Clinical Pain Research

Torbjørn Nordrik*, Elisabeth Ørskov Rotevatn, Janne Mannseth, Audun Stubhaug, Lars Jørgen Rygh

Opioid use at admittance increases need for intrahospital specialized pain service: Evidence from a registry-based study in four Norwegian university hospitals

https://doi.org/10.1515/sjpain-2025-0008
received February 14, 2025; accepted May 23, 2025

Abstract

Objectives – Acute Pain Services (APS) have significantly evolved since their establishment in the 1990s, emphasizing multimodal analgesia, which is a pivotal component of enhanced recovery after surgery, to enhance postoperative recovery. Despite improvements, variability in pain trajectories among patients necessitated the development of transitional pain units to address individual needs and ensure safe opioid tapering. The Norwegian National Registry for Advanced Acute Pain Services (AAPS), known as SmerteReg, was established to further enhance understanding of pain treatment in these patients. In this study, we aimed to analyze opioid use patterns and characteristics of opioid users referred to AAPS compared to non-opioid users.

Methods – Data from SmerteReg (2016–2020) were analyzed, including patient demographics, diagnoses, pain treatment, and patient-reported outcome measures. Patient characteristics at admittance were compared between opioid users and non-opioid users. Multivariate logistic regression was used to explore factors associated with opioid use.

Results – Of 1,068 patient tracks, 64% were opioid users at admittance. Opioid users were older and more frequently female, reporting higher levels of anxiety, depression, catastrophizing, and sleep problems before admission. Sleep problems before admittance was reported three times more frequent by patients using opioids compared to patients not using an opioid at admittance.

Conclusion – Pre-admittance opioid use was prevalent among patients referred to AAPS, emphasizing the need for tailored pain management strategies. Women, older patients, and those reporting sleep problems before admittance were more likely to use opioids. The finding that sleep problems before admittance were strongly associated with opioid use, suggests the importance of addressing sleep disturbances in pain management protocols. This study contributes to understanding opioid use patterns and factors influencing pain management in hospitalized patients.

Keywords: Acute Pain Service, acute pain, opioids, registry, pain registry, sleep problems

Previous presentations Some results from the study were previously presented as a poster at the IASP 2022 congress in Toronto, Canada, September 21, 2022.

*** Corresponding author: Torbjørn Nordrik,** Department of Clinical Science, Faculty of Medicine, University of Bergen, Postboks 7804, 5020, Bergen, Norway; Department of Anaesthesia and Intensive Care, Haukeland University Hospital, Postboks 1400, 5021, Bergen, Norway, e-mail: tnordrik@online.no, tel: +47 48190302
Elisabeth Ørskov Rotevatn: Department of Clinical Science, University of Bergen, Bergen, Norway; Department of Anaesthesia and Intensive Care, Haukeland University Hospital, Postboks 1400, 5021, Bergen, Norway; Children and Youth Clinic, Haukeland University Hospital, Bergen, Norway, e-mail: elisabeth.orskov.rotevatn@helse-bergen.no
Janne Mannseth: Department of Clinical Science, University of Bergen, Bergen, Norway, e-mail: janne.mannseth@uib.no
Audun Stubhaug: Department of Pain Management and Research, Oslo University Hospital, Oslo, Norway; Faculty of Medicine, University of Oslo, Oslo, Norway, e-mail: astubhau@ous-hf.no
Lars Jørgen Rygh: Department of Clinical Science, University of Bergen, Bergen, Norway; Department of Anaesthesia and Intensive Care, Haukeland University Hospital, Postboks 1400, 5021, Bergen, Norway, e-mail: lars.jorgen.rygh@helse-bergen.no

1 Introduction

Acute Pain Services (APS) were established in many countries during the 1990s [1]. Multi-modal analgesia was the leading concept with the aim of minimizing the side effects, reduce acute pain, and improve mobilization and recovery following surgery or acute illness [2,3]. This advancement was accompanied by implementation of new techniques like epidurals, peripheral local anesthetic blocks, and patient-controlled

analgesia in both day surgery and surgical wards [4,5]. Multimodal analgesia is also a pivotal component of enhanced recovery after surgery [6].

