

Outpatient Prescription Opioid Use in Pediatric Medicaid Enrollees With Special Health Care Needs

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abstract

BACKGROUND AND OBJECTIVES: Although potentially dangerous, little is known about outpatient opioid exposure (OE) in children and youth with special health care needs (CYSHCN). We assessed the prevalence and types of OE and the diagnoses and health care encounters proximal to OE in CYSHCN.

METHODS: This is a retrospective cohort study of 2 597 987 CYSHCN aged 0-to-18 years from 11 states, continuously enrolled in Medicaid in 2016, with ≥ 1 chronic condition. OE included any filled prescription (single or multiple) for opioids. Health care encounters were assessed within 7 days before and 7 and 30 days after OE.

RESULTS: Among CYSHCN, 7.4% had OE. CYSHCN with OE versus without OE were older (ages 10–18 years: 69.4% vs 47.7%), had more chronic conditions (≥ 3 conditions: 49.1% vs 30.6%), and had more polypharmacy (≥ 5 other medication classes: 54.7% vs 31.2%), $P < .001$ for all. Most (76.7%) OEs were single fills with a median duration of 4 days (interquartile range: 3–6). The most common OEs were acetaminophen-hydrocodone (47.5%), acetaminophen-codeine (21.5%), and oxycodone (9.5%). Emergency department visits preceded 28.8% of OEs, followed by outpatient surgery (28.8%) and outpatient specialty care (19.1%). Most OEs were preceded by a diagnosis of infection (25.9%) or injury (22.3%). Only 35.1% and 62.2% of OEs were associated with follow-up visits within 7 and 30 days, respectively.

CONCLUSIONS: OE in CYSHCN is common, especially with multiple chronic conditions and polypharmacy. In subsequent studies, researchers should examine the appropriateness of opioid prescribing, particularly in emergency departments, as well as assess for drug interactions with chronic medications and reasons for insufficient follow-up.



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Dr Feinstein conceptualized and designed the study, analyzed and interpreted the data, and drafted the initial manuscript; Mr Rodean and Drs Hall and Berry conceptualized and designed the study, analyzed and interpreted the data, and revised the manuscript; Drs Douplik, Gay, Markham, Bettenhausen, Simmons, and Ms Garrity contributed to the conception or design of the work, contributed to the acquisition, analysis, and interpretation of data for the work, revised it critically for important intellectual content, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; and all authors approve the final manuscript as submitted.

WHAT'S KNOWN ON THIS SUBJECT: Outpatient prescription opioid use in children is associated with harmful consequences, including increased emergency department visits and critical care hospitalizations. Children and youth with special health care needs (CYSHCN) frequently use medications, yet little is known about their use of opioids.

WHAT THIS STUDY ADDS: Approximately 7% of all CYSHCN and 14% of CYSHCN with a complex chronic condition received ≥ 1 opioid annually in the outpatient setting. Only 35% and 62% of opioid exposures were associated with follow-up visits within 7 and 30 days, respectively.

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Approximately 3% of US children receive opioid prescriptions in the outpatient setting for the management of acute and chronic pain.¹ Opioids can be dangerous to children, as evidenced by the dramatic rise in opioid-related pediatric emergency department (ED) visits and ICU hospitalizations over the past decade.^{2,3} Much research has focused on opioid use and the risk of subsequent misuse or development of an opioid use disorder.^{4,5} However, even during the course of proper administration of an opioid prescription, patients may be at increased risk of adverse drug events (ADEs) from direct drug effects or drug-drug interactions.^{6,7} Children and youth with special health care needs (CYSHCN) represent a particularly vulnerable group of children who may be at higher risk for necessary opioid exposures (OEs) and subsequent ADEs due to their underlying chronic conditions, surgical and procedural-related needs, and to their exposure to polypharmacy with other high-risk drugs.⁸⁻¹² However, researchers for recent large-scale studies of medication or opioid use in children either have not included or have not specifically analyzed CYSHCN.^{3,6,7}

