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Candice D. Donaldson
Chapman University

Zeev N. Kain
University of California, Irvine, zkain@hs.uci.edu

Louis Ehwerhemuepha
Children's Hospital of Orange County

Michelle A. Fortier
University of California, Irvine, mfortier@hs.uci.edu

Michael T. Phan
Chapman University

See next page for additional authors

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Authors

Candice D. Donaldson, Zeev N. Kain, Louis Ehwerhemuepha, Michelle A. Fortier, Michael T. Phan, Daniel M. Tomaszewski, Sun Yang, William Feaster, and Brooke N. Jenkins

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Candice D. Donaldson[a,b], Zeev N. Kain[bc], Louis Ehwerhemuepha[d], Michelle A. Fortier[b,e], Michael T. Phan[f], Daniel M. Tomaszewski[f,g], Sun Yang[h], William Feaster[d], Brooke N. Jenkins[a,b,c]

[a]Chapman University, Department of Psychology, Orange, CA

[b] University of California Irvine, Center on Stress & Health, Irvine, CA

[c] University of California Irvine, Department of Anesthesiology and Perioperative Care, Irvine, CA

[d]Children's Hospital of Orange County, Department of Information Systems, Orange, CA

[e]University of California Irvine, Sue & Bill Gross School of Nursing, Irvine, CA

[f]Chapman University, School of Pharmacy, Department of Biomedical and Pharmaceutical Sciences, Orange, CA

[g]University of Southern California, School of Pharmacy, Schaeffer Center for Health Policy and Economics, Los Angeles, CA

[h]Chapman University, School of Pharmacy, Department of Pharmacy Practice, Orange, CA

Address correspondence to: Dr. Brooke N. Jenkins, PhD, (bjenkins@chapman.edu) Crean College of Health and Behavioral Sciences, Chapman University, One University Drive, Orange, CA 92866

Running Head: Anxiety, Mood Disorders, and Opioid Prescribing

Abstract

This research examined whether pediatric inpatients without an anxiety/mood disorder are more likely to receive opioids in response to pain compared to patients diagnosed with a mental health condition. Research questions were tested using cross-sectional inpatient electronic medical record data. Propensity score matching was used to match patients with a disorder with patients without the disorder (anxiety analyses: $N = 2{,}892$; mood analyses: $N = 1{,}042$). Although patients with anxiety and mood disorders experienced greater pain, physicians were less likely to order opioids for these patients. Analyses also disclosed an interaction of anxiety with pain—the pain-opioid relation was stronger for patients without an anxiety disorder than for patients with an anxiety diagnosis. Instead, physicians were more likely to place non-opioid analgesic orders to the manage the pain of patients with anxiety disorders. Findings imply that pain management decisions might be influenced by patient mental health.

Keywords: opioids; pediatric pain; pain management; mood disorders; anxiety disorders

Introduction

The opioid epidemic has emerged as a public health crisis in the U.S., with about 47,000 Americans dying from an opioid-related overdose annually (Center for Disease Control and National Center for Health Statistics, 2018). Children and adolescents have also been impacted by this opioid epidemic. A study of pediatric deaths from opioids suggests a 268.2% increase in mortality rates between 1999-2016 (Gaither, Shabanova, & Leventhal, 2018), with approximately 16.2% of all emergency department visits for patients ages 13 – 17 being associated with opioid use (Tomaszewski, Arbuckle, Yang, & Linstead, 2018). Nationally, about 3.6% of adolescents between the ages of 12 and 17 report misusing an opioid in the past year (Substance Abuse and Mental Health Services Administration, 2017). This is troubling, as initiating opioid misuse between the ages of 10 and 12 years old has been linked with a high risk of transitioning to heroin use in adolescence and young adulthood (Cerdá, Santaella, Marshall, Kim, & Martins, 2015).

Despite this risk of opioid misuse and its adverse consequences, research on the legitimate use of prescribed opioids in pediatric patients is relatively scarce. Notably, prescribed opioid use from a physician in a pediatric hospital setting has been identified as a risk factor of youth opioid misuse (McCabe et al., 2017). A national study showed that legitimate opioid use during adolescence was associated with a 33% increase in the risk of future nonmedical use during young adulthood (Miech, Johnston, O'Malley, Keyes, & Heard, 2015). Similarly, pediatric patients prescribed opioids for postoperative pain have been shown to be at risk for persistently using opioids 3 to 6 months after the surgical recovery period (Harbaugh et al., 2018). Given the link between medical opioid use with misuse (McCabe et al., 2017) and persistent use (Edlund et al., 2014), researchers have begun to assess the relationship between

pain and opioid prescribing in both the outpatient (Donaldson et al., 2020; Kain et al., 2020) and hospital setting (Womer et al., 2014).

Pain in hospitalized children is common (Friedrichsdorf et al., 2015), with about 27% of pediatric patients experiencing moderate to severe pain (Groenewald, Rabbitts, Schroeder, & Harrison, 2012). Specifically, pain is defined as "an unpleasant sensory and emotional experience, associated with actual or threatened tissue damage, or described in terms of such"(International Association for the Study of Pain, 1994), signifying that pain is a cognitive, and emotional response to nociception (Bushnell, Čeko, & Low, 2013). However, the intensity of pain experienced can greatly vary for a given noxious stimulus based on the interactive effects of biological (e.g., genetics), psychological (e.g., distress, emotions, coping strategies), and social (e.g., culture, family relationships) factors (Rahim-Williams, Riley, Williams, & Fillingim, 2012; Taylor, 2015).

A link between anxiety and depression severity with pain has been established in both adult and pediatric samples. In a longitudinal study with adult patients being treated for chronic musculoskeletal pain and depression, Bair and associates (2013) found that baseline anxiety symptomology predicted pain during a 12 month follow-up assessment. Specifically, patients scoring higher on the Generalized Anxiety Disorder scale (Spitzer, Kroenke, Williams, & Löwe, 2006) reported greater pain severity one year later. Similar trends have been found for pediatric patients. Stanford and associates (2008) showed that depression and anxiety severity were associated with recurrent head, stomach, and back pain in a sample of 10 to 11 year old respondents followed longitudinally overtime. In contrast, the diagnostic relationship between common psychiatric disorders (e.g., anxiety and depression) with pain is less understood. Dorn et al. (2003) conducted a cross-sectional study with children and adolescents between the ages of 8

and 16 and found that 50% of youth with recurrent abdominal pain met the diagnostic criteria for an anxiety disorder. However, additional research is needed to better understand differences in pain severity based on the presence or absence of a mental health disorder.

