

ORIGINAL RESEARCH

Opioid use and prescription in emergency departments visits in Taiwan: a nationwide population-based retrospective study

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Abstract

The emergency departments (EDs) prescribed opioids in acute pains and had thus been one of its major sources. We aimed to describe the features of EDs opioid use in Taiwan from 2008 to 2018. A retrospective cross-sectional study was conducted through Taiwan's National Health Insurance Database. The patients having an index EDs visit from 2008 to 2018 were identified who had been administered or prescribed opioid at discharge. The general trend and the trend for each type of opioid prescribed from EDs in Taiwan were explored along with the diagnosis resulting in opioid prescriptions in EDs. The opioid prescription from EDs in the study period accounted for 9.72% to 11.97% of the total opioid prescriptions in Taiwan. The rate (prescriptions per 10⁴ persons) of opioids prescription in EDs peaked from 282.64/10⁴ in 2008 to 330.24/10⁴ in 2015, and declined to 286.47/10⁴ in 2018. The pethidine prescription rate had downward trend from 123.05/10⁴ in 2008 to 23.69/10⁴ in 2018 in EDs. Morphine was the most administered opioid in 2009 (121.11/10⁴) which increased to 180.99/10⁴ in 2018. The reasons for opioid prescriptions in EDs were the abdominal pain followed by chest pain, respiratory discomfort and cancer-related pain. It was noted that EDs prescriptions of morphine, codeine and fentanyl had an increasing trend in Taiwan between 2008 to 2018, while pethidine had a declining trend. Morphine was the most used and prescribed opioid in EDs, and the leading cause for opioid usage was abdominal pains.

Keywords

Emergency departments; Opioids; Trend; Prescription

1. Introduction

Patients having acute pains visit emergency departments (EDs) [1, 2]. Opioids are the main analgesics for treating moderate to severe pains, especially the acute pain [3, 4]. However, opioids negatively impact the society through misuse disorders, and overuse-associated deaths [5–8]. In a survey of opioid-dependent patients on methadone treatment, 13% claim EDs as their opioid source [9]. In US, there has been an increase of opioids analgesic prescriptions in EDs from 20.8% to 31% between 2001 and 2010 [10]. A retrospective analysis depicts that the patients receiving higher opioids in EDs have increased rate of becoming chronic opioid users [11]. Another US retrospective cohort study finds the patients receiving opioid prescriptions from EDs have higher risk of persistent opioid prescriptions [12]. The acute pain management in EDs can impact the incidences of chronic opioid usage, dependence and overuse problems [13, 14]. A recent US study has shown that there has been a decrease in the percentage of EDs visits that result in prescribed opioids at discharge, dropping from 12.2% in 2017–2018 to 8.1% in 2019–2020 [15]. These findings

demonstrate the importance of improving acute pain management policy in EDs to reduce patient reliance on opioids.

Opioid overuse is an issue of public health. Many countries have launched awareness programs regarding opioid usage and have investigated its prevalence in EDs. The American College of Emergency Physicians has issued clinical guidelines for improving the opioid utilizations in EDs and reduce opioid-associated risks [16, 17]. Moreover, the studies in other countries have examined the prescription patterns of opioids in EDs [18–24]. Opioids prescription patterns and prevalence are different for western and Asian countries [25–29]. However, limited data is available on the opioids usage in EDs of Asian countries in recent decade. Therefore, the main objective herein is to describe the features of EDs opioid usage in Taiwan from 2008 to 2018. A nationwide retrospective study is conducted to achieve this goal by examining the trend of opioid prescription rates between 2008 and 2018 in Taiwan.

2. Methods

2.1 Data source

In 1995, Taiwan launched a single-payer National Health Insurance (NHI) program with comprehensive health care coverage to all the legal Taiwan residents. More than 99.99% of Taiwan's 22.96 million residents were enrolled to this program [30]. The National Health Insurance Research Database (NHIRD) was consulted for the encrypted patients' identification numbers, sex, date of birth, records of outpatients, ED visits, hospital inpatients, the ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification, before 2016) or ICD-10-CM (International Classification of Diseases, 10th Revision, Clinical Modification, after 2016) codes of diagnoses, prescription details and costs covered by NHI. Furthermore, the accuracy and validity of diagnoses in NHIRD were confirmed.