In 2016, the Centers for Disease Control released national guidelines for safer opioid prescribing, but pediatric-specific recommendations were not included.¹³ Still, pediatric health care systems have begun to implement clinical guidelines for opioid prescribing and monitoring, although CYSHCN-specific recommendations are lacking.¹³⁻¹⁶ Some states have legislated maximum limits for the prescribing of opioids.¹⁷ Although no universal policy exists, it is generally recommended to (1) dispense a maximum of 3 to 7 days of opioid pain medications at the time of discharge from an outpatient clinic, ED, or hospitalization, and (2) ensure primary, specialty, or other outpatient follow-up within 7-30 days for

children likely to experience ongoing pain.¹³⁻¹⁶ It is unclear how often these safety practices are implemented during the course of clinical care, especially for CYSHCN.

To ensure the safest possible use of opioids among CYSHCN, it is essential to understand the clinical characteristics of CYSHCN who receive prescription opioids, as well as the types of health care use before and after prescription of an opioid. We thus designed this study to advance knowledge of OE in CYSHCN. Our specific aims were to (1) examine demographic and clinical characteristics of CYSHCN associated with OE, (2) describe the types of opioids prescribed to CYSHCN and the duration of therapy provided, (3) assess the most common diagnoses associated with OE in CYSHCN, and (4) analyze health care use by CYSHCN in the 7 days preceding OE and at 7 and 30 days after OE.

METHODS

Study Design, Population, and Setting

We performed a retrospective cohort study of CYSHCN using the MarketScan Medicaid Database (IBM Watson Health, Armonk, NY). This database contains claims data from fee-for-service and managed care plans from 11 deidentified states representing all geographic regions of the United States and has been extensively used for studies of CYSHCN.^{18,19} We included children ages 0-18 years continuously enrolled in Medicaid (≥ 11 months) in 2016. Continuous enrollment was chosen for study inclusion because the database does not contain pharmacy claims that could have occurred during enrollment gaps. CYSHCN were defined by the presence of ≥ 1 chronic conditions as defined by the Agency for Healthcare Research and Quality (AHRQ) Chronic Condition Indicator (CCI) system.²⁰ The AHRQ CCI system classifies

*~68 000 International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes as chronic or not chronic and assigns each chronic condition code to 1 of 18 mutually exclusive categories that are largely organized by organ system (eg, digestive or respiratory).*²¹⁻²³ In the CCI algorithm, a chronic condition is defined as a condition that lasts 12 months or longer and has 1 or both of the following effects: (1) it places limitations on self-care, independent living, and social interactions; and/or (2) it results in the need for ongoing intervention with medical products, services, and special equipment. Adapted for use in children, the AHRQ CCI system is all-inclusive of childhood chronic conditions across the spectrum of prevalence, severity, and complexity.^{19,23-25}

Definition of OE

For the patient-level analysis, an OE was defined as any filled prescription for an opioid based on the 2-digit generic product indicator (GPI) code for opioids (2-digit GPI = 65). We reported exposures to specific opioids at the level of the generic product name. For the prescription-level analysis, OEs were further classified as single- or multiple-fill episodes. Single-fill episodes consisted of an opioid fill without a refill or a new fill in the subsequent 7 days. Multiple-fill episodes consisted of an opioid fill with a refill or a new fill in the subsequent 7 days and could comprise several sequential fills. We identified children with multiple fills because they likely indicate ongoing pain and/or prolonged opioid therapy.

Demographics and Clinical Characteristics of CYSHCN With OE

We described demographic characteristics including age, sex, and race and/or ethnicity. We assessed the type and number of chronic conditions for each child with ICD-10-CM codes using the AHRQ CCI system.