Opioid use is also associated with mental health in adult patients. Specifically, previous studies advocate that adults with mental health co-morbidities have a higher likelihood of receiving an opioid prescription (Davis, Lin, Liu, & Sites, 2017) and regularly using prescription opioids (Halbert, Davis, & Wee, 2016; Sullivan, Edlund, Zhang, Unützer, & Wells, 2006). Research (Goesling et al., 2015) also suggests that pain and mental health might interact to influence opioid prescribing and use. Goesling and associates (2015) examined the relationship between pain and opioid use in depressed adults with chronic pain, and found that depression moderated the pain-opioid use relationship. For patients with no depressive symptoms, there was a positive association between pain severity and opioid use. However, for patients with symptoms of depression, there was no significant relationship between pain severity and opioid use.

In adolescents, studies have established a link between adolescent depression with opioid misuse (Havens, Young, & Havens, 2011), persistent use (Whiteside et al., 2016), and abuse (Edlund et al., 2015). However, the relationship between pain and opioid prescribing for pediatric patients diagnosed with anxiety and mood diagnoses has been understudied (Groenewald, Zhou, Palermo, & Van Cleve, 2019; Quinn et al., 2018). Quinn and associates (2018) investigated relationships between mental health and opioid prescribing using a database of commercial insurance claims. In this study, patients with anxiety and mood disorders were more likely to be prescribed a prescription opioid and to receive long-term opioid therapy. Similarly, Groenewald et al. (2019) found that anxiety and mood disorders were related with an

increased risk of opioid overdose in a retrospective analysis of privately insured adolescent patients. Still, despite the utility of these studies, there is a lack of research assessing statistical interactions between pain severity and diagnosis on the prescription of opioid medications in one multivariable model for pediatric inpatients.

Given this gap in the literature, research examining differences in pain and opioid use based on mental health in a pediatric inpatient setting is important for encouraging appropriate and safe pain management across diverse groups, before patients develop future problems with misuse and persistent use. As such, the current study aims to determine whether differences in pain and physician opioid ordering exist for patients with mental health comorbidities, and whether, the relationship between pain and opioids differs based on mental health diagnosis during the patient's visit. It is hypothesized that patients diagnosed with anxiety and mood disorders during their inpatient stay will experience higher levels of pain during their hospital admission. Additionally, the presence or absence of an anxiety/mood disorder diagnoses is postulated to moderate the relationship between inpatient pain and the number of opioid medications ordered (Goesling et al., 2015). Specifically, patients without an anxiety or mood disorder diagnosis are anticipated to be more likely to receive opioid orders in response to clinically significant pain compared to patients with a mental health diagnosis.

Method

Data Source

Research questions were assessed using cross-sectional inpatient encounter data from June 2013 to June 2018 that was retrieved from a pediatric children's hospital. Electronic medical record information (EMR) was extracted from pediatric patients between the ages of 0 and 18 (N = 81,018) that were admitted as inpatients across a variety of care settings and were prescribed

medication to manage pain. Records were de-identified and patients were assigned a unique encounter identifier, allowing medical record information to be linked.

Inclusion Criteria and Data Cleaning

Given the low prevalence of anxiety and mood disorders in patients under the age of 2, only patients between the ages of 2 and 18 were included in the analysis (N = 63,195). Further, the objective of this research was to examine differences in opioid prescribing for patients without cancer-associated chronic pain; thus, information on neoplasms was extracted using International Classification of Diseases, Ninth/Tenth revision (ICD-9/10), Clinical Modification codes C00 through D49. Patients with neoplasms (n = 8,017) were identified using the diagnosis codes and excluded from the analyses (Chung et al., 2018; Richardson et al., 2011). Patient length of stay was then examined for outliers. Patients in the 99th percentile (n = 647) were excluded from the remaining analyses (N = 54,531).

Variables

Pain severity. Patient pain is assessed by healthcare providers throughout the in-patients' hospital stay using several developmentally and situationally appropriate measurement tools (i.e., Faces, Legs, Activity, Cry, and Consolability scale [Voepel-Lewis, Merkel, Tait, Trzcinka, & Malviya, 2002], Faces Pain Scale [Hicks, von Baeyer, Spafford, van Korlaar, & Goodenough, 2001], Numeric Rating Scale [Miró, Castarlenas, & Huguet, 2009], and Neonatal Pain, Agitation and Sedation Scale [Hummel, Puchalski, Creech, & Weiss, 2008]). For the purpose of the present study, patient maximum pain score ratings during the hospital stay were included in the analyses (as done in Ehwerhemuepha, Schultz, & Feaster, 2018). Across all scales, pain level ranged from 0 (*no pain*) to 10 (*high pain*). Additionally, pain score was standardized (using a z-score) in the final analysis.

Anxiety and mood disorder diagnosis. Anxiety and mood disorders were diagnosed by the patient's provider during their inpatient visit. Patients were classified as having a mental health disorder if they displayed the symptoms presented in Table 1. Using the ICD-9/10 coding system, and grouping strategy implemented in prior studies (see Carballo et al., 2010; Pedersen et al., 2014; Waghorn, Chant, White, & Whiteford, 2005), patients were categorized as having an anxiety disorder if they were diagnosed with at least one of the following conditions during their inpatient visit: phobic and social anxiety disorders (F40-F40.9); generalized anxiety, panic disorder, and other anxiety disorders (F41-F41.9), stress-related and adjustment disorders (F43-F43.9); and somatoform disorders (F45-F45.9). Patients were classified as having a mood disorder diagnosis if they were diagnosed with one or more of the following conditions during their visit: manic episode (F30-F30.9); bipolar disorder (F31-F31.9); major depressive disorder (F32-F33.9); persistent mood disorders (F34-F34.9); and unspecified mood disorder (F39).

Opioid and non-opioid analgesic medication orders. The primary outcome variable examined in this research was the number of opioid orders made by the patient's provider during a single patient hospitalization encounter, regardless of the quantity/dose of the medication per order (as done in Ehwerhemuepha et al., 2020). Specifically, this variable represented the total number of opioids requested by the physician. Opioids included codeine, hydrocodone, hydromorphone, meperidine, sufentanil, fentanyl, morphine, oxycodone, remifentanil, nalbuphine, methadone, and tramadol. A sum of the total number of opioid analgesic medications ordered was computed as a sum score across all the different possible opioid types to indicate the total number of opioids ordered. Patients with more than one opioid order could have had the same opioid medication ordered multiple times, multiple opioid medications, or a combination of the two. In addition, information on the number of non-opioid analgesics (e.g.,

ibuprofen, acetaminophen, naproxen, gabapentin, pregabalin, celecoxib, triptan) orders was calculated in the same way.