2.2 Study design, patients' identifications and variables

A retrospective cross-sectional study was designed to analyze the patients visits in EDs using NHIRD 2008–2018. EDs visits with the record of opioids (schedule I–III controlled drugs: morphine, fentanyl, pethidine, codeine, oxycodone, hydromorphone and buprenorphine) prescriptions in EDs or at the time of discharge were identified as the study population. All the single-agent and combination opioid preparations were included in the study. Tramadol was excluded as it was a weak mu-opioid agonist and classified as a schedule IV drug in Taiwan [31]. Moreover, methadone was excluded as it was employed only for the drug addiction treatment rather than for pain management in Taiwan [32]. The retrieved data assessed the clinical characteristics of opioid prescription-related visits including patient demographics, opioid prescription and ICD-9-CM or ICD-10-CM based diagnosis. The unit of analysis was EDs visit wherein a person visiting EDs multiple times during the study period was counted each time as the separate ED visit.

The diagnosis or symptoms were classified into 8 groups based on ICD-9-CM or ICD-10-CM codes (**Supplementary Table 1**) to analyze the cause or contributing factor for opioid usage. The groups included abdominal pain, chest pain, respiratory disease, cancer pain, urinary tract disease, headache, back pain and unclassified.

2.3 Study endpoints

Primary endpoint was the trend in opioids prescriptions in EDs (usage in EDs and prescriptions at the time of discharge), *i.e.*, the rate per 10⁴ visits over time, and the associated diagnosis of EDs visits resulting in opioids usage and prescriptions from 2008 to 2018. The secondary endpoints included the trends of opioid prescription in EDs and hospitals.

2.4 Statistics

The descriptive statistics described trends of opioid prescription in each calendar year. The characteristics such as age groups, sex, hospital levels, diagnosis and opioid usage were presented as rate/10⁴ visits. The linear regression analysis estimated the trend of opioid prescriptions in EDs from 2008

to 2018. A *p*-value of < 0.05 was statistically significant. All the statistical analyses were conducted by RStudio 2021.09.0 (©2009–2021 RStudio, Public Benefit Corporation, Boston, MA, USA).

3. Results

3.1 Temporal trend of opioid usage during EDs visits from 2008 to 2018

Table 1 exhibited that the annual opioids prescriptions in Taiwan were 1.66 million (year 2008) and 1.95 million (year 2017), while the number of opioids prescriptions in EDs was 161,091 (year 2008), 219,320 (2015) and 187,000 (2018). The prescriptions in EDs and at the national level were 9.72% and 11.97%, respectively. There was no significant trend change. Besides, the opioids were prescribed in ~3% of EDs visits each year.

The total opioid prescription rate (prescriptions per 104 visits) from EDs in Taiwan touched its maximum to 330.24/10⁴ in 2015 from 282.64/10⁴ in 2008, as shown in Fig. 1. The rate decreased to 286.47/10⁴ in 2018, though the change was not significant (*p* = 0.49 by linear regression). Regarding the opioids type, the prescription rates for morphine, codeine and fentanyl increased during the study period (*p* = 0.001, <0.001 and = 0.002, respectively), whereas that of pethidine decreased (*p* < 0.001). In 2008, pethidine was the most prescribed opioid from EDs in Taiwan (123.05/10⁴), followed by morphine (121.11/10⁴), and codeine (33.15/10⁴). By 2018, morphine (180.99/10⁴), codeine (70.29/10⁴), and pethidine (23.69/10⁴) were the three most prescribed opioids in EDs. Hydromorphone and oxycodone were launched in Taiwan in 2014 and 2016, respectively, however their prescriptions had lower rates.

3.2 The diagnoses associated with opioid prescriptions in EDs

The three common symptoms or diagnoses associated with opioid prescriptions from EDs in Taiwan between 2008 and 2018 were the abdominal pain, chest pain and respiratory diseases, as shown in Fig. 2. The opioid prescription trend in abdominal and chest pains remained unchanged. However, an increase was noted in prescription trends for respiratory disease and back pain during 2008 to 2018 (*p* = 0.006 and <0.001, respectively). Conversely, a decreasing trend was noticed for urinary tract diseases (*p* < 0.001).

