Published in final edited form as:

Clin J Pain. 2019 June ; 35(6): 515–520. doi:10.1097/AJP.0000000000000707.

Opioid prescribing patterns for pediatric patients in the USA

Cornelius B. Groenewald, MBChB

Department of Anesthesiology and Pain Medicine, University of Washington School of Medicine,
4800 Sand Point Way NE, Seattle, WA 98105, USA

Abstract

The opioid crisis in America affects both adults and children. However, children are often excluded from health care policies and guidelines aimed at curbing the opioid crises. For example, recent guidelines on opioid prescribing authored by the Center for Disease Control and Prevention (CDC), has exclusively focused on adults. Stakeholders such as patients, providers, and public health agencies feel increased pressure to address the opioid crises and thus guidelines intended for adults may inadvertently be generalized to children. Indeed, some health agencies in the United States have advocated for more restrictive opioid prescribing to children as compared to adults. In order to better address the opioid crises we urgently need more evidence to guide decisions. Thus, this topical review aims to provide a brief overview of the opioid crises affecting children, followed by a synopsis of recent research on opioid prescribing patterns and data on the links between legitimate opioid use and risk for problematic opioid use behaviors.

Introduction

The field of pediatric pain medicine has undergone a paradigm shift over the past 30 years, with a growing understanding that undertreated pediatric pain is common^{1–3}. Furthermore, untreated or undertreated pain in children can substantially disrupt neurobiological⁴ and psychosocial⁵ development resulting in significant short and long term disability^{6, 7}. Yet, research clearly shows that pediatric pain continuous to be inadequately managed in many situations, including both inpatient and outpatient populations^{8, 9}. Opioids are an important component in ensuring acute pain relief, yet excessive opioids may result in harm. Indeed, the United States has seen the development of a significant opioid epidemic over the past 20 years. While the opioid epidemic is a complex process, increasingly driven by street drugs such as heroin and fentanyl, many believe the crises were precipitated by excessive opioid prescribing that health care providers initially considered safe and pharmaceutical companies marketed as low-risk for addiction. In adults it is now asserted that increased opioid prescribing over the past 20 years have resulted in increased rates of opioid misuse and opioid use disorder¹⁰. Consequently, federal and state health agencies in the United States have expended considerable effort on establishing guidelines for opioid prescribing among adults, in an attempt to address the opioid epidemic¹¹.

Correspondence to: Cornelius B. Groenewald, MB,ChB, cornelius.groenewald@seattlechildrens.org.

Conflict of Interest: No conflict of interest to report.

Yet, it also relevant to understand if and how opioid prescribing drives opioid misuse and abuse among children and adolescents. Currently, there is a lack of data associating pediatric opioid prescribing to adverse opioid-related outcomes, which has limited our ability to tailor guidelines specific to children. Therefore, the objectives of this topical review are to 1) describe the opioid crisis facing children <18 years of age in the United States, 2) describe the work to date that has analyzed patterns of opioid use among children, 3) describe studies linking legitimate opioid use to problematic opioid use behaviors, and 4) highlight strategies that providers could implement to reduce the opioid crises affecting children.

This review necessarily focusses on opioid use patterns and associated problematic opioid use specific to children and adolescents in the United States. The United States is disproportionately affected by the opioid crisis: while only about 5% of the world's population resides in the United States, about 80% of all opioids are prescribed to Americans¹². However, the opioid crisis is not a uniquely American problem. The Institute for Health Metrics and Evaluation found that worldwide 15 million people are addicted to opioids¹³. Thus, it is the hope that some of the findings in this review could be translated to other parts of the world. Table 1 contains common terms used throughout this manuscript. While there are currently no uniform definitions related to describing opioid use and problematic opioid use, it is important to use consistent terminology throughout studies. Presented here are the ones currently recommended by the CDC, and found in several recent excellent guidelines and reviews on problematic opioid use^{11, 14–18}.

