weekend		2.63 (2.52-2.75)	2.22 (2.13-2.32)
Era	2001-2006 (ref)	1	1
	2007-2011	0.84 (0.80-0.89)	0.95 (0.90-1.00)
	2012-2018	0.91 (0.86-0.96)	1.17 (1.11-1.24)

- OAT status is adjusted for demographic variables (age, sex, Aboriginal and/or Torres Strait Islander), primary cause of admission, comorbidities, and era. Primary cause of admission is adjusted for demographic variables, comorbidities, and era. Comorbidities and era are adjusted for demographic variables. Weekend is adjusted for all other variables.
- Age is centred and standardised such that the effect size represents the risk ratio associated with an increase of one standard deviation in age. A visualisation of the association between age and the risk of discharge against medical advice is provided in Supplementary Information.

### 3.2 Crossover-cohort analysis

7,793 individuals (30%) had at least one admission both on-OAT and off-OAT, and these individuals had 63,296 admissions (54% of the total). These individuals were similar to

individuals excluded from this analysis in terms of age, sex, Aboriginal and/or Torres Strait Islander status, but had higher risk of discharge against medical advice and substantially more hospitalisations than the sample used in the main analysis. A comparison between the main sample and the crossover-cohort subsample is provided in Supplementary Material. Conditional Poisson regression showed that individuals admitted to hospital during periods on-OAT had 0.84 (95% CI 0.76-0.93;  $p < 0.001$ ) times the risk of self-discharge compared to periods off-OAT, corresponding to an absolute risk reduction of 2.3%.

## 4 Discussion

This study shows that hospital inpatients with a history of opioid dependence have a high risk of discharge against medical advice, and community provision of OAT is associated with a partial reduction of this risk.

### 4.1 Relation to other studies

Studies in North America have observed similar risk of discharge against medical advice in samples of hospital inpatients who use illicit drugs. Out of 11,365 patients with a history of substance misuse admitted to acute hospitals in New York, 1,344 (11.8%) ended in self-discharge (Southern et al., 2012); out of 24,768 admission to hospitals in Canada with a primary cause of 'alcohol or drug abuse' 2,900 (11.7%) ended in self-discharge (Kraut et al., 2013); and out of 287,627 hospital admissions with a primary cause of substance use disorder in the United States, 31,245 (10.9%) ended in self-discharge (Zhu and Wu, 2019). Discharge against medical advice is likely to be even more common among people who inject drugs with, some studies showing that one in four patients self-discharge (Anis et al., 2002; Chan et al., 2004; Ti and Ti, 2015).

We are aware of three studies that have examined the association between OAT and discharge against medical advice. Consistent with our study, two found that OAT is associated with reduced risk of discharge against medical advice (Chan et al., 2004; Ti et al., 2015). The third study did not find evidence of an association, which may have related to low power (Suzuki et al., 2020). These studies had limitations compared to ours in that they focus on small, selected, high-risk groups, and were conducted in single. One used a composite outcome that did not distinguish between hospital admissions during periods on- and off-OAT (Ti et al., 2015).



Several studies have shown that younger age and male sex are associated with discharge against medical advice across different populations; not just people who use illicit drugs (Alfandre, 2009; Anis et al., 2002; Ibrahim et al., 2007; Yong et al., 2013).

## **4.2 Strengths and limitations**

We studied all hospital admissions among people with a previous OAT permit in New South Wales. The data were derived from complete datasets of hospital admissions and OAT permits in the state, which may increase the generalisability of our results to other populations who are dependent on opioids (as the study is not based on a specific population subgroup). We used two methods of estimating the association between OAT and self-discharge, with both finding reduced risk when hospital admissions occurred during periods on-OAT. The self-controlled method used a selected subsample of participants and the estimates are not directly comparable to the main analysis. The slightly smaller effect size in the self-controlled analysis may relate to residual confounding in the main analysis, or reduced benefit of OAT due to less consistent engagement with treatment in this group. The use of both approaches allowed us to show that the benefit of OAT was robust in different study designs.