To better understand the potential severity of the chronic conditions, we further identified the subset of CYSHCN with complex chronic conditions (CCCs), known to be associated with increased medical complexity (eg, multiple comorbidities, technology dependence, polypharmacy), higher morbidity and mortality, and increased resource use.²⁶

Diagnoses Associated With OE

For each opioid fill, we used the AHRQ Multi-level Clinical Classification System (CCS) to comprehensively assess all health problems (eg, injury) that were filed during health care encounters across the care continuum (ie, inpatient or outpatient) during the 7 days preceding OE. The AHRQ CCS system groups related ICD-10-CM codes into mutually exclusive categories. We determined frequencies of all CCS level 2 diagnoses to determine the most prevalent health problems in the 7 days preceding OE. Of these, we associated OE first to diagnoses with clinical indications for OE (eg, traumatic injury, malignancy). If there was not a forthcoming clinical indication for OE, we then considered other related diagnoses (eg, infection, nontraumatic musculoskeletal condition) and lastly the categories of symptoms or descriptions of the health care encounter itself (eg, ill-defined symptoms, signs, and conditions).

Health Care Use Before and After OE

Health care use across the continuum was assessed by using preestablished service categories in the data set. These categories included primary care, outpatient specialty, home health care, ED, inpatient (including inpatient surgery), outpatient surgery, dental surgery, and mental health. Overall, and by single versus multiple-fill episodes, we reported health care use during the 7 days before an opioid fill, and during the 7 and 30 days after an opioid fill.²⁷ In

the case of multiple fills, only outcomes surrounding the first fill were considered. Only prescriptions filled between January 8 and December 1 of the calendar year of study were considered for analysis to allow for complete use data.

Statistical Analysis

We used descriptive statistics to describe key characteristics of the study population, including the exposure of CYSHCN to opioids, the exposure by specific chronic condition, and the most common specific chronic medications taken by CYSHCN. Comparisons between categorical variables of interest were conducted by using the χ^2 test. Statistical significance was set at $P < .001$. All analyses were performed by using SAS 9.4 (SAS Institute, Cary, NC). This study of deidentified data was exempt from review by the policies of the Colorado Multiple Institutional Review Board.

RESULTS

Among 4 032 955 continuously enrolled children, 64.4% were CYSHCN. Overall, OE occurred in 3.5% of children without a special health care need, 7.4% of CYSHCN, and 14.0% in CYSHCN with a CCC. CYSHCN represented 80.0% of all children who had OE. The 2 597 987 CYSHCN comprised the study population for all subsequent analyses (Table 1).

Demographics and Clinical Characteristics of CYSHCN With and Without OE

Children with versus without OE were older (eg, ages 10–18 years: 69.4% vs 48.7%), more likely to be girls (52.0% vs 47.7%), non-Hispanic white (55.0% vs 46.9%), and had more chronic conditions (eg, ≥ 3 conditions: 49.1% vs 30.6%) as well as CCCs (18.8% vs 9.0%), $P < .001$ for all. Children with OEs were also more likely to have filled prescriptions from multiple other

medication classes during the study year (eg, ≥ 5 additional medication classes: 54.7% vs 31.2%, $P < .001$). Specifically, 6.5% of children with OEs had concomitant prescriptions for an anticonvulsant at some point during the study period, 5.9% for an anxiolytic, and 5.4% for a benzodiazepine.

Rates of OE in CYSHCN by Number and Type of Chronic Condition

As the number of chronic conditions increased from 1 to 5 or more, the rate of OE increased from 4.9% to 15.2%, $P < .001$ (Fig 1). The highest rates of OE were observed in children with immune (26.9%), cancer (24.0%), hematology (22.8%), and neurologic (17.8%) conditions. Specific, common examples of these conditions were hypogammaglobinemia (immune), benign neoplasm of skin (cancer), sickle cell anemia (hematology), and migraine headaches and cerebral palsy (neurologic). Also, based on the CCC classifications system, OE was high (22.0%) in children assisted with medical technology.