The opioid epidemic facing children and adolescents

Nonmedical use of opioids by children is a public health crisis. In 2016, 891,000 children (about 3.6% of the population) in the United States 12–17 years of age reported opioid misuse¹⁹. Adolescents who misuse opioids are a heterogeneous group, but can broadly be categorized as either misusing opioids for the purpose of self-treating physical pain symptoms (self-treaters) or misusing opioids for the feelings elicited, i.e. to “get high” (sensation-seekers)²⁰. Self-treaters and sensation-seekers each constitute about 50% of opioids misusers and have different characteristics. Self-treaters are more likely to have somatic complaints (e.g. pain), internalizing mental health symptoms (e.g. anxiety and depression), and history of victimization by peers. In contrast sensation-seekers are more likely to have a propensity toward rule-breaking, aggressive behavior, risk for substance dependence, and misuse of other illicit substances²¹. Distinguishing between them is of clinical importance, because treatment calls for different forms of intervention. Self-treaters could benefit from relatively low-intensity methods, such as education about risks, frequent follow-up for pain complaints, and the introduction of non-opioid pain therapies¹⁴. On the other hand, sensation-seekers could benefit from external regulation of aberrant behaviors and substance abuse treatment²¹. However, regardless of the cause, among adolescents opioid misuse is associated with adverse consequences such as reduced employment²², sexual victimization²³, and driving under the influence. Opioid misuse is also a key antecedent for other opioid-related problems, including opioid use disorder. Indeed, in 2016, 153,000 adolescents (about 0.6% of the population) in the United States 12–17 years of age reported having opioid use disorder¹⁹. Most cases of opioid use disorder were related to prescription opioids (99%), with about 1% related to heroin use disorder¹⁹. Among children,

opioids are now the most frequent cause of serious injury or death resulting from drug overdose [3] and from 1999 to 2008 the number of accidental opioid overdoses in the United States more than quadrupled²⁴. In 2008, the annual rate of unintentional deaths related to opioids was 0.1 per 100,000 for children 0–14 years of age and 3.7 per 100,000 for adolescents 15–18 years of age [30]. Following 2008, opioid-related deaths among adolescents slightly decreased to a rate of 2.0 per 100,000 adolescents in 2011, and 2.5 per 100,000 in 2015²⁵.

Opioid prescribing patterns for pediatric patients in the USA.

At present, considerable literature has been published on opioid use by adults in the United States, among whom rates of legitimate opioid use in the United States have grown substantially over the past 30 years^{26–28} with an associated increase in rates of problematic opioid use^{29–31}. As a result, a major focus of regulatory agencies is to reduce opioid prescribing to adults in the United States¹¹. Yet, drivers for an increase among children are less well known. Recently increased opioid prescribing to adults were associated with a parallel increase in *accidental* opioid overdoses in children and adolescents^{32, 33} who are exposed to adults' left-over opioids. However associations between children's own legitimate opioid use and subsequent problematic opioid use behaviors has not been well described.

Research has shown significant increase in opioid prescribing to children and adolescents over the past 20 years³⁴. In 2010, Fortuna et al. used data from two nationally representative surveys, the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey to examine changes in rates of opioid use among adolescents in the United States. Their main finding was that rates of opioid prescribing had almost doubled between 1994 and 2007: in 1994 opioids were prescribed at 3% of all ambulatory care or emergency department visits to adolescents, and this had increased to 5.5% of all ambulatory care or emergency department visits by 2007. Furthermore, rates of opioid prescriptions for common pain complaints were high: 12.7% of children presenting with headache received opioids, as did 11.3% of those with musculoskeletal complaints, 21.5% of those with back pain, and 13% of those with abdominal complaints. Richardson et al. in 2011 also found that opioid prescriptions had increased among adolescents with non-cancer pain diagnosis captured in both a national, commercially insured population and a state Medicaid plan. In their cohort opioids were often prescribed to adolescents with common pain complaints, between 21–40% of adolescents with headache, musculoskeletal, back, and abdominal pain diagnoses received opioids, with most receiving between 10–15 days of short acting opioids.