Covariates. Information on admittance year, age, sex, race/ethnicity (Hispanic/Latinx versus all others), insurance (Medicare/Medi-Cal versus all other insurance types), and length of stay were included in all analyses as control variables. Patient visit diagnoses were also retrieved and controlled for using the ICD-9/10 coding system (see Table 2).

Data Analytic Strategy

Propensity score case-control matching was performed using R's "MatchIt" package (Ho, Imai, King, & Stuart, 2011). The nearest neighbor matching algorithm with a caliper width set = 0.2 of the SD of the logit of the propensity score was implemented (Austin, 2011). Both the anxiety and mood disorder diagnoses were submitted to a propensity score matching procedure. The propensity that each participant received a diagnosis of an anxiety or mood disorder was calculated using a regression model that included the demographic and visit medical diagnosis covariates. “Case” (presence of an anxiety/mood disorder) and “Control” (absence of an anxiety/mood disorder) sets of patients were matched based on the resulting propensity scores. Matching was conducted without replacement. All patients who were not matched in the propensity score procedure was excluded from subsequent analyses. Following the recommended guidelines (Zhang, Kim, Lonjon, & Zhu, 2019), the standardized mean difference of covariates before and after matching was calculated and assessed to diagnose the balance each covariate distribution between the case and control groups.

Two separate Poisson regression models assessed the relationships between anxiety/mood disorder diagnoses with medication ordering using the propensity score matched samples. A linear multiple regression model assessed the association of pain level with

medication ordering. Admission year, demographic variables, and visit diagnosis covariates were controlled for in all analyses. All variables were standardized using z-scores in the final model. The graphing and interpretation of the interaction terms followed recommended procedures (Aiken & West, 1991). The simple slope of maximum pain score was graphed on the anxiety/mood disorder moderator at one standard deviation below the mean, at the mean, and one standard deviation above the mean.

Results

Descriptive information on the final samples is displayed in Table 3. The earliest age of onset for all mental health conditions was 2 years old. Overall, 2.90% (n = 1,586) of the sample was diagnosed with a clinical anxiety disorder and 1.30% (n = 711) were diagnosed with a mood disorder during their inpatient visit (see Tables 2 and 3). Approximately 92.60% of patients classified as having an anxiety disorder and 95.2% of patients with recorded as having a mood disorder were diagnosed with at least one other diagnostic condition during their inpatient admission. Furthermore, 140 cases could not be matched in the anxiety disorder matching procedures and 190 were unmatched in the mood disorder matching analysis. Large group differences in the demographic and diagnosis covariates across diagnosis groups were largely eliminated in the propensity score case-control matching.

Multivariate Regression Models

Pain severity. The multivariate regression models examining the effect of anxiety (Table 4) and mood (Table 5) disorders on pain severity, showed that after controlling for all demographic and diagnosis covariates, patients diagnosed with an anxiety and/or mood disorder (both $p < .001$) expressed higher pain levels during their hospitalization.

Ordered opioid analgesics. The model testing the effect of anxiety on ordered opioid analgesics (Table 4), indicated that physicians ordered fewer opioids for patients with lower pain scores and anxiety disorders (both $p < .001$). There was also a significant interaction of pain and anxiety diagnosis ($p < .001$; Figure 1). The relationship between pain and the number of opioids ordered was stronger for patients without an anxiety disorder ($\beta = 0.21$, $SE = 0.01$, $p < .001$), than for patients with an anxiety disorder ($\beta = 0.16$, $SE = 0.01$, $p < .001$). When patients expressed high pain levels (+1SD above the mean), physicians placed an average of 2.53 opioid orders for patients without anxiety and 1.83 orders for those with an anxiety disorder diagnosis. Thus, although patients with anxiety disorders expressed greater pain, physicians ordered 32.11% more opioids for patients without anxiety diagnoses. In contrast to the anxiety disorder findings, the model examining the effect of mood on ordered opioid analgesics (Table 5), did not reveal a significant interaction of pain level and mood disorder. Instead, findings disclosed significant main effects of pain and a mood disorder diagnosis, indicating that patients with lower pain scores and mood disorders (both $p < .001$) received fewer opioids.

Ordered non-opioid analgesics. The regression model scrutinizing the impact of anxiety on ordered non-opioid analgesics (Table 4), showed that physicians ordered a greater number of non-opioids for patients with higher pain scores ($p < .001$). There was also a significant interaction of pain and anxiety disorder diagnosis ($p < .001$; Figure 2)—the relationship between pain and the number of non-opioids ordered was stronger for patients with an anxiety disorder ($\beta = 0.10$, $SE = 0.01$, $p < .001$), than for patients without an anxiety diagnosis, ($\beta = 0.07$, $SE = 0.01$, $p < .001$). When patients expressed high pain, physicians ordered 2.61 non-opioid medications for patients without an anxiety disorder and 2.96 non-opioid analgesics for patients with anxiety disorders (representing a 12.57% difference). The model analyzing the effect of mood on ordered

non-opioids (Table 5), showed that pain score was associated with non-opioid orders ($p < .001$). The main effect of mood disorder diagnosis and the interaction with pain were not statistically significant.

Auxiliary Analysis

Although visit diagnosis was controlled for in all analyses, a possible alternative explanation of the presented findings is that patient medical diagnosis confounded the results. Findings in both analyses revealed that patients diagnosed with diseases of the musculoskeletal system and connective tissue (M00-M99) and/or injury, poisoning and certain other consequences (S00-T88) were more likely to receive an opioid order than patients without these diagnoses. In response, an auxiliary analysis was conducted with a subset of patients with these two diagnostic classifications ($N = 11,501$). Within this selected sample, 4.60% ($n = 526$) had an anxiety disorder diagnosis and 3.00% ($n = 344$) were classified as having a mood disorder. The same analytic plan incorporating propensity score case-control matching used in the main analysis was implemented. Three hundred and thirty six patients were matched in the anxiety disorder analysis; 141 were matched in the mood disorder analysis.

