OPEN ACCESS

ISSN: 3069-1192

Mahaveer SS, et al. (2025): 21-28
Ameri J Reg Anes Pain Med; 2(4): 100102
DOI: 10.71010/3069-1192/ajrapm-e102

Research Article

American Journal of Regional Anesthesia & Pain Medicine

Assessing Patient Discharges with Opioid Analgesia and Development of Iatrogenic Chronic Opioid Use in The United Kingdom (UK): Single Centre and Department Retrospective Cohort Study

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Abstract

Background: The impact of opioid prescriptions leading to long-term use/dependence has not been extensively assessed in the United Kingdom. The aim is to assess the number of opioid-naïve patients discharged on opioids, assess the proportion of patients regularly using opioids 3- and 6-months post-discharge, and assess variables correlating with discharge on opioid analgesia and persistent use.

Method: A retrospective cohort study conducted in accordance with STROBE Guidelines in general/emergency surgery department at a single NHS trust. The study population included opioid-naïve adult (>18 years-old) patients discharged by Buckinghamshire Healthcare NHS Trust General Surgery Department between 1st September 2022 and 30th September 2022. The main outcome measures included the number of patients discharged on any opioid medication, number of patients continuing opioid medication at 3- and 6-months post discharge. Descriptive, Chi^2 and tetrachoric (TC) statistical analyses were conducted accordingly.

Results: 391 patients were discharged in September 2022. 75 admissions were elective and 316 emergencies. 216 cases were managed surgically and 175 conservatively. 48 surgical cases involved laparotomy and 92 laparoscopies. 95 patients were discharged with opioid analgesia (85 codeine, 2 oxycodone, 3 morphine, 5 tramadol). TC analyses showed an association between opioids and admission type (TC=-0.85, correlating with emergency), management (TC=-0.99, correlating with conservative), and surgery type (TC=-0.97, correlating with laparoscopy). At 3- and 6-months post-discharge, 5(5%) patients had continued opioid use.

Conclusion: A significant portion of surgical patients are discharged on opioids. Future studies will examine for continued opioid use 6 and 12-months post-discharge. We found that approximately 5% of patients discharged on opioids following emergency or elective procedure under general surgery will develop chronic use. Discharge with opiates correlates with the type and urgency of surgery. Further work is required to assess the extent of iatrogenic opioid use in the UK.

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Citation: Mahaveer SS, Pooja S, Shoomena A, William E, Vrettos I, et al. (2025) Assessing Patient Discharges with Opioid Analgesia and Development of Iatrogenic Chronic Opioid Use in The United Kingdom (UK): Single Centre and Department Retrospective Cohort Study. *Ameri J Reg Anes Pain Med*: AJRAPM-102.

Received Date: 29 January, 2025; **Accepted Date:** 04 February, 2025; **Published Date:** 10 February, 2025

Keywords: opiate, surgery, analgesia, addiction, chronic.

Introduction

Post-operative pain management presents a clinical equipoise between judicious pain control with potent opioids and the risk of addiction. In 2017/18, 12.8% of the adult population in England were prescribed opioids (excluding treatment for cancer pain) [1].

Prior to the COVID-19 pandemic, an increasing volume of surgery was performed on an out-patient basis, putting onus on patients to independently manage their pain and weaning without direct guidance from healthcare professionals [2]. Worryingly, a mismatch between prescribed opioids and actual opioid use has enabled unregulated opioid availability in the community [3]. Indeed, a study from Ontario, Canada investigated 2833 opioid-related deaths over a 4-year-period and found half of all deaths involved prescription opioids (both prescribed and diverted) [4]. Literature from North America on chronic opioid use and related increase in opioid related deaths secondary to inappropriate prescribing has coined this phenomenon the 'opioid epidemic'.