3.3 Opioid prescriptions in EDs as stratified by hospital levels

The total opioid usage among EDs visits depicted stable trend in medical centers (*p* = 0.074) when categorized by hospital class and adjusted for the number of EDs beds. However, an upward trend in regional (*p* = 0.003) and local hospitals (*p* < 0.001) was recorded between 2008 and 2018, as depicted in Fig. 3.

TABLE 1. Trend* of opioids usage in nation and emergency departments of Taiwan, 2008–2018.

Opioids use	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
ED opioid prescriptions (A)	161,091	183,594	205,306	206,366	214,437	195,968	211,317	219,320	213,891	199,923	187,769
Total national opioid prescriptions (B)	1,657,871	1,694,034	1,716,238	1,753,601	1,791,098	1,758,148	1,838,697	1,859,456	1,890,447	1,945,930	1,884,408
Opioid prescriptions in ED (A/B)	9.72%	10.84%	11.96%	11.77%	11.97%	11.15%	11.49%	11.79%	11.31%	10.27%	9.96%
Annual ED visits (C)	5,699,514	6,354,308	6,478,162	6,671,304	6,730,946	6,328,423	6,498,546	6,641,236	6,893,527	6,497,739	6,554,591
ED visit opioid prescriptions (A/C)	2.83%	2.89%	3.17%	3.09%	3.19%	3.10%	3.25%	3.30%	3.10%	3.08%	2.86%

*Linear regression analysis of trend changes in ED opioid prescription percentage: $p = 0.710$. ED: emergency department.