This improved APS was well received, but it quickly became apparent that the individual need for analgesia varied significantly after identical surgery [7,8]. Moreover, painful trajectories were commonly observed across surgical and non-surgical wards, with considerable differences noted among individuals with similar conditions [9]. Recognizing this inter-individual variation in pain-trajectories, a new service emerged, commonly referred to as "transitional pain unit" (TPU) [10,11]. In these units, individuals at risk for poor trajectories are identified early and referred to the TPU either upon hospital admittance or upon identification of a poor trajectory [10]. These units serve to facilitate the transition from the operating room and wards back to normal life, while ensuring a safe tapering of opioids, particularly for risk patients [12].

Concurrently, persistent pain following surgery and medical diseases has been in focus, and it has been established that persistent pain is a major problem affecting a large proportion of hospitalized patients [13–15]. Important risk factors for persistent pain include previous opioid use, previous and ongoing pain conditions, and psychological distress [16,17]. The opioid use has received particular interest in light of the "opioid crisis" in the United States.

Despite documented benefits of TPU [11,12], gaps remain in understanding risk factors for prolonged opioid use and development of persistent pain. While clinical trials have stringent inclusion and exclusion criteria, registries include a broader spectrum of typical patients, providing additional insights on patients' characteristics [18]. Hence, the Norwegian National Registry for Advanced Acute Pain Services [19] (AAPS), also known as SmerteReg, was established to improve knowledge and pain treatment further. This registry now collects comprehensive data from patients in several major hospitals in Norway.

Given the link between previous opioid use and adverse outcomes such as persistent pain, poorer recovery [20], and prolonged opioid use [21] shown in clinical trials, we aimed with this study to analyze opioid use patterns and characteristics of opioid users referred to AAPS, comparing them with non-opioid users in the registry-based population of SmerteReg.

2 Methods

2.1 Study population

Patients included in SmerteReg from April 1, 2016 to December 31, 2020, at four Norwegian university hospitals, were included in this study. For registration in SmerteReg, patients had to meet the following inclusion criteria: at least one visit by the AAPS, 18 years of age or older, not being cognitively impaired, Norwegian speaking, and have given written informed consent. We investigated separate patient tracks for each referral to the AAPS. Patients referred to the AAPS multiple times during the inclusion period were registered several times as individual patient tracks.

A total of 17 patients (making a total of 27 patient tracks) in SmerteReg withdrew their consent for participation in this study.

2.2 Data

Data obtained from SmerteReg included patient age, sex, diagnoses (both an admission diagnosis and a "pain diagnosis"), information about earlier received pain treatment before and during the admittance, and the pain treatment the patient received upon assessment by the AAPS. In addition, we obtained data on pain scores at first and last visit by AAPS measured using the verbal Numeric Rating Scale (NRS), the patients' general experience of the pain treatment along with mapping of factors known to affect the experience of pain [22]. These factors included occurrence of catastrophizing, sleep problems before admittance and during hospitalization, anxiety, and depression. Catastrophizing was measured using two questions from Sullivan's Pain Catastrophizing Scale: 1. "When I'm in pain it is terrible and I think it is never going to get any better", and 2. "When I'm in pain I become afraid that the pain will get worse." The scale is graded with scores from 1 to 6, where 1 represented "never" and 6 represented "always" [23]. Sleep problems were measured using a linear scale from 1 to 6 were 1 represented "no sleep problems" and 6 represented "sleep problems all the time". The occurrence of anxiety and depression was measured using the Hospital Anxiety and Depression Scale (HADS score) [24].

In addition to data obtained in SmerteReg, detailed information on opioid use at admittance (type of opioid and dosage) for the 657 patient tracks of patients admitted at Haukeland University Hospital (HUH), Bergen, were obtained from the electronic patient records.