There are four key limitations. First, we were unable to measure OAT provision in hospitals. Patients are not usually allowed to use their own medications in hospital, and in Australia many OAT patients receive daily doses (hence would not be able to stockpile medication for a hospital admission anyway). OAT provided in hospitals is not well-recorded in our dataset, meaning we did not know if OAT was continued during admissions. We were therefore unable to assess the effect of OAT provided in hospital on the risk of discharge against medical advice.

Second, our sample is limited to people with at least one episode of OAT, and excludes people who are dependent on opioids but have never engaged with OAT. Australia has high coverage of OAT. In a community-recruited sample of people who inject drugs in Melbourne, for example, only one in four had never been prescribed an opioid agonist, and this study explicitly aimed to recruit participants with limited contact with drug treatment services (Horyniak et al., 2013). In addition, patients only need to receive one OAT permit to appear in the dataset (and do not need to formally start OAT treatment). Given this high coverage, the sample is likely to be reasonably representative of people who use illicit opioids in Australia, though the relatively small group that is excluded may differ in important ways.

Third, we were unable to measure the degree of opioid dependence at the point of hospital admission. People who use illicit opioids such as heroin have various trajectories of drug use. Onset is typically in the late teens or early 20s, and studies with long follow-up suggest that drug use can last decades (Oppenheimer et al., 1994). During this time people may have varying or episodic drug use and engagement with OAT. We have used this variation (and the fact that individuals have periods 'off-OAT' that can act as control periods) to estimate the association between OAT and discharge against medical advice. However, reasons for being 'off-OAT' may vary. For some people, engagement with an OAT programme may occur during more stable periods of life, with time off-OAT being more chaotic periods of illicit drug use. Other people may stop needing OAT during more stable periods of life when they are not using illicit opioids. Hence, the association between OAT and discharge against medical advice may be biased toward the null by cessation of drug use during periods off-OAT.

Fourth, our data did not include information about the hospital where patients were admitted. This meant we were unable to describe differences between hospitals, or account for clustering of patients in hospitals in our analysis.

### 4.3 Policy relevance

People who use opiates have poor experiences of healthcare, and discharge against medical advice is an indication that some of a patient's needs have not been met. This study shows that people in NSW with a history of opioid dependence have a high risk of discharge against medical advice, and that community-prescribed OAT is associated with reduced risk compared to patients not enrolled in OAT at the time of admission. We did not have information about OAT continuation between the community and hospital, but believe that reduced risk of self-discharge during periods on-OAT relates to OAT provision in hospital and therefore reduced risk of withdrawal. This supports investigation of programmes that aim to improve timeliness and continuity of OAT between the community and hospitals, or initiate OAT in hospital. Hospital clinicians in Canada reported a case where a patient was retained through injectable OAT, which may be helpful for patients with more severe dependence (McAdam et al., 2020).

The results highlight sub-groups who are at particularly high risk of self-discharge, and may suggest that 'acute' presentations have higher risk of self-discharge. Injecting-related injuries, accidents, drug-related problems, and 'signs and symptoms' had the highest cumulative incidence (Supplementary Information). Where patients have bacterial infections, self-discharge may lead to incomplete antibiotic courses, antibiotic resistance, and serious sequelae such as invasive infections.

The results also show that discharge at the weekend is associated with higher risk of discharge against medical advice. Previous studies in Canada have shown that risk of self-discharge varies through the week, and is higher at the weekend (Anis et al., 2002; Chan et al., 2004). The weekly distribution of admissions and discharges, and the risk of self-discharge, is shown graphically in Supplementary Information. Admissions were spread evenly across the week, with risk of discharge against medical advice not varying by day of

admission. In contrast, there were fewer discharges at weekends than on weekdays, suggesting that patients are held in hospital for longer at weekends. This may result from limited availability of staff to complete treatment and arrange discharge. It may also be because drug and alcohol liaison teams are not working at weekends, leading to delays in OAT provision in hospital.

#### **4.4 Conclusion**

Among patients with a history of opioid dependence, one in eight hospital admissions ends in discharge against medical advice, compared to approximately one in a hundred in the general population. Opioid agonist therapy is associated with a reduction of this risk. Future research should (a) investigate the quality of OAT in hospital for patients who are prescribed OAT in the community, and (b) develop interventions that can improve the quality of OAT in hospitals and test whether they reduce the risk of discharge against medical advice.