New persistent opioid use in US adult surgical patients without opioid use the year before surgery was found to be 6% compared with 4% in a non-operative control cohort [5]. The adverse effects of opioids are manifold, from dependence [6] to opioid induced hyperalgesia [7], and in extreme cases opioid-induced respiratory depression and fatality [8]. From a public health perspective, there are also economic costs in increased use of healthcare and lost productivity. Opioids should ideally not be the first-line analgesic therapy administered, as per the WHO pain ladder, and use of non-opioid adjuvant medication and techniques such as regional anaesthesia can be integral in reducing post-operative opioid use.

The peri-operative period is an important driver of new persistent opioid use. The aims of this single-centre retrospective cohort were to preliminarily 1) assess the number of opioid-naïve patients who were discharged on opioids from the General/Emergency Surgery Department at Buckinghamshire Healthcare NHS Trust in September 2022, 2) assess the proportion of these patients still regularly using opioids 3- and 6-months post-discharge, and 3) assess for variables associated with discharge on opioid analgesia and persistent use 3- and 6-months post-discharge.

Methods

Study Design

The design of this retrospective cohort study was conducted in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) Guidelines [9].

Structure of the General/Emergency Surgery Unit and Pain Team

The Emergency Surgery Unit at Stoke Mandeville Hospital consists of two dedicated wards with 40 beds in total, a Surgical Assessment Unit where stable 'fit-to-sit' patients are assessed, and between one and two emergency theatre lists operating at one time. The emergency surgery unit manages both upper and lower gastrointestinal surgical emergencies, vascular surgery is not present, endocrine and breast surgery is conducted electively at the sister site - Wycombe General Hospital. High-dependency and intensive care facilities are available as required at both sites. Patients admitted are generally clerked by a Foundation Doctor or Core Trainee (between one and four-years post-medical qualification) under supervision of a specialist trainee (between 5 years post-medical qualification and immediately pre-completion of training/consultancy). This involves conducting a formal clinical examination, gathering of a patient's history (including previous medical, surgical and mental health history, drug history, tobacco, alcohol and recreational drug history, and details of the patient's socioeconomic circumstances) and details of current symptoms. Details of a patient's history are confirmed using the NHS Spine service, an only platform that provides secondary care clinicians with access to primary care records, after permission has been granted by the patient.

Both sites additionally have a Pain Management service made up of specialist nurses and consultant anaesthetists who assist in the management and safe discharge of patients with complex analgesia requirements. The Pain Team's protocol for escalation and de-escalation of analgesia can be summarised as follows: analgesia is tailored to the patient's specific requirements – with a mixture of regional analgesia, opioid and non-opioid medication with an aim to discharge when pain is manageable and allowing each patient to perform their usual activities of daily living. The Pain Team's protocol for analgesia on discharge can be summarised as follows: patient should be discharged without opioids, or with weak opioids and a clear de-escalation plan agreed with the patient and relayed to their general practitioner.

Inclusion and exclusion criteria

Patients admitted and/or discharged by the General/Emergency surgery department between 1st September 2022 and 30th September 2022 were used as the cohort for this study, this month was chosen arbitrarily and non-randomly. No power analysis was used to approximate the necessary sample size. All patients ≥18 years of age and opioid-naïve were included in this study. Opioid-naïve was defined as not regularly taking prescribed or recreational opioid drugs prior to admission when questioned during clinical history (regularly defined as fewer than seven days in the preceding month and no recent than two weeks prior to admission) [10] and investigated on primary care record review. No restrictions were placed on the type of opioid medication discharge with in this study.

Patients violating any part of the inclusion criteria or admitted/discharged by a different specialty/department were excluded. Patients admitted more than once within the month of September were not counted separately unless for a new primary diagnosis completely unrelated to the initial (for example: first admission due to acute appendicitis and second admission due to elective parathyroidectomy), and the second admission was only counted if the patient could be considered opioid-naïve.

Variables

The following variables were extracted from electronic patient records where available: age, sex, type of admission (emergency vs. elective), diagnosis, primary procedure/surgery, length of admission (rounded up to nearest day), other medical, surgical or mental health conditions (as reported by the patient or identified after interrogation of primary care records, including substance abuse disorders), whether opioid analgesia was supplied on discharge (including dose, frequency and recommended duration) and whether safety advice was given to patients on discharge. Subjective and objective measurements for received pain were not collated due to infrequency of documentation.

