Opioid Use After Intensive Care: A Nationwide Cohort Study

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OBJECTIVE: To describe opioid use after ICU admission, identify factors associated with chronic opioid use after critical care, and determine if chronic opioid use is associated with an increased risk of death.

DESIGN: Retrospective cohort study.

SETTING: Sweden including all registered ICU admissions between 2010 and 2018.

PATIENTS: Adults surviving the first two quarters after ICU admission were eligible for inclusion. A total of 265,496 patients were screened and 61,094 were ineligible.

INTERVENTIONS: Admission to intensive care.

MEASUREMENTS AND MAIN RESULTS: Among 204,402 individuals included in the cohort, 22,138 developed chronic opioid use following critical care. Mean opioid consumption peaked after admission followed by a continuous decline without returning to baseline during follow-up of 24 months. Factors associated with chronic opioid use included high age, female sex, presence of comorbidities, preadmission opioid use, and ICU length of stay greater than 2 days. Adjusted hazard ratio for death 6–18 months after admission for chronic opioid users was 1.7 (95% CI, 1.6–1.7; $p < 0.001$). In the subset of patients not using opioids prior to admission, similar findings were noted.

CONCLUSIONS: Mean opioid consumption is increased 24 months after ICU admission despite the lack of evidence for long-term opioid treatment. Given the high number of ICU entries and risk of excess mortality for chronic users, preventing opioid misuse is important when improving long-term outcomes after critical care.

KEY WORDS: cohort studies; critical care; follow-up studies; mortality; opioid epidemic; opioid-related disorders

Over the past decades, the misuse of opioids has turned into a major public health problem in many countries. Starting in the 1990s in the United States, pharmaceutical companies marketed and promoted liberal opioid prescribing (1). This, in combination with the American Pain Society presenting pain as the fifth vital sign (2), leads to generous prescribing and subsequently widespread misuse of opioid medication. From 1999 until now, more than 750,000 people in the United States have died from a drug overdose (3), and on average, 130 Americans die every day from an opioid overdose (4). In contrast to the discussion about an opioid epidemic in the United States, little is known about prescription patterns over the last decades in Sweden. An opioid epidemic similar to the one seen in the United States is yet not evident in any Scandinavian or European country (5, 6). There is, however, an upward

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trend in opioid prescription in western and central Europe (7).

Opioids such as morphine, remifentanil, and fentanyl are commonly used in critical care for sedation and pain management (8). During intensive care, there are numerous sources of pain such as surgery, endotracheal intubation, placement of invasive catheters, or other painful conditions. Despite the liberal use of opioids, a majority of patients report pain and discomfort for several years after ICU discharge (9). Opioids are the primary pharmacologic therapy for moderate-to-severe pain but entail risks including physical dependence and addiction (10) and prolonged use can lead to tolerance and increasing doses (11). The evidence for long-term opioid treatment is weak (12) and opioid use for management of chronic pain is controversial (13, 14). Whether or not intensive care treatment per se is contributing to the current opioid crisis is not clear, neither is the prevalence of chronic opioid use after ICU care.

Our first study objective was to describe opioid use after ICU admission. Our secondary objective was to identify factors associated with chronic opioid use following ICU care. Our final objective was to determine if chronic opioid use after ICU care is associated with increased risk of death.

MATERIAL AND METHODS

Ethics Approval

The Regional Ethical Review Board in Stockholm, Sweden, approved the study (approval numbers 2018/2541-31 and 2019-00213) and waived requirement for informed consent. All research was performed in accordance with national guidelines and regulations.