Following these two studies, Kaiser³⁵ and Groenewald³³ then examined rates of opioid prescribing between 2001–2010 and 1996–2012 respectively. Kaiser et al. found no increased rates of opioid prescribing among nationally representative samples of children participating in the National Hospital Ambulatory Medical Care Survey between 2001–2010. Furthermore, Groenewald et al. found stable rates of opioid prescribing in nationally representative samples of children participating in the Medical Expenditure Panel Surveys between 1996 and 2012. Thus, both studies came to the same conclusion that rates of opioid

prescribing to children had stabilized between these time periods. The study by Groenewald et al. included a large nationally representative sample and found that, overall, 2.7% of all children in the United States received an opioid in 1996 while 2.9% of all children received an opioid prescription in 2012. Following 2012, rates of opioid prescribing to children in the United States appear to be decreasing³⁶. McCabe et al. examined trends in prescription opioid use among forty cohorts of high school seniors (modal age 18) participating in the Monitoring the Future study between 1976 and 2015³⁷. Similar to the previously mentioned studies McCabe found increased rates of opioid prescribing between 1994 and 2002, then rates appeared to stabilize between 2002 and 2012, before decreasing in 2013–2015. These changes mirror what is happening among adults^{38, 39}. Of note, a recent study found that 40% of children receive opioid during hospitalization⁴⁰. Despite decreasing rates of opioid prescribing to children in the USA, these rates continue to be greater than published reports from other developed countries. National data from Norway indicated that only 0.79% of Norwegian children receiving opioids in 2007⁴¹ and in Denmark only 1.1% of children received an opioid in 2013⁴². Thus, opioids remain among a commonly prescribed medications to children in America⁴³ and by the age of 18 almost 20% of children in the United States report having received an opioid prescription at some point during their lifetime^{37, 44}.

Problematic opioid use behaviors following a legitimate prescription

Some evidence suggests that adolescents who are prescribed opioids may be at increased risk for later problematic opioid use behaviors, including opioid misuse and unintended prolonged opioid use. To date, only 2 studies have addressed the link between legitimate opioid use and future risk for opioid misuse by children, with a major limitation that they both rely on the same data source: the Monitoring the Future Study (MTF)⁴⁵. MTF annually includes students who were in the 12th grade from 130 high schools in the USA. Miech et al. examined the association between legitimate adolescent opioid use and future risk for opioid misuse using population based data from the MTF⁴⁶. Students were randomly selected to complete the survey with a random subset selected to complete annual follow-up surveys. The authors evaluated 6,200 students surveyed between 1990 and 2012 and who completed follow-up until they were 23 years of age. The major finding from their study was that adolescents who had legitimately used prescribed opioids prior to 12th grade were 33% more likely to report opioid misuse following high school. This association was concentrated among low risk individuals, i.e. those who have little to no history of drug use and who also strongly disapprove of illegal drug use at baseline. In addition, the authors found that, among these low risk individuals, prescription opioid misuse events were rare with >80% of low risk participant limiting their misuse to fewer than 5 times over the past year. While the authors did not specifically report reasons for misuse, they speculated that most of these children misused opioid for pain relief. In contrast, among high risk individuals, for example those with a history of illicit marijuana use, alcohol use, or other drug use, legitimate opioid prescriptions did not independently predict an increased risk for prescription opioid misuse. Presumably these high risk individuals were more likely to use opioids for feelings elicited or to “get high”. Thus, the overall conclusion from the Miech study was that *risk for opioid misuse was slightly increased* in low risk individuals, who misused opioids only in a low risk

manner. On the other hand, *prescribing opioids to more experienced adolescent drug users did not increase their risk for misuse.*

McCabe et al. in 2016 also used MTF with the goal of examining associations between prescription opioid use in adolescence and the subsequent risk of opioid misuse and opioid use disorder at age 35. Similar to Miech's study multiple cohorts of U.S. 12th graders (n=4072) were followed through self-administered questionnaires, however Miech included early MTF cohorts (1976–1996) and reported on follow-up through age 35 (as compared to age 23 in the Miech et al. study). Similarly, to Miech et al., McCabe also found that medical use of prescription opioids was associated with opioid misuse at age 35. In contrast medical use of prescription opioids were not associated with the development of opioid use disorder at age 35.