2.3 Statistical analysis

Patients in each patient track were divided into two groups and defined as opioid users if they were using any opioid at the time of admittance and as non-opioid users if they were not using opioids at the time of admittance. Categorical

variables were tested for differences between the two groups using the Chi-squared test while continuous variables were tested for differences of the mean using Welch's *t*-test or analysis of variance. To further explore the factors associated with opioid use at admittance, we used multivariate logistic regression.

For anxiety and depression, we did analyses on HADS scores comparing the groups with regards to HADS as both a continuous variable and after grouping the patient tracks into "no anxiety," "anxiety," no "depression," and "depression" setting the cut-off for both significant anxiety and depression at a HADS score of 11 or higher. For catastrophizing, we divided the group into two where the cut-off for clinically significant catastrophizing was set to a summed score of eight or higher for the two questions from Sullivan's Pain Catastrophizing Scale. For sleep problems, we did the same and a score of four or higher was considered as clinically significant. For both these variables, patients that had answered "I don't know" were removed from the analyses explaining the variation in numbers for each variable. In the regression model, the highest NRS recorded for each patient track was used. We performed regression analyses using several multiple logistic regression models with the outcome of being an opioid user or not using opioids at admittance. All models included the covariates age and sex. Then, each of the following covariates were included in separate models: HADS score for anxiety, HADS score for depression, the patient tracks' highest recorded NRS, level of sleep problems (before and after admittance), and catastrophizing (i.e., adjusting for age and sex in each model).

As a sensitivity analysis, we ran all regression models and comparison tests on a data set including only unique patients (the first AAPS assessment for each patient).

Missing data were handled with listwise deletion, meaning that the complete patient track was deleted if it had one or more missing values. The level of significance was considered as *P* values below 0.05.

After preliminary analyses on the entire study population, we investigated whether there was a dose response to the observed differences. This analysis was performed using data from the patients registered from HUH. Each patient's total daily opioid dose at admittance was converted to oral morphine equivalents (OMEQ) for comparison, using the Norwegian Health Authorities official OMEQ calculation table [25]. To investigate if the level of OMEQ could explain any associations, we did two sub-analyses where we considered only the opioid-using patients and divided them into two groups of high OMEQ at referral or not. We did these analyses with cut-off for high OMEQ at both OMEQ ≥ 300 and OMEQ ≥ 100.

The primary outcome of being opioid using or not were defined and established *a priori.* Subgroup and sensitivity analyses were identified and established *post hoc.*

All data handling and analyses were performed using the R statistical software (v4.2.2; R Core Team 2022) [26].

The manuscript adheres to the STROBE guidelines.

3 Results

3.1 Basic characteristics

A total of 1,068 patient tracks based on 821 unique patients from four university hospitals in Norway were included (Bergen, n = 657 [491 unique patients, included 2016–2020];

Table 1: Basic demographic characteristics of opioid using patients and non-opioid using patients

	Non-opioid users	Opioid users	Total	*P*-value
Number of patients	386 (36%)	682 (64%)	1,068 (100%)	
Sex				<0.001
Male	214 (55%)	301 (44%)	515 (48%)	
Female	172 (45%)	381 (56%)	553 (52%)	
Age in years				<0.001
Mean (SD)	45.2 (16.2)	50.1 (15.2)	48.4 (15.8)	
Median	46	51	49	
Range	18–82	19–90	18–90	
Number of assessments by the AAPS				0.81
Mean (SD)	5.4 (4.6)	5.9 (6.2)	5.7 (5.7)	
Median	4	4	4	
Range	1–38	1–83	1–83	

Categorical variables were compared using the Chi-squared test; continuous variables were compared using the Welch's *t*-test. AAPS: Advanced Acute Pain Services, SD: standard deviation.

Oslo, $n = 164$ [149 unique patients, included in 2020]; Trondheim, $n = 128$ [97 unique patients, included in 2019–2020]; and Tromsø, $n = 119$ [87 unique patients, included 2019–2020]). For the following analyses we report results based on patient tracks. The mean age of the patients was 48 years, and 553 (52%) were female. About 832 (78%) of the patient tracks were "surgical patients", meaning that they had undergone some kind of surgery, and their problematic pain was most likely due to that.