Study Design

We created a cohort based on all patients registered in the Swedish Intensive Care Registry (SIR) from January 2010 to December 2018. SIR collects individual data from all 83 Swedish ICUs since 2001 and operates within the legal framework of the Swedish National Quality Registries (15). This framework does not require written informed consent from the patients, but patients may withdraw their data from the registry at any time. The register contains data on diagnoses, interventions, and follow-up. For patients with multiple ICU entries during the study period, only the first episode of care was included. Estimated mortality rate (EMR) was based on Acute Physiology and Chronic Health Evaluation for patients included until 2012, and thereafter based on Simplified Acute Physiology Score. Information on comorbidities was assessed up to 5 years prior to ICU admission and obtained from the Swedish National Patient Register (16) and socioeconomic factors from the Longitudinal Integration Database for Health Insurance and Labour Market Studies (17). Additional data on patient outcomes and dispensed drugs were assessed using The Swedish Cause of Death Register (18) and The Swedish Prescribed Drug Register (19).

Outcomes

The primary outcome was chronic opioid use after ICU discharge and the secondary outcome was all-cause mortality 6–18 months after ICU admission.

Definition of Opioid Use

Opioid use before ICU admission was defined as at least one written and dispensed prescription during 12 months preceding admission. Chronic opioid use was defined as repeated prescriptions equaling at least one prescription in the first as well as in the second calendar quarter (1–90 and 91–180 d, respectively) following ICU admission (20, 21). Individuals who died within the first two quarters after ICU admission, and therefore not able to fulfill the criterion of becoming a chronic user were excluded. Quarter periods were used, since a prescription covers 3 months in Sweden. Equipotent doses were calculated using oral morphine equivalents (OMEQs) to facilitate better comparison of opioids with varying potency (**Table S1**, http://links.lww.com/CCM/G126) for a list of included opioids and conversion rates. A subset of patients not using opioids 12 months prior to ICU admission were examined separately and are referred to as opioid naïve. Methadone and selected preparations of buprenorphine (Anatomical Therapeutic Chemical code N07BC) are predominately used in opioid agonist therapy for individuals with problematic drug use, and individuals using these drugs were excluded.

Statistical Analysis

Generalized estimating equations regression models were used to estimate differences in mean opioid consumption before and after ICU admission. Multivariable logistic regression was used to estimate odds ratios for the association between chronic opioid use and known or potential risk factors (age, sex, level of education, income, somatic comorbidity, psychiatric comorbidity, substance abuse, preinjury opioid use, EMR, and ICU length of stay).

Cox regression models were performed to analyze the association between chronic opioid use and all-cause mortality 6–18 months after ICU admission; results are presented as hazard ratios (HRs). Potential confounders (age, sex, somatic comorbidity, psychiatric comorbidity, substance abuse, EMR, and ICU length of stay) were selected a priori.

Sensitivity Analysis

Probability weights were used in the multivariable logistic regression model to account for nonrandom dropout from the study due to death (22). The probability of death within 180 days following ICU admission was estimated with a logistic regression model including all the variables used in the multivariable analyses as well as year of ICU admission.

Due to missing data on EMR, a separate analysis was performed excluding these individuals. A p value of less than 0.05 was considered statistically significant; all tests were two-tailed. Data analysis was performed using Stata/SE 14.2 (StataCorp, College Station, TX). The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology recommendations for cohort studies (23).

RESULTS

From January 2010 to December 2018, a total of 265,496 individuals were registered in SIR. After exclusion of 2,621 individuals receiving methadone or buprenorphine and 58,473 individuals who died within the first two quarters after ICU admission, 204,402 individuals were included in the final analysis (**Fig. 1**). Characteristics of the final study cohort are presented in **Table 1**. Mean opioid consumption (with 95% CIs) for the entire study cohort (n = 204,402) along with opioid consumption for a subset of patients not using opioids 12 months prior to ICU admission (n = 157,925) is presented in **Figure 2**, ***A*** and ***B***.