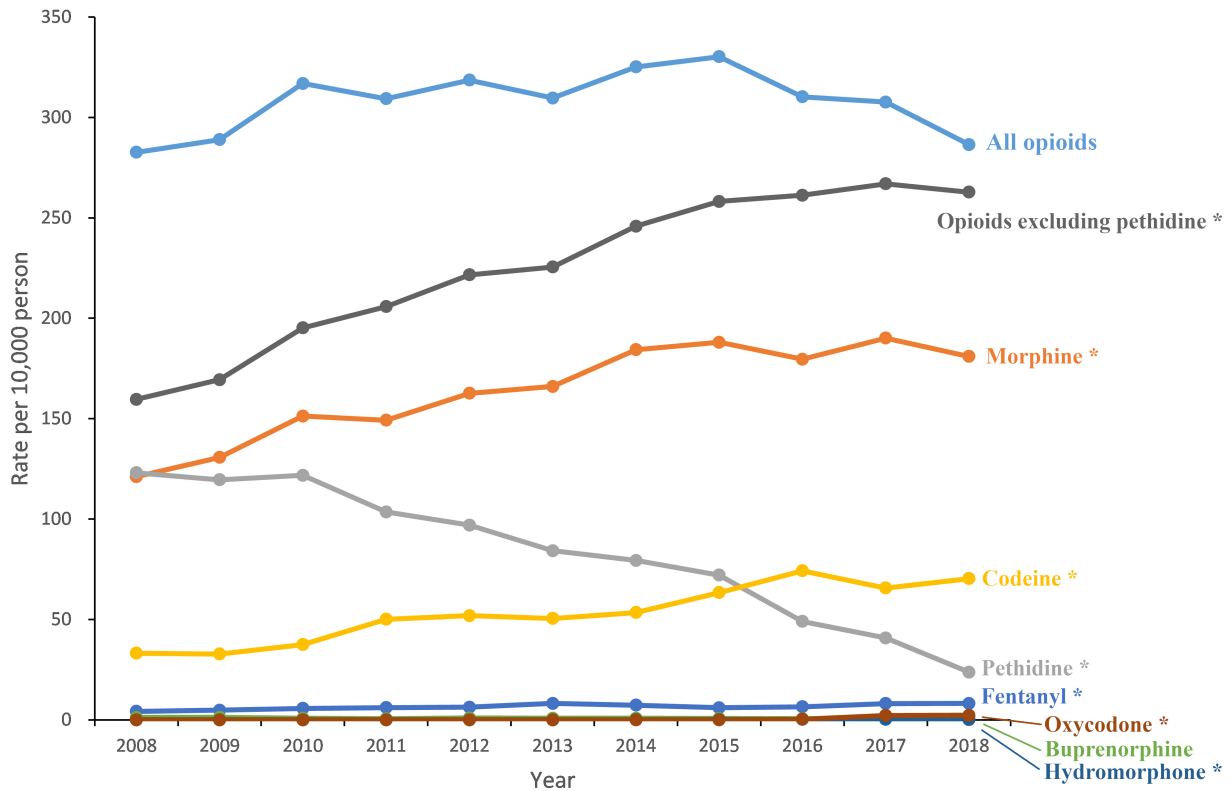


FIGURE 1. Opioid prescription trends in Taiwan’s emergency departments (2008–2018), categorized by all opioids and specific opioids. Footnote: *indicated $p < 0.05$ by trend test.

Fig. 4a illustrated that morphine had an upward trend in EDs prescription rate from 2008 to 2018 at all hospital levels ($p < 0.001$). Contrarily, pethidine (Fig. 4b) had downward trend in EDs of medical centers and regional hospitals (both $p < 0.001$). The codeine prescription rate (Fig. 4c) was enhanced at all hospital levels ($p < 0.001$), with regional hospitals EDs having the most significant change ($p < 0.001$). The fentanyl (Fig. 4d) had higher prescription rate in EDs of medical centers compared to the local and regional hospitals. However, the rate increased in medical centers and local hospitals between 2008 and 2018 ($p < 0.001$ and 0.006 , respectively).

The buprenorphine prescription rate (Fig. 4e) in EDs of medical centers declined during the study period ($p = 0.018$) however increased in the EDs of regional hospitals ($p = 0.006$), especially between 2016 and 2018. The oxycodone (Fig. 4f) and hydromorphone (Fig. 4g) had low prescription rates and mainly prescribed in EDs of medical centers. The hydromorphone prescription rate in medical centers was increased from 2014 to 2017, and dropped in 2018. Conversely, the oxycodone had an increased prescription rate in medical centers since 2017.

4. Discussion

A nationwide database was utilized in this retrospective study. It was demonstrated that the total opioid prescription rate in EDs of Taiwan’s hospitals did not change within a decade (2008 to 2018). However, morphine, codeine and fentanyl had upward trends contrary to pethidine with downward trend. The most frequent diagnosis with opioid prescription in EDs was

abdominal pain followed by chest pain, respiratory disease and cancer. This was the first study to examine opioid prescription pattern in EDs setting. Moreover, this was also the largest to-date reporting of EDs opioid usage in real-world setting of Asia. The study got its strength from nationwide population data stored in 10-year database of 23 million beneficiaries. It was statistically strong and the results were convincing compared to small-scale studies.

The study exhibited that 11% of opioid prescriptions in Taiwan were attributed to EDs visits, which were lower than that of in United States however comparable to the European countries. The proportion of opioid prescriptions in EDs visits ranged from 2.83% to 3.30%, which was low compared to other countries. The United States witnessed surge in opioid prescriptions during EDs visits where percentage increased from 20.8% to 31.0% in the period of 2001 to 2010 [10]. Moreover, 25% of EDs visits from 2005 to 2016 were identified as the opioid-using visits [33, 34]. This study however had not considered tramadol and methadone. Tramadol usage was 1.7% (2007) and 2.9% (2018) of EDs visits in United States. Swiss report revealed that 7.3% patients had opioid prescriptions on admission to EDs from 2017 to 2018 [21]. A study noted rise of total tramadol consumption in Taiwan between 2002 and 2016 [35], however no specific epidemiological reports could be found on tramadol usage in EDs of Taiwan. Thus, comparisons with other countries were not available because of the heterogeneity in opioid usage among regions and countries.

This study found that the overall trend of opioid prescription rates in EDs were unchanged from 2008 to 2018 in Taiwan.