The model testing the effect of anxiety on ordered opioid analgesics for patients with diseases of the musculoskeletal system and connective tissue, and/or injury, poisoning and certain other consequences ($N = 672$) revealed a significant interaction of pain and anxiety diagnosis ($\beta = -0.13$, $p < .001$). Findings replicated the main analyses—the relationship between pain and opioids orders was stronger for patients without an anxiety disorder ($\beta = 0.12$, $SE = 0.01$, $p < .001$), than for patients with an anxiety disorder ($\beta = 0.08$, $SE = 0.02$, $p < .001$). The model testing the effect of mood disorders on ordered opioid analgesics for the selected subset of patients ($N = 282$) disclosed a main effect of mood diagnosis ($\beta = -0.18$, $p < .01$), suggesting that

patients diagnosed with a mood disorder received fewer prescribed opioids regardless of pain severity.

Discussion

Under the conditions of this study, pediatric inpatients with anxiety and mood disorders were rated as having greater pain severity during their admittance as an inpatient in a hospital setting. Physicians also ordered fewer opioids for patients diagnosed with anxiety and mood disorders. Additionally, for patients diagnosed with an anxiety, physicians were less likely to place opioid orders in response to severe pain, and were instead more likely to place non-opioid analgesic orders to the manage significant pain severity.

These findings are consistent with past studies conducted among adult patients demonstrating a link between mental health with pain severity and frequency (Bair, Robinson, Katon, & Kroenke, 2003; Stanford et al., 2008). Current theoretical explanations propose an interplay of biological, emotional, and cognitive factors for explaining relationships between mental health conditions and the experience of pain (Weersing, Rozenman, Maher-Bridge, & Campo, 2012). Specifically, anxious youth might be biologically sensitive to stress (Biederman et al., 1993), demonstrating overactivity in brain regions used to suppress fight or flight response (Mathew, Coplan, & Gorman, 2001). Similarly, theories of pain for individuals diagnosed with depression imply a genetic vulnerability to mood dysregulation when faced with stressful life events (Caspi et al., 2003). Anxious and depressed individuals may experience heightened levels of anticipation and hypervigilance to threatening cues (Mogg & Bradley, 2005; Simpson, Neria, Lewis-Fernández, & Schneier, 2010), increasing the severity of pain experienced. Youth diagnosed with mood and anxiety disorders might also exhibit inaccurate, overly threatening

(Barlow, 2004) or negative cognitive styles (Gladstone & Kaslow, 1995), impacting how they perceive and express pain.

Although research with adults show that patients diagnosed with psychiatric disorders have a higher likelihood of receiving a prescription for opioid analgesics (Davis et al., 2017; Goesling et al., 2015), studies examining this association in pediatric patients is scarce (Groenewald et al., 2019; Quinn et al., 2018). A previous investigation with pediatric patients showed that being diagnosed with an anxiety or mood disorder was related with an increased likelihood of opioid prescription (Quinn et al., 2018); but this study did not assess interactions between pain severity and mental diagnosis on opioid prescribing in one multivariable model. In contrast, the current research examined opioid orders and demonstrated that patients with mental health diagnoses (anxiety and mood disorders) were less likely to receive prescription opioids when controlling for pain.

Together with prior studies on mental health and pediatric opioid use (Groenewald et al., 2019; Quinn et al., 2018), the complex results of this investigation support that the decision to order or prescribe a prescription opioid is complicated, and relies on the interaction of patient, provider, medical, and social factors (Turk & Okifuji, 1997). For example, the finding that physicians were less likely to order prescription opioid medications to treat severe pain in patients perceived to have a mental health disorder is not surprising, as there is an established relationship between prescription opioid use and later misuse in adolescent patients (Miech et al., 2015). As such, it is logical that physicians might decide to be more conservative when deciding whether to order opioid analgesics over non-opioid alternatives in this setting. Also, within the context of the opioid epidemic, governmental and professional organizations have implemented programs designed to monitor and implement consistent clinical guidelines for opioid therapy,

with guidelines recommending that physicians screen for mental health conditions prior to prescribing opioid analgesics (Nuckols et al., 2014). The finding that physicians made fewer opioid orders for pediatric inpatients with anxiety and mood disorders, even at high levels of pain, might therefore support the influence of social factors on the decision to order opioid medications.

A challenge with pain management is that no biological objective measure currently exists to assess the efficacy of opioid treatment. Nurses and physicians must therefore interpret patient pain experiences. The observed differences in ordered opioids might be explained by patient, provider, psychological, and social factors that influence how health care providers interpret pain and subsequently decide the best plan of management. Specifically, providers may perceive that patients exhibiting symptoms of anxiety and mood disorders express exaggerated pain levels due to feelings of psychological distress, worry, or depression (Hansen & Streltzer, 2005). If patient pain expression is perceived to be amplified due to the patient's current psychological state (e.g., excessive worry, fear, or sadness), it is likely that providers would decide to seek alternative lower risk pain management strategies. It is also important to highlight that despite their possible negative side effects, opioids are shown to effectively help with acute pain management (Manchikanti & Singh, 2008). Thus, patients with mental health disorders should not completely be denied opioid analgesics for pain relief, as undermanagement of pain is also a concern. Instead, future investigations should examine potential relationships between inpatient opioid use and later opioid misuse, persistent use, and abuse, and the ways in which parents can be educated about the risks of opioid use and safe storage behaviors (McDonald et al., 2017).

Strengths and Limitations

Findings should be interpreted in light of several limitations. Data were cross-sectional, and as a result, causal conclusions about the relationship between mental health conditions and physician opioid ordering could not be drawn. However, the use of propensity score matching which is a casual inference technique aids in ameliorating this limitation. The current investigation involved inpatients at a single tertiary pediatric institution. Although it is expected that studies with inpatients from similar institutions would establish similar results, the current findings might not be generalizable to all pediatric facilities. Although similar effects have been found in prior secondary data analytic research examining substance use outcomes (Donaldson, Nakawaki, & Crano, 2015), the low effect sizes in the main analyses might also represent a limitation. Still, differences in opioid ordering were relatively large at high levels of pain (representing a 33.45% difference in the anxiety analysis and a 51.90% difference in the mood disorder analysis). Thus, findings are likely to have practical and clinical implications, suggesting that physicians might possess biases outside of their awareness, and that patients with mental health conditions might be suffering disproportionally from pain in a pediatric hospital setting.