Specific Opioids Used by CYSHCN

Of the 271 869 opioid prescriptions, 189 040 (76.7%) were dispensed as part of a single-fill episode, and the remainder were dispensed as part of 57 542 multiple-fill episodes (Table 1). Single-fill episodes had a median duration of 4 days (interquartile range [IQR]: 3–6 days), and multiple-fill episodes consisted of a median of 2 fills with a total median duration of 10 days (IQR: 7–19 days). Table 2 lists the most commonly filled opioids and the median total days supplied. Acetaminophen-hydrocodone comprised 47.5% of all opioid fills, followed by acetaminophen-codeine (21.5%), oxycodone (9.5%), acetaminophen-oxycodone (9.0%), and tramadol (6.2%).

TABLE 1 Demographic and Clinical Characteristics of CYSHCN Enrolled in Medicaid

	All Subjects, <i>N</i> = 2 597 987		
	<i>n</i> (%)	Opioid Prescription	
		No, <i>n</i> = 2 406 816	Yes, <i>n</i> = 191 171
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
Demographics			
Age in y			
1	12 989 (0.5)	12 688 (0.5)	301 (0.2)
1–5	635 903 (24.5)	608 373 (25.3)	27 530 (14.4)
5–9	642 644 (24.7)	612 065 (25.4)	30 579 (16.0)
10–12	479 739 (18.5)	455 761 (18.9)	23 978 (12.5)
13–18	826 712 (31.8)	717 929 (29.8)	108 783 (56.9)
Sex			
Male	1 350 873 (52.0)	1 259 024 (52.3)	91 849 (48.0)
Female	1 247 114 (48.0)	1 147 792 (47.7)	99 322 (52.0)
Race and/or ethnicity			
Non-Hispanic white	1 234 155 (47.5)	1 128 993 (46.9)	105 162 (55.0)
Non-Hispanic African American	822 472 (31.7)	770 136 (32.0)	52 336 (27.4)
Hispanic	212 695 (8.2)	201 419 (8.4)	11 276 (5.9)
Other	328 665 (12.6)	306 268 (12.7)	22 397 (11.7)
Clinical characteristics			
CCC			
Yes	252 994 (9.7)	217 510 (9.0)	35 484 (18.6)
Technology assistance			
Yes	21 909 (0.8)	17 098 (0.7)	4811 (2.5)
No. additional nonopioid prescription classes ^a received			
0	449 008 (17.3)	442 260 (18.4)	6748 (3.5)
1–2	720 362 (27.7)	686 918 (28.5)	33 444 (17.5)
3–4	605 602 (23.3)	562 965 (23.4)	42 637 (22.3)
5–6	395 568 (15.2)	357 961 (14.9)	37 607 (19.7)
≥7	427 447 (16.5)	356 712 (14.8)	70 735 (37.0)

^a Based on 2-digit GPI code, which categorizes major classes of medications.

Specific Diagnoses and Procedures Associated With OE for CYSHCN

Table 3 lists the top categories of recorded diagnosis codes preceding OE. Those diagnoses most frequently included infections (25.9%), injury (22.3%), nontraumatic musculoskeletal issues (9.6%), dental issues (6.7%), mental health issues (6.6%), gastrointestinal issues (3.7%), nontraumatic neurologic issues (1.6%), and malignancy (1.5%). Among specific types of infection, respiratory infections comprised the majority (64.1%). There was no diagnosis recorded for 12.9% of CYSHCN with an OE.

Health Care Use Before and After OE for CYSHCN

Approximately 86.3% of all OEs were preceded by contact with a health care provider (Fig 2). ED visits preceded 28.8% of all exposures,

followed by outpatient surgery (28.8%), outpatient specialty (20.8%), primary care (18.3%), dental care (7.3%), and inpatient (6.5%) visits. Of the remaining 13.7% without care in the preceding 7 days, 12.0% had a “not elsewhere specified/injections/durable medical equipment” claim and the rest had no claims at all. Regarding follow-up care, 35.1% of single-fill OEs were associated with a follow-up visit within 7 days and 62.2% within 30 days, with the majority of follow-up visits occurring in the primary care or outpatient subspecialist office settings. Examining multiple-fill episodes only, this rose to 51.6% within 7 days and 74.7% within 30 days.