Data Collection and Statistical Analysis

Eligible patients were identified, anonymised and collated by the Buckinghamshire Healthcare NHS Trust audit department, variables were extracted from electronic records by four authors (M.S., S.A., P.S., W.E.) and reviewed once again by a single author (M.S.). Records of patients initially on opioid medications were then reviewed once more three and six months later, as three months has been previously defined as the point at which opioid use is classified as chronic [11]. Descriptive analyses were used as a cursory assessment of variables, Tetrachoric and Chi [2] analyses, and Student's T-tests were used to compare binary, non-parametric and parametric variables respectively. For Tetrachoric analyses, a value greater than ±0.7 was considered a strong correlation. All statistical analyses were conducted using IBM SPSS version 27.0.1 [12].

Results

In total 514 patients were identified as being discharged in September 2022 by the audit team, 391 patients remained after identification of duplicate entry, admitted and/or discharged by a specialty other than General/Emergency surgery.

Demographics

The mean age of this cohort was 53.5 years (range: 19 to 93 years). 201 patients were female and 190 patients were male. For males the average age was 56.3 years and 50.8 years for females (p=0.0039, 95% Confidence Interval [CI]: 9.3-1.8). 208 patients were ≥50 and 183 were below the age of 50. 233 patients had at least one medical comorbidity. 4 patients had a history of fibromyalgia and/or chronic pain. 5 patients had a previous history of substance abuse/dependence and 20 patients had a previous history of mental illness. 95 patients (24.3%) were discharge with opioid analgesia, 46 females and 49 males (χ^2=0.448, p=0.503). The mean age of patients discharged with opioid analgesia was 59.3 (p=0.345, 95% CI: -9.20-3.2, compared to overall mean). 85 patients were discharged with codeine, 3 with morphine, 2 with oxycodone modified release (MR) and 5 with tramadol.

Diagnoses

The most frequent diagnosis was an abscess which was provided to 57 patients, this was followed by acute biliary disease – provided to 51 patients, and abdominal hernias – provided to 41 patients. 26 patients were diagnosed with non-specific abdominal pain. Of those discharged with opioids, the most common diagnosis was acute biliary disease – provided to 21 patients, followed by appendicitis – provided to 16 patients, and hernia – provided to 9 patients.

Factors Correlating with Opioid Prescription at Discharge

316 patients had emergency admission and 75 patients had elective admissions. 175 patients had non-operative management and 216 had operative. All elective patients were managed operatively. Of the emergency admissions, 162 were managed non-operatively and 154 managed operatively. Of those managed operatively, 92 had a minimally invasive approach (either laparoscopic or robot-assisted) and 48 required laparotomies.

66 patients were managed operatively and required an opioid prescription on discharge, 150 did not. 29 patients managed non-operatively required an opioid prescription, 146 did not. Tetrachoric analysis found opioid prescription correlated with conservative management (*Tc*= -0.99) (Figure 1).