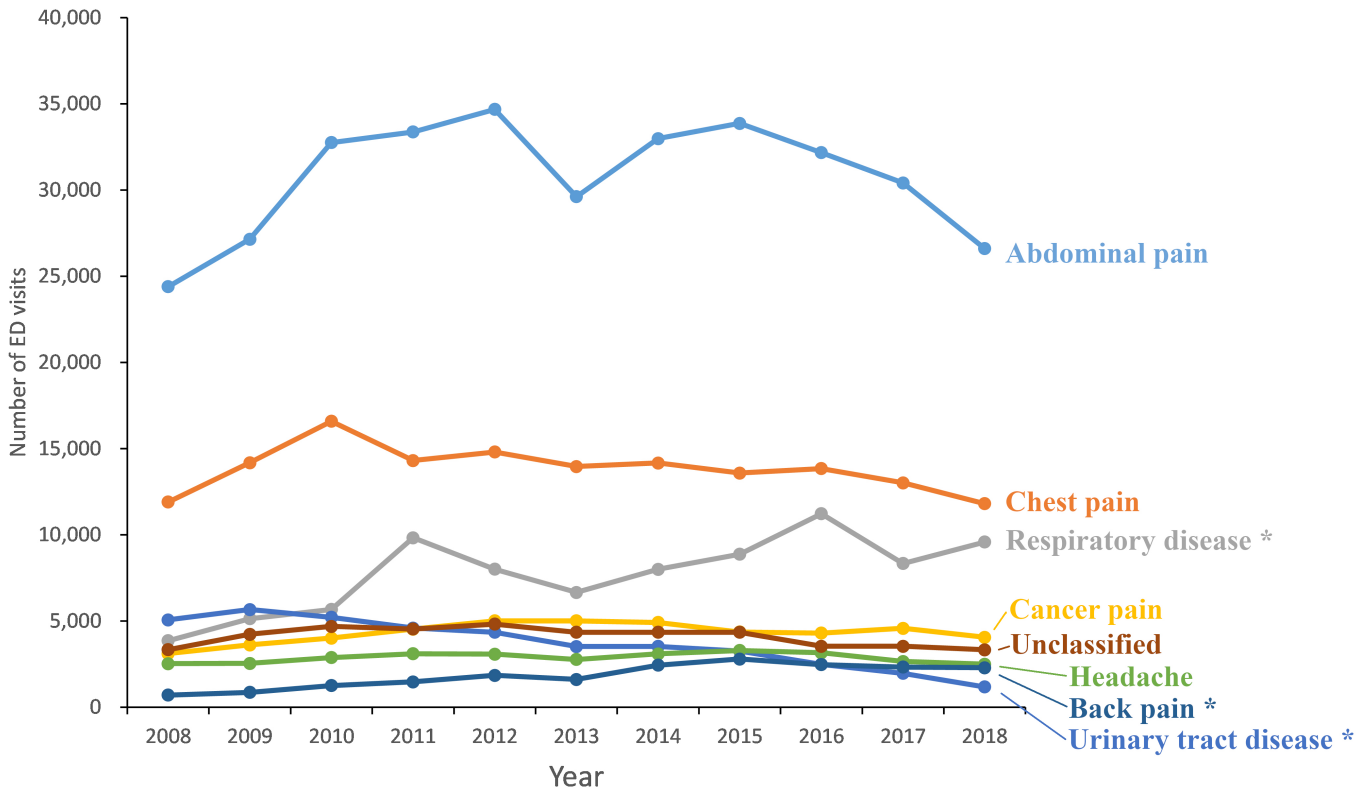


FIGURE 2. Opioid prescription trends in Taiwan’s emergency departments, classified by diagnosis (2008–2018). Footnote: *indicated $p < 0.05$ by trend test.