Previous research suggests that electronic medical record mental health diagnostic information is not always accurate (Davis, Sudlow, & Hotopf, 2016). Consequently, the validity of the anxiety and mood disorder diagnoses made by provider's during the patient's visit also represents a study limitation. Regardless, provider perceptions were the focus of this work, suggesting that diagnostic validity might not be as critical in this context. Instead, it is important to highlight that when physicians perceived patients as exhibiting symptoms associated with anxiety (see Table 1; e.g., persistent fear and worry) and mood (e.g., mood swings, elation, sadness) disorders, they were less likely to order opioid medications. As such, findings imply

that symptoms of mental health disorders influence provider willingness to prescribe opioid analgesics.

The aim of this work was to examine physician prescribing decisions (under the assumption that physicians ordered the appropriate medication dose). Thus, the examination of opioid orders is appropriate in this setting, as opioid orders have been examined as a proxy for opioid prescriptions in other studies of patient EMR data (Lail, Sequeira, Lieu, & Dhalla, 2014). Still, the use of opioid orders represents both a strength and limitation. Most studies of opioid use in this context have examined prescriptions or orders as a binary (yes/no) variable. A strength of this research is the examination of opioid ordering as a continuous outcome. However, the use of opioid order is also a limitation, as the number of opioids ordered did not necessarily reflect the number of doses administered to patients. To offset this limitation, visit diagnoses were controlled for in all analyses, and logistic regression models were estimated treating ordered opioid analgesics as a binary outcome, which replicated the pattern of results revealed in this study. Still, administered opioid dose represents a more accurate conceptualization of prescribing patterns, and should therefore be examined in future studies with pediatric patients.

Conclusion

To the best of our knowledge, this is the first investigation to examine trends in opioid prescribing for pediatric patients with mental health diagnoses that have been admitted as inpatients and prescribed medication to manage pain. Results suggest that although patients with anxiety and mood disorders experience more severe pain during their hospital stay, physicians decide to make fewer prescription opioid analgesic orders for patients with these psychological co-morbidities. Specifically, findings suggest that patients with anxiety and mood disorders are less likely to be prescribed opioids, even after controlling for pain level, when compared with a

matched sample of patients that did not have an anxiety/mood disorder. However, additional research is needed to understand how opioid use as an inpatient is associated with adverse opioid outcomes, especially in the pain context. Regardless, this work suggests that future studies examining the association between mental health disorders and prescription opioid use are warranted to promote safer and appropriate opioid use among pediatric populations.

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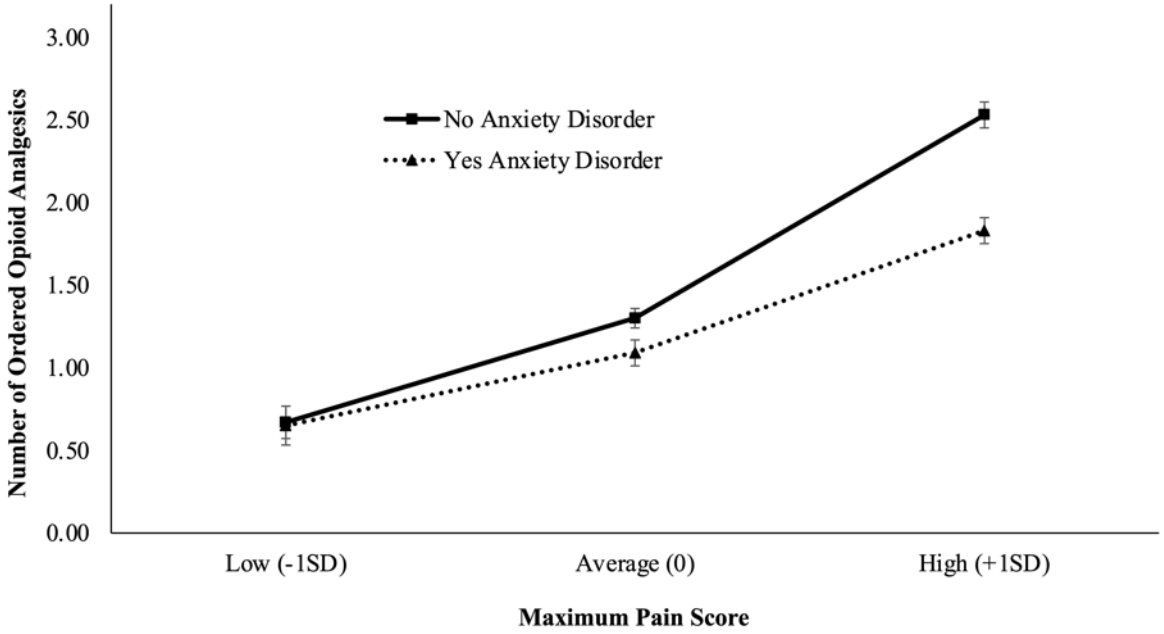
Figure Captions

Figure 1. Interaction of pain severity and anxiety disorder diagnosis on the number of opioid analgesics ordered. Values reflect standardized estimates controlling for all model covariates and 95% confidence intervals. The number of ordered opioid analgesics ranged from 0 to 10, but was truncated to maintain conceptual clarity.

Figure 2. Interaction of pain severity and anxiety disorder diagnosis on the number of non-opioid analgesics ordered. Values reflect standardized estimates controlling for all model covariates and 95% confidence intervals. The number of ordered non-opioid analgesics ranged from 0 to 9, but was truncated to maintain conceptual clarity.