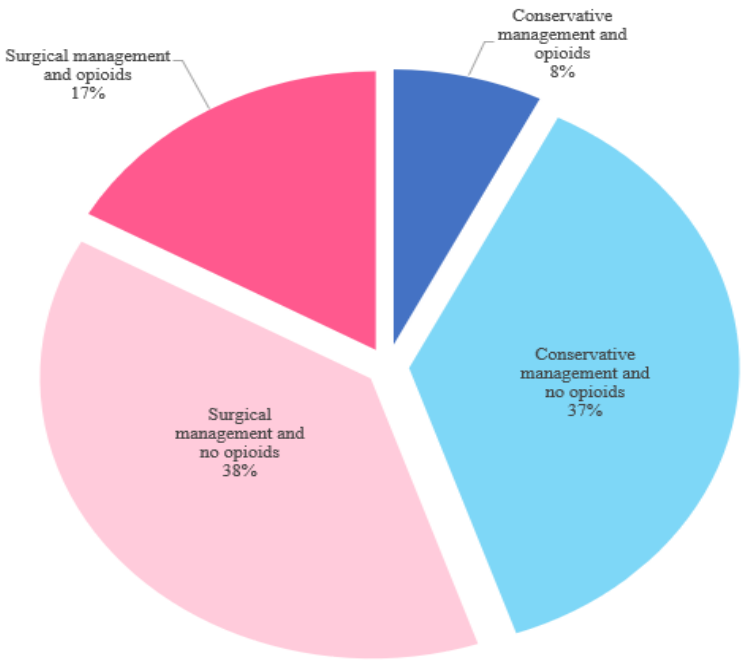

Figure 1: Comparison of opioid prescriptions given to patients undergoing surgical management vs. conservative management. **Key:** light blue: conservative management and no opioids, dark blue: conservative management and opioids, light pink: surgical management and no opioids, dark pink: surgical management and opioids.

15 patients were managed with elective surgery and required an opioid prescription on discharge, 60 did not. 80 patients managed with emergency surgery and required an opioid prescription, 236 did not. Tetrachoric analysis found opioid prescription correlated strongly with emergency surgery (*Tc*=-0.85) (Figure 2).

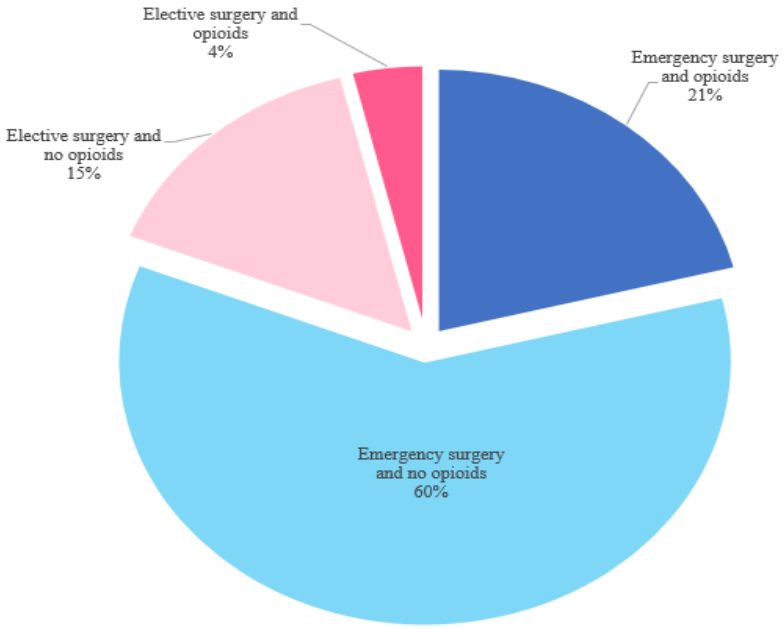

Figure 2: Comparison of opioid prescriptions given to patients undergoing emergency surgery vs. elective surgery.
Key: light blue: emergency surgery and no opioids, dark blue: emergency surgery and opioids, light pink: elective surgery and no opioids, dark pink: elective surgery and opioids.

15 patients were managed with laparotomy and required an opioid prescription on discharge, 33 did not. 46 patients managed with minimally invasive surgery and required an opioid prescription, 46 did not. Tetrachoric analysis found opioid prescription correlated strongly with minimally invasive surgery (*Tc*=-0.97) (Figure 3).