## 5 Additional information

### 5.1 Contributions

Conceptualisation: LD. Study design: DL, NJ, MH, SL, NE, SN & LD. Data curation: NJ and DL. Formal analysis: NJ and DL. Original draft preparation: DL. Review and editing: DL, NJ, MH, SL, NE, SN & LD.

### 5.2 Declarations of interest

MH reports honoraria for speaking at meetings from Gilead, Abbvie, and MSD. SN reports research funding (untied educational grants) from Indivior and Seqirus, and her institution has received honoraria from Indivior for delivery of training on opioid dependence. LD reports untied educational grant funding to conduct studies of new opioid medications in Australia from Indivior, Mundipharma, Seqirus and Reckitt Benckiser.

### 5.3 Funding

DL is funded by the National Institute of Health Research (NIHR) [Doctoral Research Fellowship DRF-2018-11-ST2016]. MH acknowledges funding from NIHR Health Protection Research Unit (HPRU) in Behavioural Science and Evaluation, NIHR School of Public Health Research (SPHR), and NIHR Biomedical Research Centre (BRC) at Bristol. This paper presents independent research. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care. The OATS study is funded by the National Institutes of Health (R01 DA144740 PI: Degenhardt). LD is supported by an Australian National Health and Medical Research Council Senior Principal Research Fellowship. The National Drug and Alcohol Research Centre is supported by funding from the Australian Government Department of Health under the Drug and Alcohol Program.

### 5.4 Acknowledgements

This research article was reviewed by the OATS Aboriginal reference group, including Alan Bennett, Doug James, Kim Sullivan, and Craig Vaughan. Record linkage was conducted by the NSW Ministry of Health and the Centre for Health Record Linkage. The Cause of Death Unit Record File (COD URF) is provided by the Australian Coordinating Registry for the COD URF on behalf of the NSW Registry of Births Deaths and Marriages, NSW Coroner and the National Coronial Information System.

## **5.5 Ethics and approvals**

This study is approved by the NSW Population and Health Services Research Ethics Committee (2018/HRE0205) and Aboriginal Health and Medical Research Council Research Ethics Committee (1400/18).

## **5.6 Data sharing**

Data from the OATS study is not publicly available, in accordance with the project's research governance. Researchers interested in using data from OATS should contact the study team: <https://ndarc.med.unsw.edu.au/project/opioid-agonist-treatment-and-safety-oats-study>