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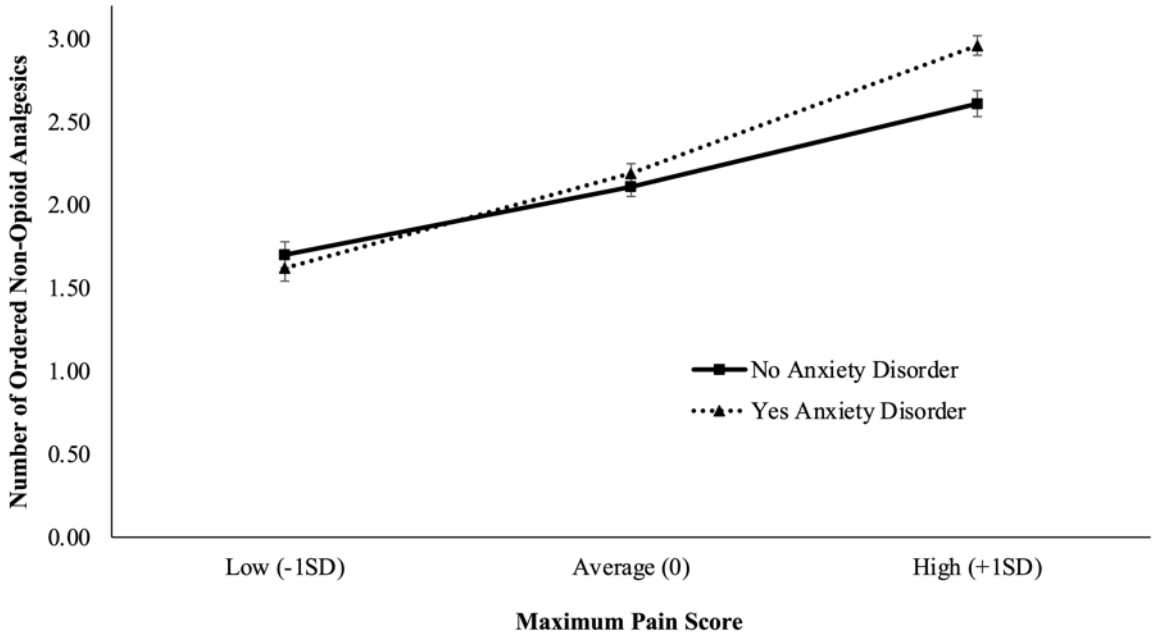

Figure 2. Interaction of pain severity and anxiety disorder diagnosis on the number of non-opioid analgesics ordered. Values reflect standardized estimates controlling for all model covariates and 95% confidence intervals. The number of ordered non-opioid analgesics ranged from 0 to 9, but was truncated to maintain conceptual clarity.

Table 1. International Classification of Diseases, Ninth/Tenth revision (ICD-9/10) Mental Disorder Diagnostic Classifications

Diagnosis	ICD 9/10 Codes	*n* (%) of Cases[a]	Symptoms[b]
Anxiety, dissociative, stress-related, and somatoform disorders (*n* = 1,586, 2.90%)			
Phobic and social anxiety disorders	F40-F40.9	220 (0.4%)	Intense, unrealistic, persistent fear and avoidance of an object, activity, or situation.
Generalized anxiety, panic disorder, and other anxiety disorders	F41-F41.9	741 (1.4%)	*Anxiety disorders*: excessive worry and feelings of fear, dread, and uneasiness that last six months or longer. *Panic disorder*: an anxiety disorder characterized by multiple unexpected panic attacks with persistent concern of recurring attacks.
Stress-related and adjustment disorders	F43-F43.9	862 (1.6%)	*Acute stress reaction and post-traumatic stress*: the development of anxiety and dissociative symptoms as a result of exposure to a traumatic event. *Adjustment disorders*: person responds to a stressful event (such as an illness, job loss, or divorce) with extreme emotions and actions.
Somatoform disorders	F45-F45.9	304 (0.6%)	The presence of physical symptoms that suggest a medical condition but are not fully explained by any known medical reasons.
Mood [affective] disorders (*n* = 711, 1.30%)			
Manic episode	F30-F30.9	201 (0.4%)	Characterized by a period of at least one week where an elevated, expansive, or unusually irritable mood.
Bipolar disorder	F31-F31.9	250 (0.5%)	Marked by severe mood swings (manic or major depressive episodes) and a tendency to remission and recurrence.
Major depressive disorder	F32-F33.9	571 (1.1%)	Ongoing feelings of sadness, loss of energy, and difficulty dealing with normal daily life. Other symptoms include feelings of worthlessness and hopelessness, loss of pleasure in activities, changes in eating or sleeping habits, and thoughts of death or suicide.
Persistent mood disorders	F34-F34.9	247 (0.5%)	Alternating and recurring periods of depression and elation. Also, can be characterized by relatively mild depressive symptoms or marked loss of pleasure in usual activities.
Unspecified mood disorder	F39	214 (0.4%)	Severe disturbance in mood (depression, anxiety, elation) accompanied by psychotic symptoms such as delusions, and hallucinations.

Note. The earliest age of onset for all disorders was 2 years old. Patients could be diagnosed with more than one disorder. a = unmatched sample (*N* = 53,292); b = symptoms from the ICD 10 website: https://www.icd10data.com/ICD10CM/Codes/F01-F99

Table 2. Sample Characteristics Before and After Propensity Score Case-Control Matching