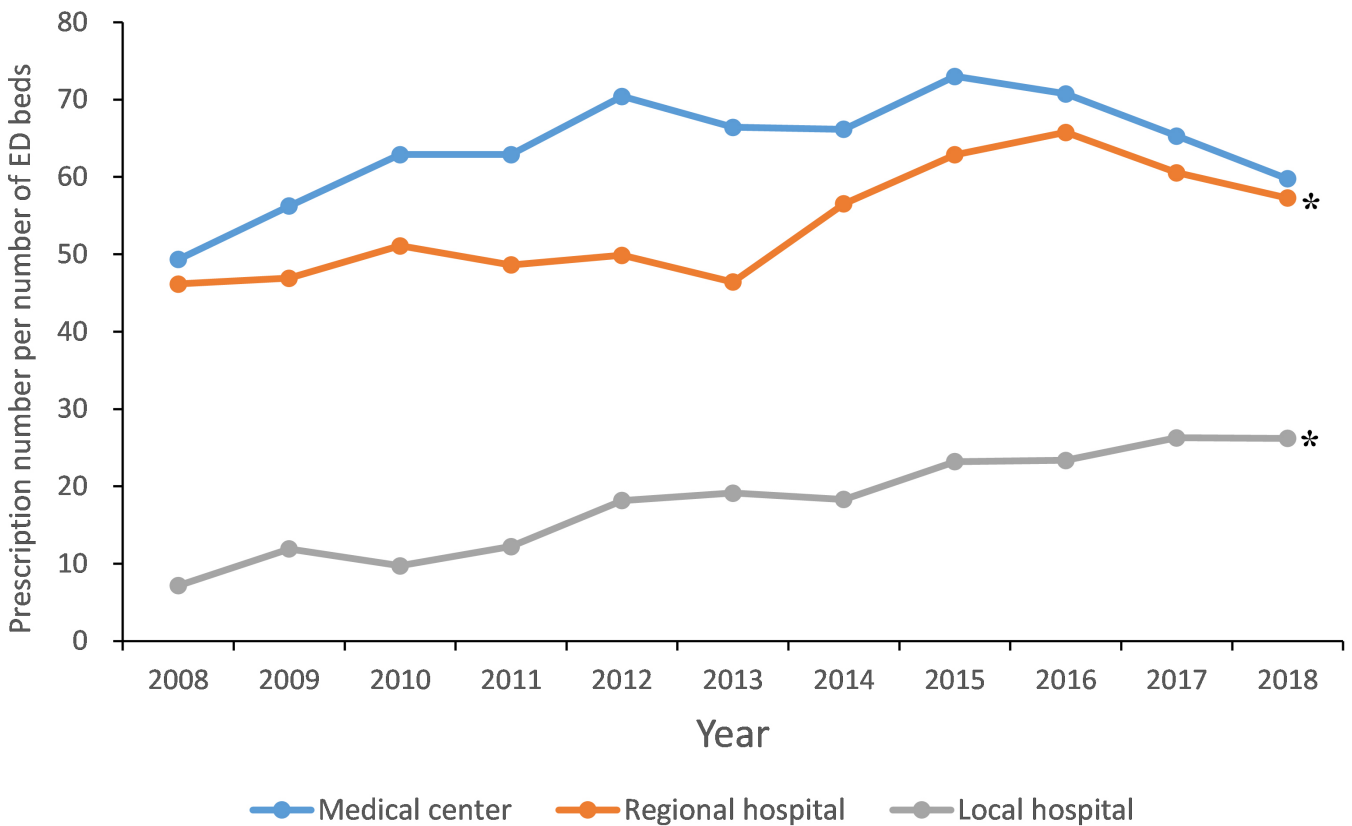


FIGURE 3. Opioid prescription trends in Taiwan’s emergency departments from 2008–2018, classified by hospital levels (medical center, regional hospital and local hospital). Footnote: *indicated $p < 0.05$ by trend test.



FIGURE 4. Opioid prescription trends in Taiwan’s emergency departments from 2008–2018, classified by hospital levels and adjusted by beds. (a) Morphine; (b) Pethidine; (c) Codeine; (d) Fentanyl; (e) Buprenorphine; (f) Oxycodone; (g) Hydromorphone. Footnote: *indicated $p < 0.05$ by trend test.

However, notable changes in prescription rates were found pertaining to the specific opioid categories. The morphine, codeine and fentanyl rates were increased over the study period, whereas pethidine rate was steadily decreased. The decreasing trend of pethidine was in line with Beers criteria [36], which recommended against the meperidine usage in older adults. This was also consistent with a prior study in Taiwan examining the national pethidine prescriptions from 2002 to 2007 [37].