DISCUSSION

The findings from the current study suggest that CYSHCN in Medicaid may

be exposed to opioids at a twofold higher rate than the general pediatric population.¹ Older, non-Hispanic white children were most likely to have OE compared with children of other race and/or ethnicities. The highest rates of OE were observed in children with immune, cancer, and hematologic conditions. Moreover, multiple chronic conditions, technology assistance, and polypharmacy were particularly associated with higher rates of OE. Consistent with previous literature, the majority of opioids were prescribed as a single-episode fill and for short durations, although ~12% of prescriptions were multiple-fill episodes.²⁸ The types of opioids used were consistent with previous studies, with codeine, hydrocodone, and oxycodone representing the majority of prescriptions.²⁹ The most frequent preceding diagnoses were consistent with potential need

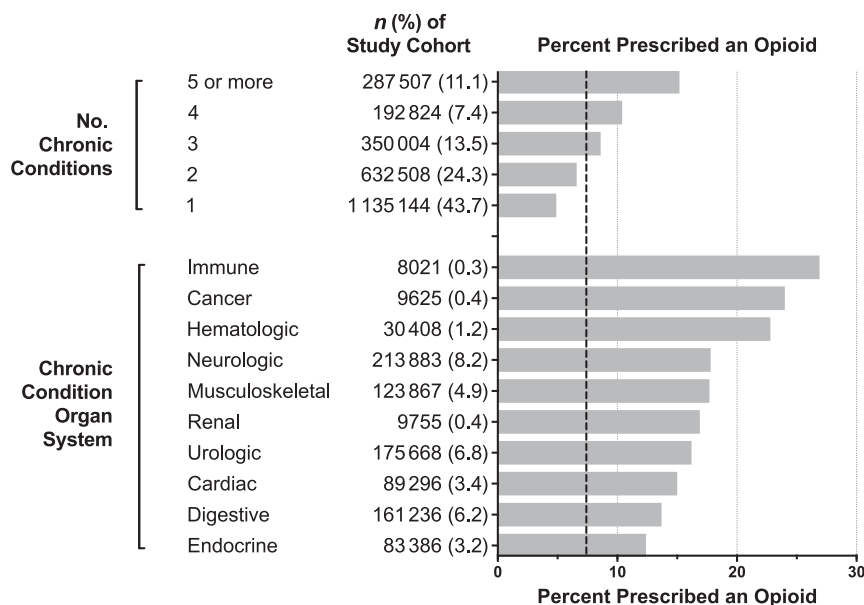


FIGURE 1

Opioid prescription by type and number of chronic conditions among CYSHCN enrolled in Medicaid. Each horizontal bar represents the prevalence of OE within that specific category. For example, 26.1% of children with an immune chronic condition had an OE. The vertical dashed reference line represents the overall prevalence of OE among the study cohort (7%); the prevalence of OE among all children is ~3%.

for opioid therapy (eg, injury). Although >80% of all children had contact with a prescribing provider in the 7 days before OE, far fewer had subsequent follow-up at 7 and 30 days. Several of these findings warrant additional discussion.