## 6 References

- Alfandre, D.J., 2009. "I'm Going Home": Discharges Against Medical Advice. *Mayo Clin. Proc.* 84, 255–260. doi:10.4065/84.3.255
- Anis, A.H., Sun, H., Guh, D.P., Schechter, M.T., O'Shaughnessy, M.V., 2002. Leaving hospital against medical advice among HIV-positive patients. *CMAJ* 167.
- Armstrong, B.G., Gasparrini, A., Tobias, A., 2014. Conditional Poisson models: a flexible alternative to conditional logistic case cross-over analysis. *BMC Med. Res. Methodol.* 14. doi:10.1186/1471-2288-14-122
- Australian Institute of Health and Welfare, 2019. Admitted patient care 2017-18. <https://www.aihw.gov.au/reports/hospitals/admitted-patient-care-2017-18/contents/at-a-glance> (accessed: 19 November 2019)
- Brook, M., Hilty, D.M., Liu, W., Hu, R., Frye, M.A., 2006. Discharge Against Medical Advice From Inpatient Psychiatric Treatment: A Literature Review. *Psychiatr. Serv.* 57, 7.
- Canadian Institute for Health Information, 2013. Leaving Against Medical Advice: Characteristics Associated With Self-Discharge. [https://secure.cihi.ca/free\\_products/LAMA\\_aib\\_oct012013\\_en.pdf](https://secure.cihi.ca/free_products/LAMA_aib_oct012013_en.pdf) (accessed: 10 February 2020)
- Chan, A.C.H., Palepu, A., Guh, D.P., Sun, H., Schechter, M.T., O'Shaughnessy, M.V., Anis, A.H., 2004. HIV-Positive Injection Drug Users Who Leave the Hospital Against Medical Advice: The Mitigating Role of Methadone and Social Support. *JAIDS J. Acquir. Immune Defic. Syndr.* 35, 56–59. doi:10.1097/00126334-200401010-00008
- Choi, M., Kim, H., Qian, H., Palepu, A., 2011. Readmission Rates of Patients Discharged against Medical Advice: A Matched Cohort Study. *PLoS ONE* 6, e24459. doi:10.1371/journal.pone.0024459
- Degenhardt, L., Larney, S., Randall, D., Burns, L., Hall, W., 2014. Causes of death in a cohort treated for opioid dependence between 1985 and 2005: Mortality among opioid-dependent people. *Addiction* 109, 90–99. doi:10.1111/add.12337
- Hines, S., Theodorou, S., Williamson, A., Fong, D., Curry, K., 2008. Management of acute pain in methadone maintenance therapy in-patients. *Drug Alcohol Rev.* 27, 519–523. doi:10.1080/09595230802245519
- Horyniak, D., Higgs, P., Jenkinson, R., Degenhardt, L., Stoové, M., Kerr, T., Hickman, M., Aitken, C., Dietze, P., 2013. Establishing the Melbourne injecting drug user cohort study (MIX): rationale, methods, and baseline and twelve-month follow-up results. *Harm. Reduct. J.* 10, 11. doi:10.1186/1477-7517-10-11
- Hwang, S.W., Li, J., Gupta, R., Chien, V., Martin, R.E., 2003. What happens to patients who leave hospital against medical advice? *CMAJ* 168.
- Ibrahim, S.A., Kwok, C.K., Krishnan, E., 2007. Factors Associated With Patients Who Leave Acute-Care Hospitals Against Medical Advice. *Am. J. Public Health* 97, 2204–2208. doi:10.2105/AJPH.2006.100164
- Kraut, A., Fransoo, R., Olafson, K., Ramsey, C.D., Yogendran, M., Garland, A., 2013. A population-based analysis of leaving the hospital against medical advice: incidence and associated variables. *BMC Health Serv. Res.* 13, 415. doi:10.1186/1472-6963-13-415
- Larance, B., Degenhardt, L., Grebely, J., Nielsen, S., Bruno, R., Dietze, P., Lancaster, K., Larney, S., Santo, T., Shanahan, M., Memedovic, S., Ali, R., Farrell, M., 2020. Perceptions of extended-release buprenorphine injections for opioid use disorder among people who regularly use opioids in Australia. *Addiction* 115, 1295–1305. doi:10.1111/add.14941
- Larney, S., Hickman, M., Fiellin, D.A., Dobbins, T., Nielsen, S., Jones, N.R., Mattick, R.P., Ali, R., Degenhardt, L., 2018. Using routinely collected data to understand and predict adverse outcomes in opioid agonist treatment: Protocol for the Opioid Agonist Treatment Safety (OATS) Study. *BMJ Open* 8, e025204. doi:10.1136/bmjopen-2018-025204