The mean opioid consumption increased in the months preceding ICU admission followed by an initial peak in the first quarter after admission and a continuous decline without returning to baseline. After 24 months (eight quarters), the mean consumption was still increased compared with baseline use (equaling 9–12 mo before admission) (**Table S2**, http://links.lww.com/CCM/G126). Baseline characteristics for opioid naïve individuals compared with individuals with opioid use are presented in **Table S3** (http://links.lww.com/CCM/G126). Among opioid-naïve patients, between the second and the eighth calendar quarter after ICU admission, the mean opioid consumption decreased on average by 4.3-mg OMEQ (95% CI, 2.9–5.8) per quarter but remained substantial during end of follow-up of 24 months.

ICU patients with subsequent chronic opioid use (n = 22 138) were older, more likely to be female, and had lower level of education as well as a higher number of somatic and psychiatric comorbid conditions in addition to more substance abuse on ICU admission.

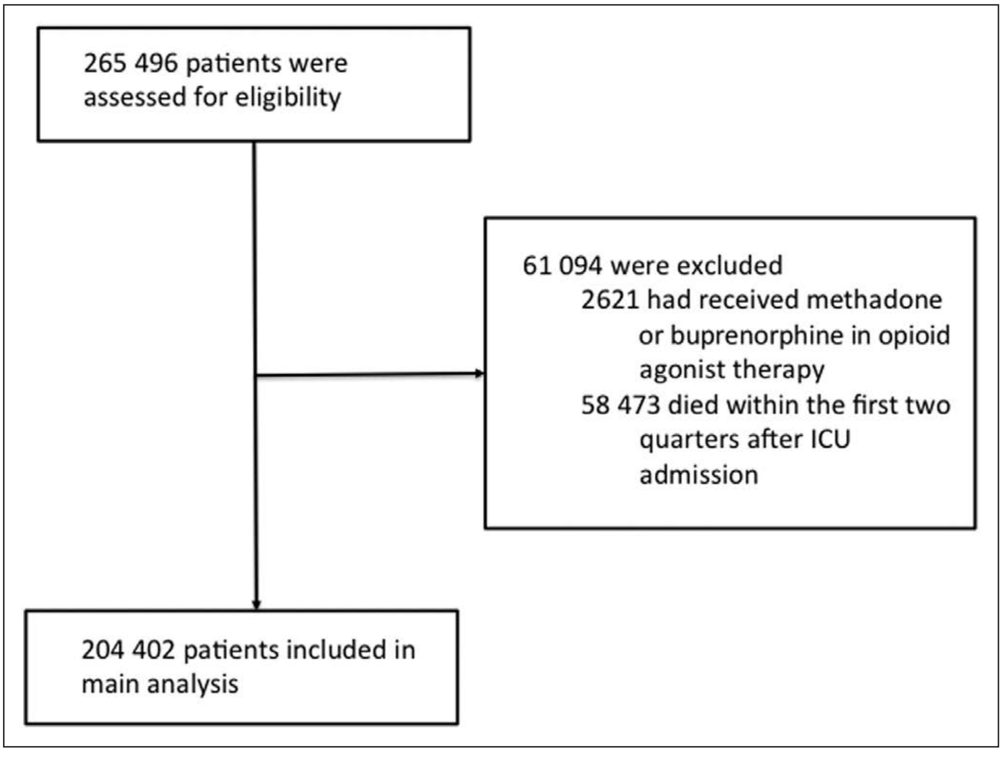

Figure 1. Flowchart of included patients.