	Anxiety Disorder Analysis				**Mood Disorder Analysis**			
	Before Matching (*N* = 54,531)		**After Matching (*N* = 2,892)**		**Before Matching (*N* = 54,531)**		**After Matching (*N* = 1,042)**	
	No Diagnosis (*n* = 52,945)	Yes Diagnosis (*n* = 1,586)	No Diagnosis (*n* = 1,446)	Yes Diagnosis (*n* = 1,446)	No Diagnosis (*n* = 53,820)	Yes Diagnosis (*n* = 711)	No Diagnosis (*n* = 521)	Yes Diagnosis (*n* = 521)
	M(*SD*)	*M*(*SD*)	*M*(*SD*)	*M*(*SD*)	*M*(*SD*)	*M*(*SD*)	*M*(*SD*)	*M*(*SD*)
Age	9.64 (4.71)	12.84 (4.08)	12.82 (4.44)	12.83 (4.06)	9.68 (4.71)	13.88 (4.11)	13.89 (4.33)	14.69 (3.48)
Length of Stay	3.26 (3.98)	6.01 (6.37)	5.99 (6.69)	6.03 (6.06)	3.33 (4.07)	4.54 (5.91)	5.30 (6.12)	5.28 (5.97)
	n(%)	*n*(%)	*n*(%)	*n*(%)	*n*(%)	*n*(%)	*n*(%)	*n*(%)
Year: 2013	3,478 (6.60)	76 (4.80)	29 (2.0)	56 (3.90)	3,485 (6.50)	69 (9.70)	27 (5.20)	22 (4.20)
Year: 2014	8,639 (16.30)	130 (8.20)	119 (8.20)	100 (6.90)	8,652 (16.10)	117 (16.50)	57 (10.90)	62 (11.90)
Year: 2015	11,320 (21.40)	154 (9.70)	231 (16.0)	140 (9.70)	11,356 (21.10)	118 (16.60)	104 (20.0)	89 (17.10)
Year: 2016	11,746 (22.20)	455 (28.70)	331 (22.90)	424 (29.30)	12,044 (22.40)	157 (22.10)	123 (23.60)	131 (25.10)
Year: 2017	11,873 (22.40)	602 (38.00)	450 (31.10)	570 (39.40)	12,295 (22.80)	180 (25.30)	147 (28.20)	155 (29.80)
Year: 2018	5,889 (11.10)	169 (10.70)	286 (19.80)	156 (10.80)	5,988 (11.10)	70 (9.80)	63 (12.10)	62 (11.90)
Male	28,451 (53.70)	678 (42.70)	618 (42.70)	635 (43.90)	28,892 (53.70)	237 (33.30)	202 (38.80)	169 (32.40)
Hispanic	28,430 (53.70)	955 (60.20)	840 (58.10)	861 (59.50)	28,943 (53.80)	442 (62.20)	320 (61.40)	326 (62.60)
Medicare/Medi-Cal	20,641 (39.00)	823 (51.90)	743 (51.40)	742 (51.30)	21,156 (39.30)	308 (43.30)	219 (42.0)	227 (43.60)
Presence of the following visit diagnoses:								
Anxiety Disorder	---	---	---	---	1,218 (2.30)	368 (51.80)	146 (28.30)	176 (34.0)
Mood Disorder	343 (0.60)	368 (23.20)	186 (12.90)	231 (16.0)	---	---	---	---
Bacterial/viral infections (A00-A99)	4,488 (8.50)	321 (20.20)	212 (14.70)	217 (15.0)	4,580 (8.50)	229 (32.20)	47 (9.0)	55 (10.60)
Blood disease (D50-D89)	6,823 (12.90)	374 (23.60)	231 (16.0)	273 (18.90)	6,963 (12.90)	234 (32.90)	60 (11.50)	63 (12.10)
Endocrine, nutritional, and metabolic diseases (E00-E89)	7,789 (14.70)	547 (34.50)	382 (26.40)	424 (29.30)	7,984 (14.80)	352 (49.50)	175 (33.60)	169 (32.40)

Nervous system diseases (G00-G99)	10,845 (20.50)	632 (39.80)	490 (33.90)	526 (36.40)	11,121 (20.70)	356 (50.10)	183 (35.10)	185 (35.50)
Circulatory system diseases (I00-I99)	3,954 (7.50)	386 (24.30)	239 (16.50)	267 (18.50)	4,068 (7.60)	272 (38.30)	109 (20.90)	96 (18.40)
Respiratory system diseases (J00-J99)	10,263 (19.40)	367 (23.10)	251 (17.40)	269 (18.60)	10,374 (19.30)	256 (36.0)	90 (17.30)	86 (16.50)
Digestive system diseases (K00-K95)	15,304 (28.90)	519 (32.70)	398 (27.50)	417 (28.80)	15,516 (28.80)	307 (43.20)	136 (26.10)	136 (26.10)
Diseases of the musculoskeletal system /connective tissue (M00-M99)	53,40 (10.10)	392 (24.70)	240 (16.60)	294 (20.30)	5,469 (10.20)	263 (37.0)	84 (16.10)	91 (17.50)
Genitourinary system diseases (N00-N99)	4,008 (7.60)	349 (22.0)	203 (14.0)	246 (17.0)	4,105 (7.60)	252 (35.40)	76 (14.60)	80 (15.40)
Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99)	8,176 (15.40)	367 (23.10)	238 (16.50)	271 (18.70)	8,299 (15.40)	244 (34.30)	76 (14.60)	76 (14.60)
Injury/poisoning (S00-T88)	6,103 (11.50)	357 (22.50)	229 (15.80)	257 (17.80)	6,168 (11.50)	292 (41.10)	108 (20.70)	118 (22.60)
Other mental, behavioral and neurodevelopmental (F01-F99)	4,065 (7.70)	448 (28.20)	307 (21.20)	320 (22.10)	4,167 (7.70)	346 (48.70)	164 (31.50)	159 (30.50)

Table 3. Descriptive Statistics

		Unmatched Sample (N = 54,531)	Anxiety Disorder Analysis Matched Sample (N = 2,892)	Mood Disorder Analysis Matched Sample (N = 1,042)
Demographic and Clinical Characteristics				
Age	Range	2 – 18	2 – 18	2 – 18
	M (*SD*)	9.73 (4.73)	12.82 (4.25)	14.29 (3.95)
Sex/Gender	Male	53.40%	43.30%	62.00%
	Female	46.60%	56.70%	38.00%
Ethnicity	Hispanic	46.10%	41.18%	38.00%
	Non-Hispanic	53.90%	58.82%	62.00%
Medicare/Medi-Cal Insurance	Yes	60.60%	48.65%	57.20%
	No	39.40%	51.35%	42.80%
Length of stay	Range	0 – 30	0 – 30	0 – 30
	M (*SD*)	3.34 (4.10)	6.01 (6.38)	5.29 (6.04)
Number of Medications Ordered				
Opioid Analgesics	Range	0 – 11	0 – 10	0 – 10
	M (*SD*)	1.94 (2.13)	1.96 (2.16)	1.58 (2.11)
Non-Opioid Analgesics	Range	0 – 9	0 – 9	0 – 8
	M (*SD*)	2.15 (1.28)	2.38 (1.54)	2.13 (1.44)

Table 4. Multiple Regression Model Results: Anxiety Disorder Diagnosis (N = 2,892)