- Lewer, D., Freer, J., King, E., Larney, S., Degenhardt, L., Tweed, E.J., Hope, V.D., Harris, M., Millar, T., Hayward, A., Ciccarone, D., Morley, K.I., 2019. Frequency of healthcare utilisation by adults who use illicit drugs: a systematic review and meta-analysis. *Addiction* 148, 14892. doi:10.1111/add.14892
- Lewer, D., Harris, M., Hope, V., 2017. Opiate Injection–Associated Skin, Soft Tissue, and Vascular Infections, England, UK, 1997–2016. *Emerg. Infect. Dis.* 23, 1400–1403. doi:10.3201/eid2308.170439
- Luo, X., Sorock, G.S., 2008. Analysis of recurrent event data under the case-crossover design with applications to elderly falls. *Stat. Med.* 27, 2890–2901. doi:10.1002/sim.3171
- Maclure, M., Mittleman, B., 2000. Should We Use a Case-Crossover Design? *Annu. Rev. Public Health* 21, 193–221. doi:10.1146/annurev.publhealth.21.1.193
- McAdam, M., Brar, R., Young, S., 2020. Initiation of injectable opioid agonist treatment in hospital: A case report. *Drug Alcohol Rev.* 39, 138–141. doi:10.1111/dar.13020
- McNeil, R., Small, W., Wood, E., Kerr, T., 2014. Hospitals as a ‘risk environment’: An ethno-epidemiological study of voluntary and involuntary discharge from hospital against medical advice among people who inject drugs. *Soc. Sci. Med.* 105, 59–66. doi:10.1016/j.socscimed.2014.01.010
- Oppenheimer, E., Tobutt, C., Taylor, C., Andrew, T., 1994. Death and survival in a cohort of heroin addicts from London clinics: a 22-year follow-up study. *Addiction* 89, 1299–1308. doi:10.1111/j.1360-0443.1994.tb03309.x
- Simon, R., Snow, R., Wakeman, S., 2019. Understanding why patients with substance use disorders leave the hospital against medical advice: A qualitative study. *Subst. Abuse* 1–7. doi:10.1080/08897077.2019.1671942
- Smith, M.W., Stocks, C., Santora, P.B., 2015. Hospital Readmission Rates and Emergency Department Visits for Mental Health and Substance Abuse Conditions. *Community Ment. Health J.* 51, 190–197. doi:10.1007/s10597-014-9784-x
- Sordo, L., Barrio, G., Bravo, M.J., Indave, B.I., Degenhardt, L., Wiessing, L., Ferri, M., Pastor-Barriuso, R., 2017. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ* 357. doi:10.1136/bmj.j1550
- Southern, W.N., Nahvi, S., Arnsten, J.H., 2012. Increased Risk of Mortality and Readmission among Patients Discharged Against Medical Advice. *Am. J. Med.* 125, 594–602. doi:10.1016/j.amjmed.2011.12.017
- Summers, P.J., Hellman, J.L., MacLean, M.R., Rees, V.W., Wilkes, M.S., 2018. Negative experiences of pain and withdrawal create barriers to abscess care for people who inject heroin. A mixed methods analysis. *Drug Alcohol Depend.* 190, 200–208. doi:10.1016/j.drugalcdep.2018.06.010
- Suzuki, J., Robinson, D., Mosquera, M., Solomon, D.A., Montgomery, M.W., Price, C.D., Johnson, J.A., Martin, B., Liebschutz, J.W., Schnipper, J.L., Weiss, R.D., 2020. Impact of Medications for Opioid Use Disorder on Discharge Against Medical Advice Among People Who Inject Drugs Hospitalized for Infective Endocarditis. *Am. J. Addict.* 29, 155–159. doi:10.1111/ajad.13000
- Ti, L., Milloy, M.-J., Buxton, J., McNeil, R., Dobrer, S., Hayashi, K., Wood, E., Kerr, T., 2015. Factors Associated with Leaving Hospital against Medical Advice among People Who Use Illicit Drugs in Vancouver, Canada. *PLOS ONE* 10, e0141594. doi:10.1371/journal.pone.0141594
- Ti, Lianping, Ti, Lianlian, 2015. Leaving the Hospital Against Medical Advice Among People Who Use Illicit Drugs: A Systematic Review. *Am. J. Public Health* 105, e53–e59. doi:10.2105/AJPH.2015.302885
- Tkacz, J., Volpicelli, J., Un, H., Ruetsch, C., 2014. Relationship Between Buprenorphine Adherence and Health Service Utilization and Costs Among Opioid Dependent Patients. *J. Subst. Abuse Treat.* 46, 456–462. doi:10.1016/j.jsat.2013.10.014
- van Boekel, L.C., Brouwers, E.P.M., van Weeghel, J., Garretsen, H.F.L., 2013. Stigma among health professionals towards patients with substance use disorders and its consequences for healthcare delivery: Systematic review. *Drug Alcohol Depend.* 131, 23–35. doi:10.1016/j.drugalcdep.2013.02.018



- Yong, T.Y., Fok, J.S., Hakendorf, P., Ben-Tovim, D., Thompson, C.H., Li, J.Y., 2013. Characteristics and outcomes of discharges against medical advice among hospitalised patients: Outcomes of self-discharges. *Intern. Med. J.* 43, 798–802. doi:10.1111/imj.12109
- Zhu, H., Wu, L.-T., 2019. Discharge against medical advice from hospitalizations for substance use disorders: The potential impact of the Affordable Care Act. *Drug Alcohol Depend.* 197, 115–119. doi:10.1016/j.drugalcdep.2018.12.032