Morphine, codeine and pethidine were the three most prescribed opioids in EDs of Taiwan. US had different patterns where morphine and hydromorphone were the most prescribed opioids from EDs in 2010 [10]. Oxycodone, transdermal fentanyl and tramadol were the most common opioids in Switzerland between 2017 and 2018 [21]. A meta-analysis suggested that the hydromorphone had slightly better analgesic effect than morphine [38], which might explain the high hydromorphone usage in US. However, hydromorphone in Taiwan was only available in slow-release oral form, which might have limited its usage for acute pain management in EDs.

A Taiwanese study examining opioid consumption in settings not limited to EDs depicted that between 2002 and 2014, opioid consumption per capita increased for fentanyl, morphine and codeine while decreased for quasi-drugs [39]. Comparing results with this study revealed that trends were similar for morphine, fentanyl and meperidine while opposite for codeine.

Morphine and codeine had increased prescription rates at all levels of EDs while pethidine had decreasing trend in medical centers and regional hospital EDs, however the prescription rates in local hospital EDs remained unchanged. The pethidine prescription rates in medical center EDs since 2016 had the lowest among all hospital levels. This might reflect that physicians at higher levels in hospitals were more inclined to gauge their clinical practice based on current recommendations.

This study identified abdominal pain, chest pain and respiratory disease as the most common diagnoses or symptoms for opioid prescriptions in Taiwan's EDs. These findings differed from those of US studies, where dental pain, urolithiasis, fractures, back pain and extremity pain were the common diagnoses for opioid prescriptions at discharge times between 2006 and 2017 [40]. In another US study analyzing the NHAMCS database between 2001 and 2010, opioid prescriptions in EDs were more for chest pain, abdominal pain and headache [10].

The opioid prescription rates for patients having pain conditions like back pain, abdominal pain and headache had shown decreasing trend in US [40]. In Switzerland, the primary indication for opioid prescription in EDs from 2017 to 2018 was musculoskeletal disease followed by neoplastic disease [21]. In Australia, opioid prescriptions with the maximum permissible quantities at discharge in 2017 were given to patients with musculoskeletal, urogenital and gastrointestinal diseases [20].

5. Limitations

This study had some limitations. First, only the number of opioid prescriptions was calculated and no assessment made for the prescription amount which limited the comprehension

of opioid usage pattern. Second, the opioid administration in EDs or prescriptions after EDs discharge were not calculated separately. Third, the tramadol was not included because it was considered a weak mu-opioid agonist and only classified as a schedule IV drug in Taiwan. Furthermore, methadone was excluded as it was employed only for the drug addiction treatment and not for pain management in Taiwan. Fourth, the pain levels were not recorded in NHIR database, which hindered the confirmation of true pain conditions of the patients. Fifth, patients' characteristics and diagnoses might be amplified if they revisited EDs multiple times during a short period. Sixth, the opioid prescribers' details were not included in this study. There was no information if the opioid was prescribed by an EDs physician or consultant specialist.

6. Conclusions

The present study highlighted noteworthy trends in opioid prescription practices in Taiwan's emergency departments. Between 2008 and 2018, the morphine, codeine and fentanyl had increased prescriptions while that of pethidine was declined. Furthermore, the most often prescribed opioids in Taiwan's EDs were morphine, followed by codeine and pethidine. The dominant indications for opioid prescriptions in EDs were the abdominal pain, chest pain, respiratory disease and malignancy.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and analyzed during the current study are not publicly available due to legal restrictions for privacy protection of susceptible populations under the regulations of Taiwan but are available from the corresponding authors on reasonable request.

AUTHOR CONTRIBUTIONS

CLK—reviewed the literature, interpreted the results and drafted the manuscript. CHH—reviewed the literature and performed the statistical analyses. KCH, YTL, PHT and JJW—reviewed the literature and interpreted the results. CCC—conceived and design the study, coordinated and interpreted the results, and revised the manuscript. All authors have read and approved the final version of this manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by Institutional Review Board of Chi Mei Medical Center (Serial No. 10812-E01) and the requirement for informed consent was waived by the Chi Mei Hospital institutional review board because of the retrospective nature of the study and all patient identification data were encrypted. All methods were carried out per relevant guidelines and regulations of Chi Mei Medical Center.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at <https://oss.signavitae.com/mre-signavitae/article/1732576605125918720/attachment/Supplementary%20material.docx>.

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