First, further investigation is needed to assess the appropriateness of OE in CYSHCN. Many CYSHCN were exposed to opioids by health care providers, including ED clinicians and dentists, who, because of their typical role and setting in the health care system, may either not have been ideally positioned to achieve strong longitudinal knowledge of the children's past medical history (ie, CCCs, polypharmacy, etc) or current overall health and well-being, or situated to provide follow-up.^{30,31} These patient attributes may be particularly important to contemplate when choosing which medication(s) to prescribe for pain in CYSHCN. Although certain chronic conditions (eg, sickle cell anemia) may necessitate opioid therapy,³²

a number of prescriptions were preceded by diagnoses not synonymous with pain (eg, respiratory infections). Recent US Food and Drug Administration warnings have been issued to minimize OE for acute respiratory infections and to reduce use of specific opioids in children (eg, codeine).^{27,33,34} High rates of OE in the current study also occurred in children with complex neuromuscular conditions, such as cerebral palsy. These conditions may make it difficult to quantify and assess pain, especially by health care providers lacking clinical familiarity with the child and family. Real-world clinical data are needed to assess the medical decision-making that led to OE in CYSHCN, including which nonopioid medications for pain in CYSHCN were trialed in advance of the exposure.³⁵

Second, the high rates of polypharmacy observed in CYSHCN with OE in the current study merit additional exploration. Emerging evidence suggests that polypharmacy

is prevalent among CYSHCN, especially those using Medicaid.³⁶ Although opioids themselves can result in dangerous ADEs, including digestive dysmotility, urinary retention, and respiratory depression, they also have the potential for drug-drug interactions with a variety of other medications.^{16,37} For example, because of the risk for severe respiratory depression, coma, and death when opioids are used concomitantly with benzodiazepines, the US Food and Drug Administration has issued a black box warning against simultaneous administration of these medications. Despite this warning, some CYSHCN (eg, those with epilepsy and musculoskeletal spasticity) using benzodiazepines in the current study were also exposed to opioids. Additional study is necessary to assess whether those CYSHCN received prescriptions from multiple outpatient providers (eg, opioid from a dental or surgical provider and antiepileptic from a neurologist), potentially without concerted collaboration, decision-making, and monitoring. This practice could lead to concurrent therapy with contraindicated drug combinations. Such combinations, like opioids and benzodiazepines, may be clinically necessary but also require extremely close monitoring to avoid adverse events when used simultaneously. Although our study was not designed to look at concurrent medication use, future pediatric polypharmacy studies should investigate simultaneous exposure to opioids and other drugs, particularly to look for signals of downstream consequences.

Finally, <50% of children with multiple-fill episodes (indicating ongoing pain) had follow-up within 7 days. Although not assessed in the current study, it is possible that the pain experienced by these children resolved or that based on family or physician preference, follow-up occurred by phone or another

TABLE 2 Opioids Prescribed for CYSHCN Enrolled in Medicaid

Opioid	Opioid Prescription		
	<i>n</i>	Percent of Total	Days Supplied, median (IQR)
Acetaminophen/hydrocodone bitartrate	129 146	47.5	4 (3–6)
Acetaminophen/codeine phosphate	58 414	21.5	4 (3–5)
Oxycodone hydrochloride	25 761	9.5	5 (3–8)
Acetaminophen/oxycodone hydrochloride	24 510	9.0	5 (3–6)
Tramadol hydrochloride	16 747	6.2	5 (3–10)
Fentanyl citrate ²	10 364	3.8	1 (1–1)
Morphine sulfate	2 893	1.1	1 (1–7)
Hydromorphone hydrochloride	1 438	0.5	1 (1–5)
Methadone hydrochloride	701	0.3	30 (9–30)
Meperidine hydrochloride	496	0.2	1 (1–1)
Acetaminophen/tramadol hydrochloride	406	0.1	4 (3–7)
Hydrocodone bitartrate/ibuprofen	386	0.1	4 (3–5)
Fentanyl patch	236	0.1	30 (18–30)
Acetaminophen/butalbital/caffeine/codeine phosphate	153	0.1	5 (5–10)
Codeine sulfate	66	0.0	5 (3–8)
Tapentadol hydrochloride	43	0.0	30 (10–30)
Aspirin/butalbital/caffeine/codeine phosphate	40	0.0	6 (4–30)
Remifentanyl hydrochloride ^a	22	0.0	1 (1–1)
Oxymorphone hydrochloride	17	0.0	30 (30–30)
Opium	11	0.0	30 (30–30)
Other ^b	19	0.0	—

—, not applicable.