3.2 Opioid users vs patients not using opioids

A total of 682 (64%) of the patient tracks were opioid users at admittance (Table 1). Mean age for this group was 50 years, and 56% were female. A total of 36% patients were not opioid users at admittance. Mean age in this group was 45 years, and 45% were female. Regarding the patient reported outcome measures (PROMs), opioid using patients reported a significantly higher HADS score for both anxiety and depression. When dividing the groups into "anxiety" or "no anxiety" and "depression" and "no depression" (with a cut-off HADS score of 11 for both anxiety and depression), there were a significantly higher occurrence of anxiety in the opioid-using group. They also reported a significantly higher occurrence of catastrophizing and sleep problems before admittance (Table 2). No differences were found for occurrence of sleep problems after admittance between the two groups.

In addition, and for the record, all patients seen by the AAPS were treated with an opioid as part of the in-hospital pain treatment.

3.3 Factors associated with being an opioid user at admittance

Multiple logistic regression models including only age and sex (no patient reported data) showed that both age and sex were significantly associated with using opioids at admittance (Table 3). Models including patient reported data (each model adjusted for sex and age), showed that both sleep problems before admittance, and higher HADS scores for anxiety and depression were associated with using opioids at admittance (Table 3).

In addition, we did the same analyses using only unique patient data at their first assessment. We found no differences in estimates and their level of significance compared to the analyses including all patient tracks (results not shown).

3.4 Dose response

A sub-analysis of patients tracks from patients admitted to HUH showed no dose response of OMEQ at admittance

Table 2: Comparison of opioid tolerant and opioid naïve patients regarding PROMs

	Non-opioid users	Opioid users	*P*-value
Anxiety			
Yes	226	288	<0.001
No	41	89	
Depression			
Yes	28	55	0.013
No	239	322	
Catastrophizing			
Yes	71	145	0.003
No	187	224	
Sleep problems (before admission)			
Yes	54	163	<0.001
No	212	215	
Sleep problems (after admission)			
Yes	123	171	0.83
No	140	204	

Two-tailed *P* value. Each *P* value is generated from comparison using the Chi-squared test considered significant if $P < 0.05$.

Table 3: Logistic regression models for estimation of variables associated with outcome of being an opioid user or not

Variable (number of patient tracks included in model)	OR	95% CI	*P*-value
Sex* (1,068)	1.73	1.35–2.26	<0.001
Age* (1,068)	1.02	1.01–1.03	<0.001
Anxiety (HADS)** (644)	1.07	1.03–1.12	<0.001
Depression (HADS)** (644)	1.06	1.02–1.11	0.002
Catastrophizing** (627)	1.60	1.13–2.28	0.009
Highest recorded NRS** (828)	1.01	1.00–1.01	0.52
Sleep problems before admission** (644)	3.12	2.17–4.54	<0.001
Sleep problems after admission** (638)	1.04	0.75–1.44	0.812

*A model including only age and sex, **adjusted for age and sex in addition to mentioned variable. CI: confidence interval, HADS: Hospital Anxiety and Depression Scale, OR: odds ratio, NRS: Numeric Rating Scale.

among the groups (opioid users vs non-opioid using patients), with analyses done with cut-offs for the high-OMEQ group at ≥100 OMEQ and ≥300 OMEQ. The outcome for the sub-analysis were the same as in the main analysis as described above.

3.5 Missing data

For patient reported data, the number of missing variables are different for each variable, e.g., for highest NRS (1,068–828:240/1,068 = 22% missing), for HADS (1,068–644: = 424/1,068 = 40% missing), for sleep problems before admission (also 40%), and for catastrophizing (1,068–627 = 441/1,068 = 41% missing).

3.6 Multiple patient tracks

A total of 55% of the 670 patients that had only one track were opioid users at admittance to hospital. In contrast 70% of the 95 patients that had two tracks and 75% of those who had three tracks were opioid users at their first track hospital admittance (Table 4).