TABLE 1.
General Characteristics for Patients Admitted to ICU

ICU patients	
Count	204,402
Age, median (IQR)	63 (46–73)
Male, *n* (%)	119,901 (58.7)
Income categories, *n* (%)	
Low	35,392 (17.4)
Medium	157,894 (77.6)
High	10,115 (5.0)
Education level, *n* (%)	
Low	69,036 (34.6)
Medium	89,324 (44.8)
High	41,053 (20.6)
CCI categories, *n* (%)	
CCI 0	93,105 (45.6)
CCI 1	40,155 (19.6)
CCI > 1	71,142 (34.8)
Psychiatric comorbidity, *n* (%)	37,735 (18.5)
Substance abuse, *n* (%)	23,505 (11.5)
Preadmission opioid usage, *n* (%)	46,477 (22.7)
Acute myocardial infarction, *n* (%)	23,385 (11.4)
Congestive heart failure, *n* (%)	22,111 (10.8)
Peripheral vascular disease, *n* (%)	16,901 (8.3)
Cerebrovascular disease, *n* (%)	18,902 (9.2)
Dementia, *n* (%)	2,243 (1.1)
Chronic obstructive pulmonary disease, *n* (%)	23,152 (11.3)
Rheumatoid disease, *n* (%)	6,619 (3.2)
Peptic ulcer disease, *n* (%)	6,312 (3.1)
Mild liver disease, *n* (%)	7,606 (3.7)
Moderate/severe liver disease, *n* (%)	2,634 (1.3)
Diabetes without complications, *n* (%)	31,544 (15.4)
Diabetes with complications, *n* (%)	11,388 (5.6)
Hemiplegia or paraplegia, *n* (%)	3,720 (1.8)

(*Continued*)

TABLE 1. (*Continued*).
General Characteristics for Patients Admitted to ICU

ICU patients	
Renal disease, *n* (%)	9,012 (4.4)
Cancer, *n* (%)	25,946 (12.7)
Metastatic cancer, *n* (%)	5,229 (2.6)
AIDS, *n* (%)	241 (0.1)
Estimated mortality rate, median (IQR)	0.058 (0.018–0.16)
ICU length of stay, median (IQR)	1.5 (1.5–2.5)
Surgery, *n* (%)	
Acute care	22,132 (10.8)
Elective	46,245 (22.6)
No surgery	136,025 (66.5)

CCI = Charlson Comorbidity Index, IQR = interquartile range.

Additionally, a higher number of individuals underwent acute care surgery and more than 70% of the chronic opioid users consumed opioids also prior to their episode of intensive care (**Table 2**). Similar differences between the chronic and nonchronic users were seen among opioid naïve patients with the exception of a greater number of surgical procedures in the chronic opioid group, a lower prevalence of psychiatric comorbidity, and no difference in substance abuse (**Table S4**, http://links.lww.com/CCM/G126).

In the multivariable logistic regression analysis, age, female sex, low level of education, low income, somatic comorbidity, psychiatric comorbidity, preadmission opioid usage, lower EMR, surgery, earlier year of ICU admission, and ICU stay for more than 2 days were associated with higher odds of chronic opioid use (**Table 3**). For opioid naïve patients, age, female sex, low level of education, somatic comorbidity, surgery, and ICU stay for more than 3 days were associated with chronic opioid use (**Table S5**, http://links.lww.com/CCM/G126).

During the follow-up time 6–18 months after ICU admission, 13,251 patients died, of which 2,872 were chronic opioid users. In the unadjusted Cox regression analysis, chronic opioid use was associated with a higher mortality, HR 2.2 (95% CI, 2.2–2.3; $p < 0.001$). After adjustment for age, sex, somatic and psychiatric comorbidities, substance abuse, EMR, and ICU length of stay, this association was still significant and HR is 1.7 (95% CI, 1.6–1.7;