^a This is an intravenous opioid that may have been administered to a child with peripheral or central vascular access by a home health professional or hospice provider.

^b Other includes (each with $n \leq 10$) sufentanil citrate, hydrocodone bitartrate, alfentanil hydrochloride, belladonna alkaloids/opium alkaloids, aspirin/oxycodone hydrochloride, codeine/dexbrompheniramine/pseudoephedrine, morphine sulfate/naltrexone hydrochloride.

communication mode that was not associated with a health care claim. However, because long-term opioid use often begins with treatment of acute pain, it is imperative that children who receive multiple fills of opioids are reevaluated in some

manner for ongoing need versus discontinuation.¹³ In a recent study investigating persistent opioid use after surgery, ~5% of opioid-naïve subjects filled additional opioid prescriptions >90 days after surgery, raising concern that acute exposure

to opioids for postoperative pain management may be associated with a risk of long-term use.²⁹ When follow-up is indicated, improved strategies for ensuring follow-up are warranted.³⁸ Medical homes for CYSHCN may be best positioned to identify patients with prescriptions for new high-alert medications like opioids and then conduct follow-up evaluations either in person, by phone, or via the electronic health record. Centralized electronic prescription drug monitoring programs contain the necessary data to ascertain such patients.³⁹ Follow-up evaluations should minimize impact on the families of children with high medical complexity who may also have medical caregivers in the home who can relay information to the prescribing provider.

Our findings must be interpreted in the context of several limitations. First, our results were based on filled opioid prescriptions. Children may

TABLE 3 CCS Diagnosis Groups Coded in 7 Days Before an Opioid Prescription for CYSHCN Enrolled in Medicaid

CCS Diagnosis Group ^a (<i>N</i> = 183 653)	Opioid Prescription	
	<i>n</i>	Percent of Total
Infection	47 530	25.9
Injury	40 916	22.3
No diagnosis recorded	23 694	12.9
Nontraumatic musculoskeletal condition	17 694	9.6
Other	16 872	9.2
Dental condition	12 293	6.7
Mental health condition	12 196	6.6
Gastrointestinal condition	6 845	3.7
Nontraumatic neurologic condition	2 893	1.6
Malignancy	2 720	1.5

^a For each opioid prescription filled, we used the AHRQ Multi-level CCS to comprehensively assess all health problems (eg, diagnoses) that were filed during health care encounters across the care continuum (eg, inpatient or outpatient) during the 7 d preceding OE. The AHRQ CCS system groups related *International Classification of Diseases, Ninth Revision, Clinical Modification* codes into mutually exclusive categories. We determined frequencies of all CCS level 2 diagnoses to determine the most prevalent health problems in the 7 d preceding OE. Of these, we associated OE first to diagnoses with clinical indications for OE (eg, traumatic injury, malignancy). If there was not a forthcoming clinical indication for OE, we then considered other related diagnoses (eg, infection, nontraumatic musculoskeletal condition), and lastly the categories of symptoms or descriptions of the health care encounter itself (eg, ill-defined symptoms, signs, and conditions).