**Hospital admissions in NSW between 1 August 2001 and 30 April 2018 where the patient had at least one episode of OAT in the community**

254,703 admissions; 35,386 patients

**Admissions prior to first known OAT episode**

32,266 admissions

**Admissions after first OAT episode**

222,437 admissions; 32,601 patients

**Not discharged to the community**

1. Died during admission: 1,662 admissions
2. Transferred to another hospital: 4,987 admissions
3. Still admitted at the end of follow-up: 245 admissions

**Discharged to community**

215,543 admissions; 32,270 patients

**Admissions due to ineligible primary causes**

1. Planned admissions: 92,161 admissions
2. Pregnancy, childbirth (XV): 3,085 admissions
3. 'Factors influencing health status' (XXI): 1,574 admissions
4. Unknown primary cause: 631 admissions

**Emergency admissions due to accidents, medical, mental health, or drug-related causes**

116,959 admissions; 26,264 patients

**Invalid data**

Linked mortality data show death prior to discharge alive: 2 admissions

**Dataset for main analysis**

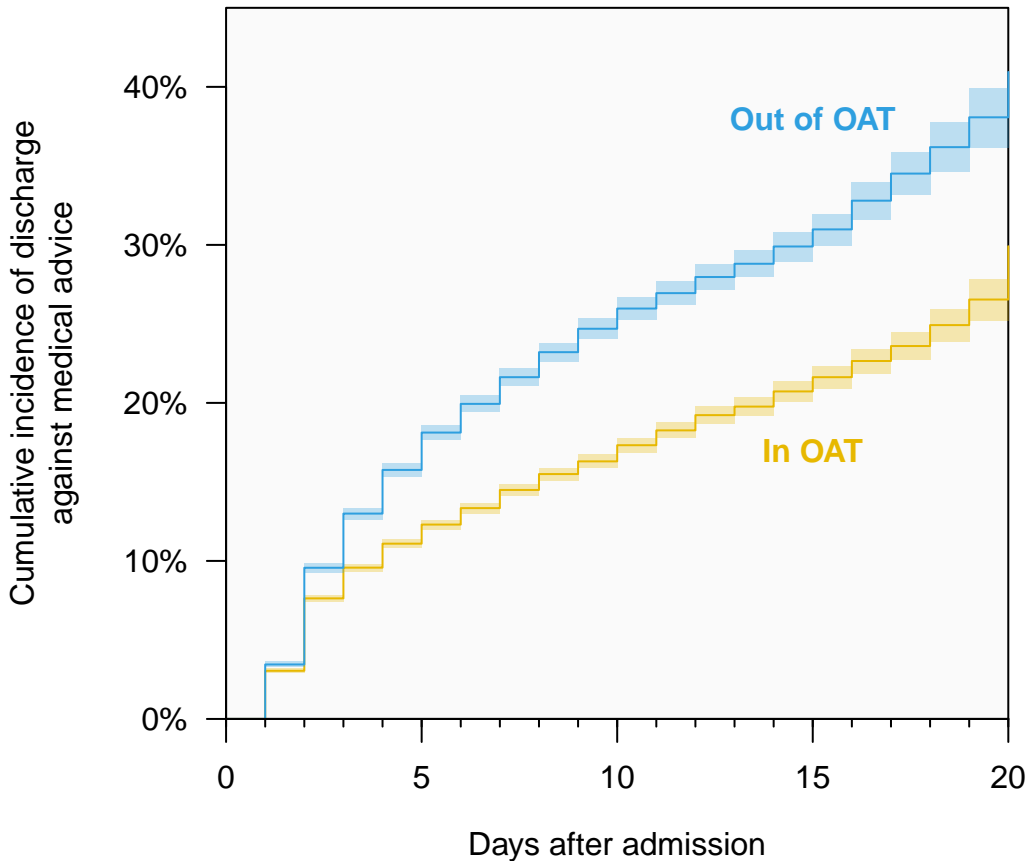