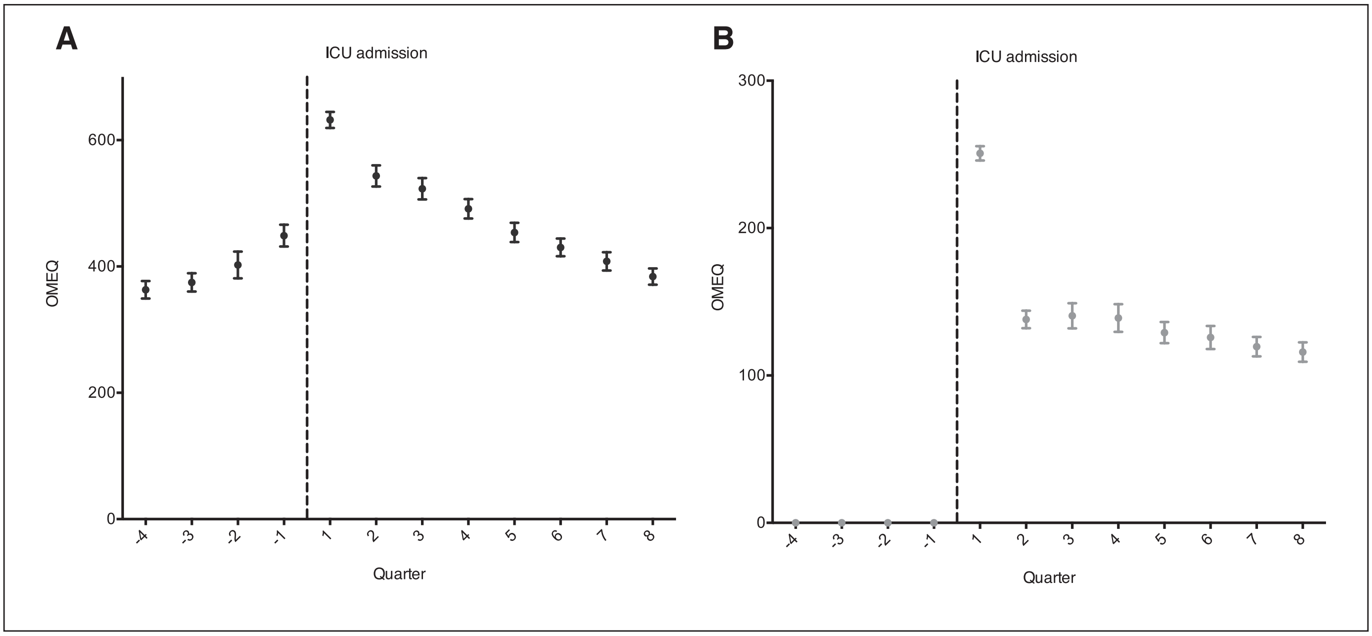

Figure 2. Opioid prescription in relation to ICU care. Opioid prescription pre- and post-ICU cares for the entire study cohort ($n = 204{,}402$) (**A**) and a subset of patients not using opioids 12 mo prior to ICU admission ($n = 157{,}925$) (**B**). OMEQ = oral morphine equivalents.

$p < 0.001$) (**Table S6**, http://links.lww.com/CCM/G126). In the subset of patients not using opioids prior to ICU admission, chronic opioid use was similarly associated with long-term mortality and adjusted HR is 1.9 (95% CI, 1.8–2.1; $p < 0.001$).

Sensitivity Analysis

In the analysis accounting for nonrandom dropout from the study due to death, length of stay greater than 7 days, low EMR, and elective surgery were no longer associated with chronic opioid use.

Missing Data

One of the important variables in our study, EMR, had a relatively large proportion of missing data (n = 28,155, 13.77%). Smaller numbers of missing data were found on education (n = 4,989, 2.44%) and income (n = 1,001, 0.49%). The presence of missing data should not be regarded as a serious limitation of our study, for at least two reasons: first, it does not pose a significant threat to the statistical power of our analysis, as the dataset is very large, and second, the variables above were only used as covariates. The proportion of missing data in education and income is less than 5%, which has been suggested as the maximum upper acceptance limit for large datasets (24). In addition, we showed that the distribution of the response variables of interest was very similar if we compared observations with/without missing EMR, indicating a noninformative missingness mechanism (25).

DISCUSSION

This large nationwide cohort study showed that mean opioid consumption increased in the months preceding ICU admission followed by an initial peak and a continuous decline without returning to baseline during follow-up of 24 months. In opioid naïve patients, mean opioid use was substantial during the same follow-up period of 24 months. Factors associated with chronic opioid use included age, female sex, comorbid conditions, opioid prescription prior to ICU admission, acute care surgery, and ICU length of stay. For individuals with chronic opioid use, mortality was increased 6–18 months after admission even after adjustment for baseline and ICU admission characteristics. In the subset of patients without prior opioid exposure, the findings were similar.