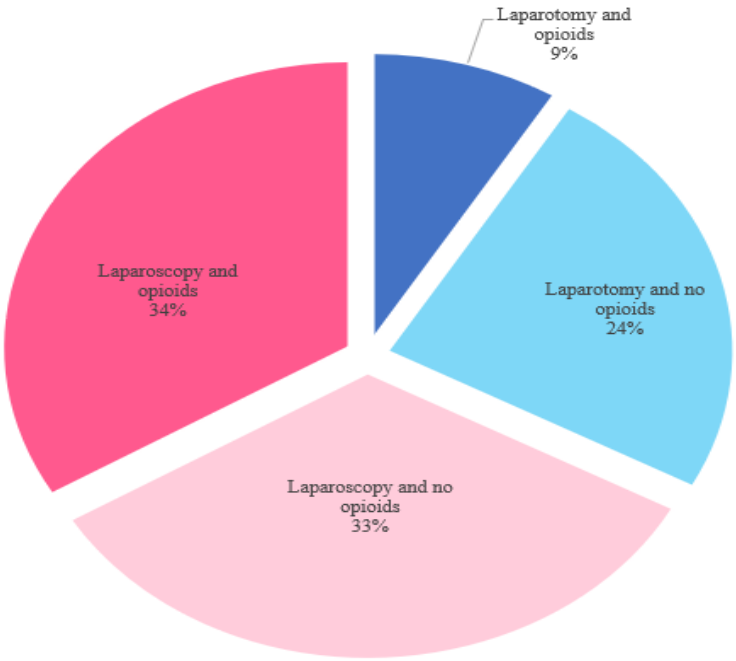

Figure 3: Comparison of opioid prescriptions given to patients undergoing laparoscopic surgery vs. open surgery.
Key: light blue: laparotomy and no opioids, dark blue: laparotomy and opioids, light pink: laparoscopy and no opioids, dark pink: laparoscopy and opioids.

Continued Opioid Use at Three and Six Months Post-Discharge

At three months, five patients had continued opioid use. 3 were male and 2 were female. The same five patients (1% of the study's cohort) were found to have continued opioid use six months after discharge (Table 1). The mean age was 46.3 years. Two patients were initially treated for acute pancreatitis, and one each for incarcerated umbilical hernia, axillary abscess and sigmoid diverticulitis. One patient was treated operatively. Four patients were discharged on codeine, and one patient was

discharged with tramadol. One patient was switched from codeine to tramadol and another was switched from tramadol to codeine. Of note, two patients were switched to neuropathic analgesia, one patient to pregabalin and one patient to amitriptyline (Table 1). Of these seven patients, two had a previous history of substance abuse. We were unable to confirm whether chronic/persistent pain was formally diagnosed in these patients.

Patient	Age	Sex	Diagnosis	Admission type	Management	Analgesia on discharge	Analgesia at 3 and 6-months
1	26	Male	Acute pancreatitis	Emergency	Non-operative	Codeine	Tramadol
2	38	Male	Alcohol induced pancreatitis	Emergency	Non-operative	Co-Codamol	Pregabalin
3	39	Female	Appendicitis	Emergency	Laparoscopic appendicectomy	Tramadol	Amitriptyline
4	44	Male	Incarcerated umbilical hernia	Emergency	Open mesh repair	Codeine	Co-codamol
5	47	Female	Acute pancreatitis	Emergency	Non-operative	Tramadol	Co-codamol
6	49	Male	Axillary abscesses	Emergency	Non-operative	Codeine	Codeine
7	65	Female	Sigmoid diverticulitis	Emergency	Non-operative	Codeine	Co-codamol

Safety Information on Discharge

Of those discharged on opioids, 14 patients (14.7%) received cessation advice on discharge, and eight (8.4%) patients received documented driving safety advice, and only four received both.

Discussion

Demographics

A large review of recent, primarily North American, literature on the gender differences of opioid misuse has reported greater opioid prescription use in females compared to men [13]. *Graziani and Nistico* (2016) posit that a possible CYP3A4, a cytochrome responsible for opioid metabolism, may have a role due to its higher activity in females [14], and *Lopes et al.* (2022) have identified further genes that correlated with clinical outcomes in opioid misuse in specific sexes during their genome wide association study [15]. Our study identified no significant difference in opioid prescriptions on discharge between the sexes, nor were there substantial numbers of patients continuing opioid use at 3- and 6-months to draw conclusions on chronic opioid use differences between the sexes. Much of the data from the 'opioid epidemic' is derived from North American literature, therefore societal and ethnographic differences may make findings non-representative of the UK/Europe. Of note, a Grey Paper report on the incidence of opioid use across Local Authorities in the UK usage rate of 4.46 per 1000 of the population in the area of Buckinghamshire in 2016/17 [16], the fourth lowest rate (range: 3.63-25.51), implying our findings may not represent the UK as whole either.