4 Discussion

In this registry-based study, we found that as much as 64% of the patients referred to AAPS used opioids at admittance. The opioid using patients were more frequently female and older compared to non-opioid using patients.

Table 4: Distribution of registered patient tracks and opioid status among the 821 unique patients in the registry

Number of patient tracks per unique patient	Non opioid users (*n*)	Opioid users (*n*)	Total (*n*)
1	301 (45%)	369 (55%)	670 (100%)
2	29 (31%)	66 (70%)	95 (100%)
3	9 (24%)	28 (76%)	37 (100%)
4	3 (30%)	7 (70%)	10 (100%)
5	1 (30%)	2 (70%)	3 (100%)
6	2 (50%)	2 (50%)	4 (100%)
7	0	1 (100%)	1 (100%)
11	0	1 (100%)	1 (100%)

Furthermore, the opioid using patients reported sleep problems before admittance three times more frequently than non-opioid using patients.

In this study, we report for the first time the characteristics of patients referred to reinforced APS registered in the Norwegian National Registry for AAPS (SmerteReg) [19], from four large university hospitals. The included patients were heterogenous regarding what diagnosis and what procedures they underwent during hospitalization, but they all shared being referred to the AAPS from the wards and experiencing particularly difficult pain where standard pain treatment was insufficient.

The impact of pre-admission opioid use has recently come into interest, and, to our knowledge, this is the first time it is reported that almost 2 of 3 patients (64%) referred to the AAPS were using an opioid at admittance. The precise number of opioid users at admittance among all hospitalized patients in the four hospitals encompassed is not known. However, most certainly, this number would be significantly lower than the observed 64% in the study population and we estimate it to be within the range of 10–20% of admitted patients. This estimation is based on findings from a recent investigation utilizing data from the Norwegian Prescription Database. Here, it was found that 9% of men and 12% of women had received an ambulatory prescription of an opioid during the last year [27]. Another study from Sweden found that 61,000 of 290,000 (21%) patients undergoing major surgery had received a prescription of an opioid at least once during 180 days prior to the surgery [28]. Thus, it may possibly be that patients using an opioid before and at admittance have a significant increased risk of not experiencing sufficient analgesic effect of standard care at the wards and therefore will need specialized acute pain care by AAPS.

Preoperative use of opioids has been shown to be a significant risk factor for extended opioid dependency and subsequent postoperative complications [29–31]. Our findings may confirm this association between prior opioid exposure and prolonged postoperative opioid usage. Our registry data show that all patients received opioid therapy throughout their hospitalization; however, the duration and extent of opioid utilization following discharge remain undisclosed for the examined period up to 2020. Starting in 2021, SmerteReg has integrated a patient questionnaire addressing opioid usage 4 weeks post-discharge, facilitating further exploration of perioperative opioid use in forthcoming investigations.

It has previously been shown that women report more pain after surgery than men, also when the surgery is identical [8]. This is in line with the findings of the current study where women were referred to the AAPS slightly

more frequently than men. Accordingly, there were significantly more women in the group using opioids when admitted to hospital compared to the group not using opioids at admittance. Sex differences between groups of opioid users and non-opioid users has previously been shown in the United States where prescriptions of opioids from 2015 to 2018 was more frequent among women than men, with an increasing difference in age [32]. Also, women in an American outpatient setting were more likely to be given opioid prescriptions than men [33]. There are similar findings in Norway, as mentioned above, showing that 9% of men and 12% of women had received an ambulatory prescription of an opioid during the last year [27].

Patients admitted while using opioids reported sleep problems prior to admittance three times more frequently than those not using opioids. While it is known that patients seeking help for opioid dependence disorders frequently report sleep problems, this study is, to our knowledge, the first to report such findings in a population of hospitalized patients referred to AAPS. It prompts speculation about whether these reported sleep problems were caused by opioid use itself or by other factors, such as sleep problems being an under-communicated reason for receiving outpatient opioids or a combination of factors. Interestingly, during their hospital stay, all patients in this study were treated with opioids, and both groups reported similar degrees of sleep problems after admission, suggesting that acute illness, pain level, or the opioids themselves may affect sleep. However, other factors, including being hospitalized, are also likely contributors to reported sleep problems [34].