116,957 admissions; 26,082 patients

**Not included in crossover cohort sub-analysis**

Patients with admissions only 'on' or 'off' of OAT: 53,661 admissions

**Dataset for crossover cohort sub-analysis**

62,296 admissions; 7,793 patients



**Number at risk**

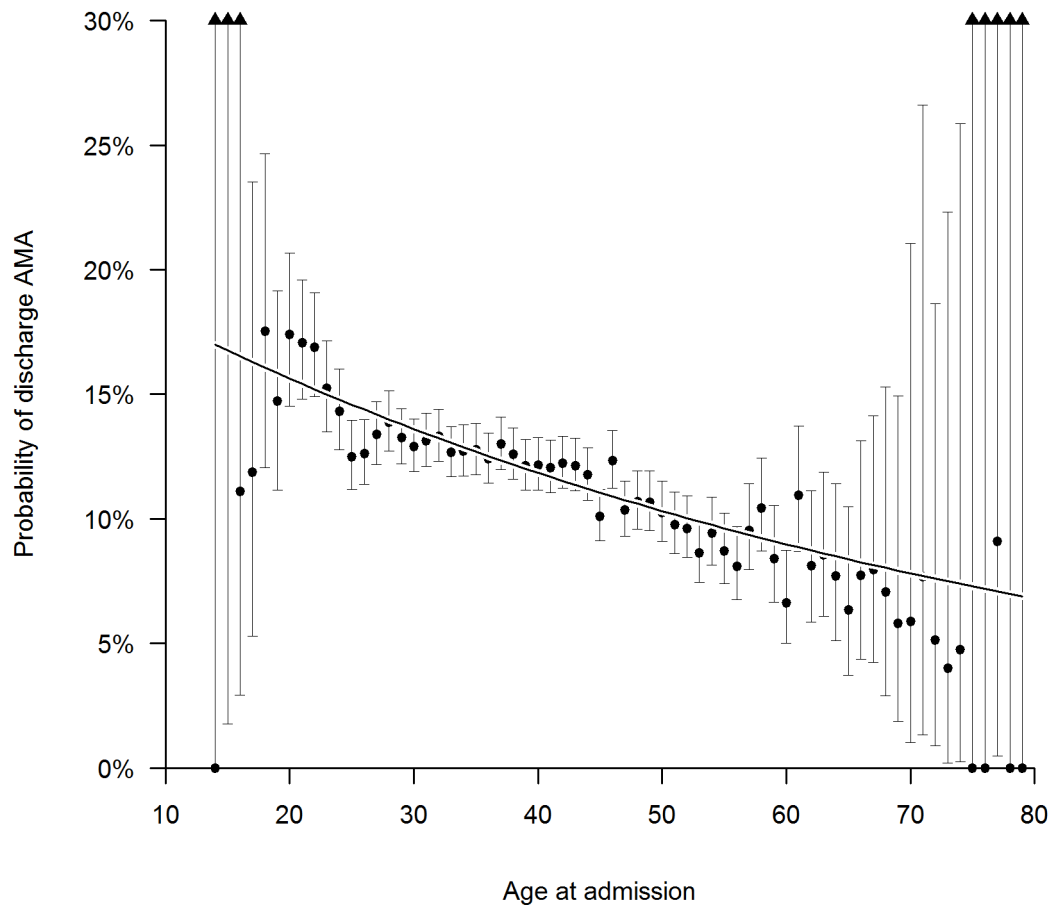
<b>Out of OAT</b>	72,008	23,258	7,946	2,904	305
<b>In OAT</b>	44,949	14,208	4,299	1,490	151

# Supplementary material

1. Visualisation of the association between age and discharge against medical advice
2. Comparison of participants included in the crossover-cohort sub-analysis with those not included
3. Discharge against medical advice by weekday of admission and discharge
4. Cumulative incidence of discharge against medical advice by primary cause of admission

# 1. Visualisation of the association between age and discharge against medical advice

Figure S1: Association between age and discharge against medical advice. Points show the risk by single-year-of-age with 95% confidence intervals, and the line shows the predicted risk based on the Poisson regression model used in the main analysis.