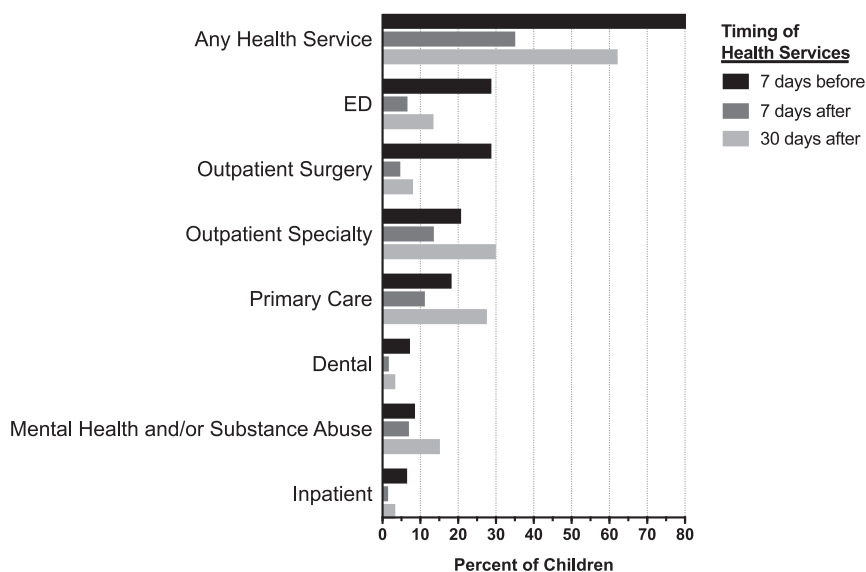


FIGURE 2

Health services before and after opioid prescription for CYSHCN enrolled in Medicaid. Each horizontal bar represents the percentage of children who used that specific type of health care service at 7 days before OE, 7 days after OE, and 30 days after OE. For example, of the total 228 019 children with OE, 177 183 (77.7%) used any health service 7 days before OE, 76 829 (33.7%) used any health service 7 days after OE, and 146 051 used any health service 30 days after OE.

have used only a portion of the filled prescription, which would lead to an overestimation of risk due to opioids. We attempted to address this issue by separately analyzing children with multiple prescription episodes, which would indicate that they were using their dispensed medication. Second, a percentage of prescribing episodes were not preceded by visits with a prescribing provider. This indicates that children may have received opioids from prescriptions made >7 days before the fill date or from other modes (eg, called-in prescription without a health care encounter). In either scenario, this raises concern that children might be receiving opioids without a timely, in-person assessment of their pain symptoms. Third, because these were administrative claims data, we were not able to determine an individual child's actual need for opioid pain control. We attempted to report prescription episodes associated with

diagnostic codes for conditions indicating likely physical pain (eg, traumatic injury). For the majority of prescription episodes, however, we were not able to identify the reasons for opioid therapy, including their use in palliative and end-of-life care. Fourth, the continuous enrollment attribute of our study population led to underrepresentation of infants, which could have affected the demographic characteristics of the cohort as well as the rate and risk factors for OE in CYSHCN. Subsequent analysis of OE in neonates and infants is warranted.

These limitations notwithstanding, we hope that the current study advances knowledge and awareness of outpatient OE in the vulnerable population of CYSHCN. Medical home clinicians for CYSHCN in particular may leverage these findings to counsel CYSHCN and their families on the likelihood of OE, especially for

children with attributes (eg, multiple chronic conditions and polypharmacy) associated with higher OE. To ensure the safety of OE in CYSHCN, the development of evidence-based opioid prescribing guidelines is paramount, including best practices for follow-up evaluation. As opioid prescribing guidelines are implemented, it will be important for subsequent studies to assess trends in OE over time for CYSHCN.

CONCLUSIONS

OE in CYSHCN is common, especially among those with multiple chronic conditions and polypharmacy. The findings may be useful to catalyze subsequent investigations on (1) the appropriateness of opioid use in CYSHCN, especially when prescribed from dental and ED settings; (2) opioid interactions with other chronic medications, especially in CYSHCN with polypharmacy; and (3) reasons for insufficient follow-up in CYSHCN prescribed opioids.

ABBREVIATIONS

ADE: adverse drug event
 AHRQ: Agency for Healthcare Research and Quality
 CCC: complex chronic condition
 CCI: Chronic Condition Indicator
 CCS: Clinical Classification System
 CYSHCN: children and youth with special health care needs
 ED: emergency department
 GPI: generic product indicator
 ICD-10-CM: *International Classification of Diseases, 10th Revision, Clinical Modification*
 IQR: interquartile range
 OE: opioid exposure

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