5 Strengths and limitations

The study benefited from comprehensive data collection, utilizing SmerteReg data, which allowed for a broad spectrum of patient characteristics and treatment outcomes to be analyzed. By incorporating PROMs such as pain scores, anxiety, depression, and sleep problems, the study provided a holistic understanding of factors influencing opioid use and pain management.

The study had several limitations. The finding that unique patients with two or more tracks are overrepresented in the opioid using group could influence the described results. However, the main finding that opioid use at admittance is a predictor for needing specialized pain treatment still stands, since 55% of those with only one track are opioid users which are significantly higher than the general population. For the patients with two or more tracks this prediction is even stronger. Furthermore, when analyzing the data for the 670 patients with only one track, the results showed the same tendency as for the whole study population (1,068 tracks).

Furthermore, listwise deletion of patient tracks with missing values may have introduced bias, potentially affecting the generalizability of the results. Additionally, the study focused exclusively on data from Norwegian university hospitals, limiting the generalizability of findings to other healthcare settings or countries with different healthcare systems. The data collected were partly based on patients' memory, which may be subject to recall bias or inaccuracies in documentation. Furthermore, the lack of long-term follow-up beyond the hospital stay limited the understanding of long-term effects and opioid-related risks post-discharge.

In this study, we analyzed anonymous, retrospective registry data. This implies that the complete electronic patient record data for each patient cannot be obtained. Thus, data concerning, e.g., specific opioid used, indication for APS admittance, or type of surgery the patients underwent is missing in the analysis. Not being able to include the exact type of opioid used as well as the specific cause of hospital admission and surgery, limits the interpretation of our data. We strongly suggest collecting detailed data on preoperative opioid use including drug, dose, administration, indication, and length of treatment for future studies. Such data may, at least partly, explain both immediate and long-term postoperative trajectory regarding pain and opioid use, and potentially the risk for persistent postsurgical pain.

6 Conclusions

This study sheds light on the characteristics of patients referred to reinforced APS, offering valuable insights into the prevalence of opioid use, demographic factors, and associated clinical implications. Notably, we observed a high prevalence of opioid use among patients referred to AAPS, with as much as 64% of patients using opioids at admittance. Sleep problems before admittance were associated with opioid use, suggesting the importance of addressing sleep disturbances in pain management protocols.

Acknowledgments: AI (ChatGPT) was used to improve the abstract.

Research ethics: Research involving human subjects complied with all relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration (as amended in 2013). The Regional Committee

for Medical and Health Research Ethics, REK Vest, Norway, approved the use of registry data and access into patient records for extraction of information about opioid usage – (reference number 139470). All patients registered within the inclusion period were informed about the current study and their right to withdraw from participation.

Informed consent: All the patients gave their written informed consent to inclusion in the registry and for their data to be used for both research and quality improvement.

Author contributions: The authors have accepted responsibility for the entire content of this manuscript and approved its submission. Torbjørn Nordrik helped with planning the study, data analysis, data interpretation, and writing of manuscript. Elisabeth Ørskov Rotevatn helped with data interpretation and writing of manuscript. Janne Mannseth helped with guiding the statistical analyses and commented on the manuscript. Audun Stubhaug helped with data interpretation and writing of manuscript. Lars Jørgen Rygh helped with planning the study, data interpretation, and writing of manuscript.

Competing interests: Audun Stubhaug is an honorary editor in *Scandinavian Journal of Pain*. All other authors state no conflict of interest.

Research funding: The study was funded by The Norwegian National Registry for Advanced Acute Pain Services (SmerteReg) and the University of Bergen.

Data availability: Data registered in SmerteReg is available for all who wish to use the data within the purpose of the registry as long as the necessary permissions from the registry professional council and the Regional Ethics Committee (REC) is obtained.

Artificial intelligence/Machine learning tools: AI (ChatGPT) was used to improve the abstract.

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