While both these studies point to weak associations between medical opioid use and future opioid *misuse* but not *abuse*, it is important to acknowledge that both have significant limitations, including the use of cross-sectional data which precludes cause-effect relationships. Thus, our knowledge in this area remains murky and speculative. There is a pressing need for research to understand longitudinal relationships between legitimate opioid use and problematic opioid use behaviors among children.

In addition to opioid misuse, researchers have also examined associations between legitimate opioid use and unintended prolonged opioid use^{47, 48}. Prolonged opioid use is infrequently indicated among children and usually limited to a small number of conditions such as sickle cell disease, cancer, and palliative care. However, 2 recent publications have identified unintended prolonged use as a significant concern following acute opioid prescribing in opioid-naïve children following surgery⁴⁹ and trauma⁵⁰. Whiteside found that 12.5% of adolescent used opioids up to 12-months following admission for traumatic injury. Similarly, Harbaugh et al. found that 3–12% of adolescents became persistent opioids users 90–180 days following a range of pediatric surgeries. Factors associated with prolonged opioid use in both cohorts included previous substance use and a history of chronic pain, and it should be emphasized that this study did not address the legitimacy of long term opioid use.

Prescribed opioids are often unused

Given increased rates of opioid prescribing to children and the potential for associated problematic opioid use behaviors, it is relevant to consider whether opioids are overprescribed to children. Evidence suggests that they are overprescribed: the vast majority of opioids prescribed to children goes unused and are not disposed of by parents. Researchers examined opioid use following orthopedic spine⁵¹, general surgery^{52, 53}, and tonsillectomy⁵⁴ and found that children were prescribed between 30–70 opioid doses (either in pill or liquid form), depending on the surgical procedure. In these cohorts, opioid use by children was extremely variable and between 25–75% of prescribed opioid doses went unused. Disposal of leftover opioids was also widely variable, with one study finding that 33% of parents planning on keeping leftover opioids for future use⁵¹, while in another study 85% of parents did not know what to do with leftover opioids⁵³. Leftover opioids are a

major source of opioid diversion, misuse and abuse, and it is estimated that the majority (>80%) of adolescent opioid abusers get them from either their own leftover prescriptions or from friends' and family members' leftover prescriptions^{19, 55, 56}. Thus, reducing opioid prescribing to children and adolescents may result in less opioid being available for misuse.

How can providers address this issue?

Opioids are mainstay for treating children's acute pain yet providers should remain cognizant that legitimate opioid use may result in problematic opioid use behaviors. To reduce problematic opioid use, several strategies may be helpful to prescribers: 1) create guidelines to guide responsible opioid prescribing and reduce leftover medications, 2) educate adolescents about risks of opioids and how to safely dispose of opioids, and 3) reduce illicit prescriptions by using state Prescription Drug Monitoring Programs (PMPs).

Data from the National Survey on Drug Use and Health suggest that most opioids are sourced from a single prescriber (>80%), as compare to multiple prescribers (<2%), or drug dealers (<10%). Thus, guidelines aimed at appropriate opioid prescribing by providers is an important first step. Recently, the Center for Disease Control and Prevention (CDC), published guidelines aimed at reducing opioids for chronic pain in adults¹¹. Unfortunately, these guidelines specifically excluded children⁵⁷. Currently there are no data to guide providers on how much opioid to prescribe children. However at very least guidelines aimed at children should be equitable to adults' guidelines. For example, the state of Washington Health Care Authority recently approved guidelines for Medicaid patient restricting opioids to children (20 years of age) to a quantity limit of 18 dosages, yet approved a quantity limit of 42 dosages per prescription for adults (21 years of age)⁵⁸. Indeed, data suggest that children are at lower risk for opioid misuse¹⁹ and overdose⁵⁹ as compared to adults, thus children should not be subject to more restrictive parameters compared to adults.