Our study shows that individuals admitted to intensive care, on average, were prescribed large amounts of opioids both before and after ICU admission compared with the general population (26, 27). The higher than expected baseline consumption might be due to underlying medical conditions (28) or the high prevalence of substance abuse and psychiatric disease; both reported

TABLE 2.
General Characteristics in ICU Patients Stratified by Chronic Opioid Use

ICU Patients	No Chronic Opioid Use	Chronic Opioid Use
Count	173,339	22,138
Age, median (IQR)	63 (45–73)	65 (52–74)
Male, *n* (%)	103,617 (59.8)	10,945 (49.4)
Income categories, *n* (%)		
Low	30,442 (17.7)	3,403 (15.4)
Medium	133,171 (77.2)	17,865 (80.9)
High	8,849 (5.1)	806 (3.6)
Education level, *n* (%)		
Low	58,288 (34.5)	8,031 (37.0)
Medium	75,186 (44.5)	10,170 (46.8)
High	35,533 (21.0)	3,527 (16.2)
CCI categories, *n* (%)		
CCI 0	82,516 (47.6)	6,817 (30.8)
CCI 1	34,093 (19.7)	4,285 (19.4)
CCI > 1	56,730 (32.7)	11,036 (49.8)
Psychiatric comorbidity, *n* (%)	31,016 (17.9)	5,225 (23.6)
Substance abuse, *n* (%)	19,587 (11.3)	3,019 (13.6)
Pre-ICU opioid use, *n* (%)	29,010 (16.7)	15,613 (70.5)
Acute myocardial infarction, *n* (%)	19,321 (11.1)	2,976 (13.4)
Congestive heart failure, *n* (%)	17,711 (10.2)	3,315 (15.0)
Peripheral vascular disease, *n* (%)	13,365 (7.7)	2,723 (12.3)
Cerebrovascular disease, *n* (%)	15,592 (9.0)	2,488 (11.2)
Dementia, *n* (%)	1,776 (1.0)	360 (1.6)
Chronic obstructive pulmonary disease, *n* (%)	17,941 (10.4)	4,173 (18.8)
Rheumatoid disease, *n* (%)	4,777 (2.8)	1,519 (6.9)
Peptic ulcer disease, *n* (%)	4,812 (2.8)	1,249 (5.6)
Mild liver disease, *n* (%)	6,078 (3.5)	1,199 (5.4)
Moderate/severe liver disease, *n* (%)	2,129 (1.2)	374 (1.7)
Diabetes, *n* (%)	25,392 (14.6)	4,554 (20.6)
Diabetes + complications, *n* (%)	8,965 (5.2)	1,909 (8.6)
Hemiplegia or paraplegia, *n* (%)	2,834 (1.6)	688 (3.1)
Renal disease, *n* (%)	7,026 (4.1)	1,504 (6.8)
Cancer, *n* (%)	20,580 (11.9)	4,141 (18.7)
Metastatic cancer, *n* (%)	3,806 (2.2)	1,125 (5.1)
AIDS, *n* (%)	200 (0.1)	25 (0.1)
Estimated mortality rate, median (IQR)	0.058 (0.018–0.16)	0.074 (0.024–0.19)
ICU length of stay, median (IQR)	1.5 (1.5–2.5)	1.5 (1.5–2.5)
Surgery, *n* (%)		
Acute care	18,099 (10.4)	2,845 (12.9)
Elective	39,442 (22.8)	4,573 (20.7)
No surgery	115,798 (66.8)	14,720 (66.5)

CCI = Charlson Comorbidity Index, IQR = interquartile range.