Diagnoses

The causes of an acute surgical abdomen presenting to the BHT General/Emergency Surgery department show consistency with previous epidemiological studies[17]. Acute biliary disease, appendicitis, and abdominal hernias predominated the diagnoses in those discharged with opioids, this reflects both acuity and brevity of admission, with these patients being readily discharged post-surgical management to control their pain independently in the community.

Such practices may represent a vector for chronic opioid misuse [18], few studies have investigated patient understanding and approach to patient-directed weaning practices and we report 14.7% of patients receiving documented safety advice on discharge. Absence of medical guidance on weaning from opioids presents an avoidable risk in preventing the development of opioid misuse.

Correlating Factors

Studies have shown minimally invasive surgery is associated with reduced post-operative pain [19], however we have identified a correlation with opioid prescription on discharge. Minimally invasive surgery is also associated with expediated discharge, therefore increased prescriptions may correspond to uncontrolled management of mild-moderate pain on discharge [20]. Alternatively, increased prescriptions may correspond to improper prescribing practices, and the mismatch between opioid prescribing and actual use has been shown to drive unregulated opioid availability in the community [3].

Opioid prescriptions also correlated with emergency surgery. Reduced patient optimisation, complex surgery, increased patient anxiety and greater severity of pathology are all linked with both emergency surgery and an increased likelihood of developing long-term opioid use [21,22].

Continued Opioid Use

5/391 patients included in this study developed new chronic opioid use. Previous studies have shown that up to 14.7% of patients develop chronic opioid use [23]. All patients continuing to take opioids at three months continued use at six months also. Two out of five patients with a previous history of substance abuse were now requiring ongoing analgesia at six months. Chronic substance misuse has been associated with mental health issues, with studies reporting a coincidence as high as 50% [24] and rate of relapse between 40.5% and 74.6% [25]. Other factors correlating with chronic opioid use in the post-operative patients include: male sex, > 50 years, history of depression, benzodiazepine or antidepressant use[21]. Two out of five patients also had a primary diagnosis of pancreatitis which

lead to chronic pancreatitis causing long-standing pain in up to 60% of patients [26].

Limitations

Our study was limited in that only a single centre and specialty were assessed, therefore results may not be representative nationally and may be biased the region of Buckinghamshire. The study also does not consider use of opioids purchased over the counter. Power assessment was not conducted, therefore the sample size needed for statistically significant results is unknown.

Future Direction

The study, at present, provides a preliminary base line for the scope of the opioid epidemic in the UK. Future iterations of this study should assess ongoing symptoms patients on opioid analgesia experience using objective measures both at the beginning and end of admission, and at follow-up intervals. Additionally, a larger and more wide-spread study, covering different specialties, should be conducted and the influence of further variables (e.g. socioeconomic) on the development of chronic opioid use should be assessed. Additionally, objective measures on the impact of providing written advice on opioids at discharge to those with prescriptions should be assessed.

Conclusion

Our study highlights the need for further assessment on the extent of iatrogenic chronic opioid use. Once high-risk individuals have been identified appropriate in-hospital and community support can be provided to prevent substance misuse.

Acknowledgements

1. **Assistance with Article:** We thank Stoke Mandeville Hospital's Audit and Quality Improvement Department for collating the data from electronic patient records.
2. **Financial support and sponsorship:** The authors did not receive funding for this study.
3. **Conflicts of interest:** The authors declare no conflicts of interest.
4. **Presentation:** preliminary data was presented at the European Society of Regional Anaesthesia 2023.

Ethics Statement

All methods were carried out in accordance with relevant guidelines and regulations pertaining to this study. Ethical approval was not sought as anonymised data was received from the Buckinghamshire Healthcare NHS Trust's audit department. Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our study.

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