## 2. Comparison of participants included in the crossover-cohort sub-analysis with those not included

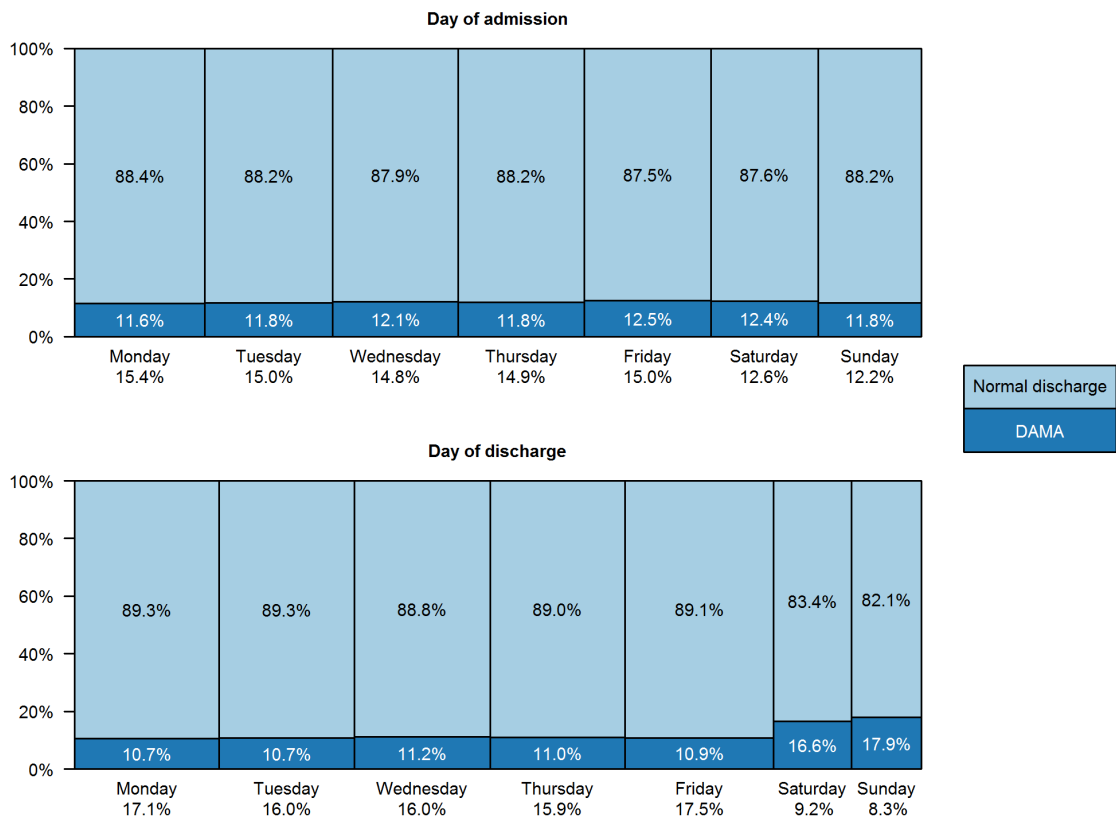
Table S1: Comparison of participants included in the crossover-cohort sub-analysis with those not included

	<b>Excluded from crossover-cohort</b>	<b>Included in crossover-cohort</b>
Number of patients	18,470	7,793
Mean follow-up time (sd)	8.0 (5.1)	10.7 (4.5)
Mean age (sd)	38.1 (10.0)	34.5 ( 9.1)
Number of female patients	6,064 (32.8%)	2,729 (35.0%)
Aboriginal and/or Torres Strait Islander	4,104 (22.2%)	2,283 (29.3%)
Mean number of hospital admissions (sd)	2.9 (3.9)	8.1 (8.8)
Rate of hospital admission per 100 person-years*	36.5	75.8

\* The numerator is the count of hospital admissions eligible for inclusion in this study, and the denominator is the number of years between the first OAT episode and the end of the time period in which eligible hospital admissions could occur (death or 30 June 2018).

### 3. Discharge against medical advice by weekday of admission and discharge

Figure S2: Risk of discharge against medical advice by day of discharge and day of admission. The width of the bars is proportional to the number of discharges / admissions (e.g. 15.4% of patients were admitted on a Monday), and the dark section of the bar represents the proportion that discharged against medical advice (e.g. 11.5% of patients admitted on a Monday discharged against medical advice).



## 4. Cumulative incidence of discharge against medical advice by primary cause of admission

Figure S3: cumulative incidence of discharge against medical advice by primary cause of admission, days 1-21 of admission, using the Kaplan-Meier method with censoring at planned discharge. Error bars are 95% confidence intervals.