TABLE 3.
Univariate and Multivariable Logistic Regression Analyses, Associations With Chronic Opioid Use Presented As Odds Ratio (95% CI)

ICU Patients	Univariate	*p*	Multivariable	*p*
Age categories, median (IQR)				
18–29	Reference		Reference	
30–39	1.88 (1.73–2.05)	< 0.001	1.54 (1.40–1.68)	< 0.001
40–49	2.83 (2.63–3.05)	< 0.001	2.13 (1.95–2.32)	< 0.001
50–59	3.00 (2.80–3.22)	< 0.001	2.22 (2.05–2.41)	< 0.001
60–69	2.77 (2.60–2.97)	< 0.001	2.08 (1.92–2.25)	< 0.001
70–79	2.63 (2.46–2.81)	< 0.001	1.88 (1.73–2.04)	< 0.001
80–89	2.83 (2.63–3.04)	< 0.001	1.84 (1.68–2.01)	< 0.001
90+	3.49 (3.04–4.01)	< 0.001	2.15 (1.83–2.53)	< 0.001
Male	0.66 (0.64–0.68)	< 0.001	0.80 (0.77–0.83)	< 0.001
Income categories, median (IQR)				
Low	Reference		Reference	
Medium	1.20 (1.15–1.25)	< 0.001	1.00 (0.96–1.05)	0.93
High	0.81 (0.75–0.88)	< 0.001	0.89 (0.80–0.98)	0.016
Education level, median (IQR)				
Low	Reference		Reference	
Medium	0.98 (0.95–1.01)	0.25	0.98 (0.94–1.02)	0.30
High	0.72 (0.69–0.75)	< 0.001	0.78 (0.74–0.82)	< 0.001
CCI categories, median (IQR)				
CCI 0	Reference		Reference	
CCI 1	1.52 (1.46–1.58)	< 0.001	1.20 (1.14–1.26)	< 0.001
CCI > 1	2.35 (2.28–2.43)	< 0.001	1.46 (1.40–1.52)	< 0.001
Psychiatric comorbidity, median (IQR)	1.42 (1.37–1.47)	< 0.001	1.27 (1.22–1.33)	< 0.001
Substance abuse, median (IQR)	1.24 (1.19–1.29)	< 0.001	1.04 (0.99–1.09)	0.16
Pre-ICU opioid use, median (IQR)	11.90 (11.54–12.29)	< 0.001	10.31 (9.96–10.67)	< 0.001
Estimated mortality rate, median (IQR)	2.00 (1.84–2.18)	< 0.001	0.87 (0.78–0.98)	0.026
ICU length of stay, d, median (IQR)				
0–2	Reference		Reference	
3–7	1.25 (1.21–1.29)	< 0.001	1.12 (1.08–1.17)	< 0.001
> 7	1.12 (1.06–1.18)	< 0.001	1.07 (1.00–1.14)	0.035
Surgery, median (IQR)				
No surgery	Reference		Reference	
Elective	0.91 (0.88–0.94)	< 0.001	1.06 (1.01–1.11)	0.028
Acute care	1.24 (1.18–1.29)	< 0.001	1.30 (1.24–1.37)	< 0.001
ICU admission year, median (IQR)				
2010–2012	Reference		Reference	
2013–2015	0.99 (0.96–1.02)	0.62	1.00 (0.97–1.04)	0.88
2016–2018	0.90 (0.87–0.94)	< 0.001	0.95 (0.91–0.99)	0.009

CCI = Charlson Comorbidity Index.

to be associated with chronic opioid use (29). Evident mechanisms explaining the increased opioid use preceding ICU admission remain speculative, but one contributing factor might be worsening of symptoms for chronic medical conditions with a subsequent increased opioid use. However, since individuals dying in the first two quarters following ICU admission were excluded, deterioration of advanced stages of malignancies is probably not the key explanation. After the initial peak in the first quarter after admission, opioid consumption decreased but did not return to preadmission baseline levels. This is analogous to previous findings in trauma populations (27, 30), but remarkable considering the lack of evidence for any long-term use of opioids (12).