Outcome Variables	**Pain Severity**			**Opioid Analgesics**			**Non-Opioid Analgesics**		
		95% CI			95% CI			95% CI	
	β	LL	UL	β	LL	UL	β	LL	UL
Predictor Variables									
Maximum Pain Score	---	---	---	0.60***	0.56	0.64	0.26***	0.22	0.30
Anxiety Disorder Diagnosis	0.13***	0.10	0.15	-0.09***	-0.11	-0.05	0.01	0.00	0.03
Maximum Pain Score x Anxiety Disorder Diagnosis	---	---	---	-0.07***	-0.09	-0.05	0.04**	0.03	0.05
Covariates									
Year	0.03*	0.00	0.06	-0.05***	-0.06	-0.04	0.03*	0.02	0.04
Age	0.10***	0.07	0.13	0.01	0.00	0.02	-0.01	-0.02	0.00
Sex	-0.07***	-0.10	-0.05	0.10***	0.09	0.11	-0.02	-0.03	-0.01
Hispanic Ethnicity	0.04**	0.01	0.07	0.00	-0.02	0.01	-0.01	-0.02	0.00
Medicare/Medi-Cal	-0.03	-0.06	0.00	0.01	0.00	0.02	0.02	0.01	0.03
Length of Stay	0.11***	0.08	0.14	0.08***	0.07	0.09	0.07***	0.06	0.08
Mood Disorder Diagnosis	0.03	0.00	0.06	-0.11***	-0.13	-0.09	-0.01	-0.02	0.00
Bacterial and viral infections	-0.02	-0.05	0.02	-0.01	-0.02	0.00	0.00	-0.01	0.01
Blood diseases	-0.05**	-0.08	-0.01	0.03*	0.02	0.04	-0.05***	-0.06	-0.04
Endocrine, nutritional, and metabolic diseases	-0.01	-0.05	0.02	-0.06***	-0.08	-0.04	-0.04**	-0.05	-0.03
Diseases of the nervous system	-0.07***	-0.10	-0.04	-0.08***	-0.09	-0.07	0.03*	0.02	0.04
Diseases of the circulatory system	0.00	-0.03	0.03	0.04**	0.03	0.05	-0.04**	-0.05	-0.03
Diseases of the respiratory system	-0.05**	-0.08	-0.01	0.01	-0.01	0.03	0.01	0.00	0.02
Diseases of the digestive system	0.05**	0.02	0.08	0.04**	0.03	0.05	0.03*	0.02	0.04
Diseases of the musculoskeletal system and connective tissue	0.02	-0.01	0.05	0.10***	0.09	0.11	0.08***	0.07	0.09
Diseases of the genitourinary system	-0.04**	-0.08	-0.01	0.06***	0.05	0.07	0.00	-0.01	0.01
Congenital malformations, deformations and chromosomal abnormalities	-0.02	-0.05	0.02	0.10***	0.09	0.11	0.01	0.00	0.02
Injury, poisoning and certain other consequences	-0.02	-0.05	0.01	0.16***	0.15	0.17	-0.02	-0.03	-0.01

Other mental, behavioral and neurodevelopmental disorders	-0.09***	-0.12	-0.05	-0.14***	-0.16	-0.12	-0.04**	-0.05	-0.03
Opioid Analgesics	0.34***	0.30	0.37				0.10***	0.09	0.11
Non-Opioid Analgesics	0.28***	0.24	0.31	0.18***	0.17	0.19	---	---	---

Note. Estimates represent standardized coefficients. CI = confidence interval; LL = lower limit; UL = upper limit.
*$p < .05$,**$p < .01$, ***$p < .001$

Table 5. Regression Model Results: Mood Disorder Diagnosis (N = 1,042)

Outcome Variables	**Pain Severity**			**Opioid Analgesics**			**Non-Opioid Analgesics**		
		95% CI			95% CI			95% CI	
	β	LL	UL	β	LL	UL	β	LL	UL
Predictor Variables									
Maximum Pain Score	---	---	---	0.68***	0.60	0.76	0.31***	0.25	0.37
Mood Disorder Diagnosis	0.10***	0.06	0.15	-0.26***	-0.29	-0.20	-0.02	-0.04	0.02
Maximum Pain Score x Mood Disorder Diagnosis	---	---	---	0.05	0.00	0.10	0.04	0.02	0.06
Covariates									
Year	0.05*	0.00	0.10	-0.10***	-0.13	-0.07	-0.02	-0.04	0.00
Age	0.13***	0.08	0.18	-0.04	-0.07	-0.01	-0.02	-0.05	0.01
Sex	-0.12***	-0.16	-0.07	0.08**	0.05	0.11	-0.02	-0.04	0.00
Hispanic Ethnicity	-0.03	-0.08	0.01	0.01	-0.02	0.04	0.00	-0.02	0.02
Medicare/Medi-Cal	0.01	-0.03	0.06	-0.03	-0.06	0.00	0.07**	0.05	0.09
Length of Stay	0.12***	0.06	0.17	0.09***	0.07	0.11	0.00	-0.02	0.02
Anxiety Disorder Diagnosis	0.08**	0.04	0.13	-0.11***	-0.14	-0.08	0.01	-0.01	0.03
Bacterial and viral infections	0.00	-0.05	0.06	0.01	-0.01	0.03	0.02	0.00	0.04
Blood diseases	-0.08**	-0.13	-0.02	0.04	0.01	0.07	-0.01	-0.04	0.02
Endocrine, nutritional, and metabolic diseases	0.01	-0.05	0.06	-0.20***	-0.23	-0.17	0.00	-0.03	0.03
Diseases of the nervous system	-0.10***	-0.14	-0.05	-0.09**	-0.12	-0.06	0.03	0.01	0.05
Diseases of the circulatory system	0.00	-0.05	0.06	0.06*	0.03	0.09	-0.02	-0.04	0.00
Diseases of the respiratory system	-0.02	-0.07	0.03	0.00	-0.03	0.03	0.01	-0.01	0.03
Diseases of the digestive system	0.04	-0.01	0.09	0.08**	0.05	0.11	0.03	0.01	0.05
Diseases of the musculoskeletal system and connective tissue	0.03	-0.02	0.08	0.14***	0.12	0.16	0.01	-0.01	0.03
Diseases of the genitourinary system	0.00	-0.06	0.05	0.08***	0.06	0.10	-0.03	-0.05	-0.01
Congenital malformations, deformations and chromosomal abnormalities	-0.05*	-0.11	0.00	0.10***	0.08	0.12	0.02	0.00	0.04
Injury, poisoning and certain other consequences	-0.04	-0.09	0.01	0.16***	0.14	0.18	-0.04	-0.06	-0.02

Other mental, behavioral and neurodevelopmental disorders	-0.01	-0.06	0.04	-0.12***	-0.15	-0.09	-0.05*	-0.07	-0.03
Opioid Analgesics	0.30***	0.24	0.36	---	---	---	0.14***	0.11	0.17
Non-Opioid Analgesics	0.33***	0.27	0.38	0.19***	0.17	0.21	---	---	---

Note. Estimates represent standardized coefficients. CI = confidence interval; LL = lower limit; UL = upper limit.
*$p < .05$,**$p < .01$, ***$p < .001$