Most ICU patients receive opioids as part of a sedation regimen or for pain management (31). It has been suggested that continuous infusions of opioids for a long period of time or at a high rate might drive risks for chronic use after discharge, but previous studies provide no evidence of this (32, 33). Furthermore, a majority of ICU survivors report pain and discomfort for several years after discharge (9), which also is a risk factor for chronic opioid treatment (34). In one of few studies investigating opioid use in ICU survivors, there was no evident association between admission to ICU and chronic opioid use (35). However, this study included patients between 2005 and 2008, and might not reflect current prescribing patterns considering the fast growing problem with misuse over the last decade. Another more recent Canadian study on opioid-naïve patients undergoing invasive mechanical ventilation included between 2013 and 2015 found that only 2.6% met criteria for persistent opioid use after hospitalization (36). Nevertheless, this study defined persistent opioid use as having filed multiple prescriptions as opposed to the current study using OMEQs making comparisons hard.

In our cohort, risk factors for chronic opioid use included increasing age and female sex. Previous studies report similar associations for increasing age, whereas sex has shown contrasting results (37, 38). In addition, chronic opioid users had lower income and level of education in line with a Norwegian report (39). Substance abuse and psychiatric disease were both associated with chronic opioid use, two conditions obviously associated with potential long-term addiction (29). The strongest risk factor was preinjury opioid consumption, a well-known risk factor for long-term opioid usage (27, 40). A more recent year of ICU admission was associated with less risk of chronic opioid use, possibly reflecting an increasing awareness of the risks entailed with chronic opioid use. Finally, surgery and ICU length of stay were associated with chronic opioid use. Previous studies have shown similar results for surgery (41), but the association between length of stay and chronic opioid use is not a consistent finding (35, 36). Increasing EMR had decreased odds of chronic opioid use, which might reflect that seriously ill patients are not capable of getting their prescriptions dispensed.

Chronic opioid use was associated with an increased mortality 6–18 months after ICU admission. Recognized adverse effects of opioids such as delirium, constipation, and respiratory depression have been reported to have an impact on ICU mortality (42, 43). However, chronic opioid use might also comprise risks of myocardial infarction, stroke, venous thromboembolism, and inappropriate immune modulation (11, 44), all of which add on to the already poor prognosis of ICU patients. These factors separately or combined might be the reason why chronic opioid use is associated with increased risk of death after ICU treatment. Interestingly, the HR was even higher in the subset of patients not using opioids prior to ICU admission. This is somewhat surprising and evidently contrasts with a Danish study where all-cause mortality following ICU only was increased for current and recent opioid users and not for nonusers (45). The same conclusion was reached in a South Korean study, where the odds of 90-day mortality were higher in chronic opioid users than opioid naïve patients (46).

Chronic opioid use after discharge from intensive care is complex and multifactorial. In addition, differences in prescribing patterns and healthcare systems make comparisons with other countries difficult. However, this study recognizes the many immediate and long-term risks involved in liberal use of opioids and highlights the fact that prescription of opioids is associated with increased risk of death after intensive care.

This study includes all registered ICU admissions in Sweden during a 9-year period. One of the strengths of this study is the use of validated health registers with low rates of missing data and minimal loss to follow-up. Limitations include the retrospective and register-based study design and the lack of information on quantities of opioids administered while treated in hospital. In addition, we cannot be sure to what extent the individuals consumed the opioids prescribed and dispensed. Differences in medical systems between the countries may limit the generalizability of the results.

CONCLUSIONS

In summary, our results demonstrate that mean opioid consumption increased in the months preceding ICU admission followed by an initial peak and a continuous decline but did not return to preadmission baseline levels during follow-up of 24 months. Chronic opioid use after critical care was associated with increased mortality. The same applied for the subset of opioid naïve individuals. It is important to continue to treat pain optimally while patients are in the ICU, but how to address pain and opioid prescriptions best after ICU discharge in the light of an ongoing opioid crisis is not clear and needs to be studied further.

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