Adolescents and their parents should be educated about the risks associated with medical use of opioids and should be encouraged to dispose of opioids once they are no longer needed. A recent survey found that 1 in 4 adolescents believe that there were no risk in using an opioid without a prescription⁶⁰. Indeed, risk for opioid misuse following a legitimate prescription is concentrated among adolescents who strongly disapprove of drug use⁴⁶. Furthermore, unsafe storage of opioids is common, with less than 30% of adults reporting locking up opioids at home⁶¹. Adolescents and their parents should be informed about the dangers of opioid misuse, safe storage and disposal, as well as how to respond to an overdose. When informed of the risks associated with opioids, parents may opt for non-opioid alternatives.

Although relatively rare, another way that adolescents obtain prescription opioids for misuse is to visit multiple providers or by filling opioids at multiple pharmacies. Prescription Drug Monitoring Programs (PMPs) are state-level programs that identify patterns of aberrant prescribing and their use has been endorsed by the CDC^{11, 62}. PMPs provide prescribers with information about patients possibly receiving too much opioid or risky combinations of medications (e.g. benzodiazepines along with opioids) and gives prescribers the opportunity to refer patients to substance use treatment programs. PMP use are associated with a reduction in intentional opioid exposures⁶³. Currently not all states mandate that prescribers

check PMPs before providing opioids, however those that do such as Kentucky⁶⁴ and New York⁶⁵, have seen a reduction in problematic opioid behaviors. Whether these changes may be attributable to the PMP or to other social and statutory changes is unknown. To date, 49 states have PMP programs, however the minority *require* their use. Requiring that health care providers register for their PMP⁶⁶ and use it to check their patient's opioid prescription pattern may play an important part in reducing the opioid epidemic affecting children.

Conclusions

In summary, this manuscript presents a topical review of opioid use and related problematic behaviors affecting children in the United States. Children 18 years of age, constitute 25% of the entire United States population, yet have unique needs related to opioids. Over the past 2–3 decades health care providers have significantly increased opioid prescribing to children. During the same time period nonmedical use of opioids has emerged as a public health crises affecting children. However, it is not clear whether increased opioid prescribing to children has driven the opioid crises. Furthermore, knowledge on risks for problematic opioid use behaviors following a legitimate prescription remains severely limited. An urgent need exist to better understand the risks associated with opioid use. Future research in this critical area could be facilitated by well designed longitudinal studies tracking children's opioid use and problematic behaviors over time.

References

1. King S, Chambers CT, Huguet A, et al. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. *Pain*. 2011;152:2729–2738. [PubMed: 22078064]
2. Groenewald CB, Wright DR, Palermo TM. Health care expenditures associated with pediatric pain-related conditions in the United States. *Pain*. 2015;156:951–957. [PubMed: 25734992]
3. Schechter NL, Allen DA, Hanson K. Status of pediatric pain control: a comparison of hospital analgesic usage in children and adults. *Pediatrics*. 1986;77:11–15. [PubMed: 2415909]
4. Schwaller F, Fitzgerald M. The consequences of pain in early life: injury-induced plasticity in developing pain pathways. *Eur J Neurosci*. 2014;39:344–352. [PubMed: 24494675]
5. Palermo TM, Valrie CR, Karlson CW. Family and parent influences on pediatric chronic pain: a developmental perspective. *Am Psychol*. 2014;69:142–152. [PubMed: 24547800]
6. Rabbitts JA, Zhou C, Groenewald CB, et al. Trajectories of postsurgical pain in children: risk factors and impact of late pain recovery on long-term health outcomes after major surgery. *Pain*. 2015;156:2383–2389. [PubMed: 26381701]
7. Howard RF. Current status of pain management in children. *JAMA*. 2003;290:2464–2469. [PubMed: 14612483]
8. Groenewald CB, Rabbitts JA, Schroeder DR, et al. Prevalence of moderate-severe pain in hospitalized children. *Paediatr Anaesth*. 2012;22:661–668. [PubMed: 22332912]
9. Goyal MK, Kuppermann N, Cleary SD, et al. Racial Disparities in Pain Management of Children With Appendicitis in Emergency Departments. *JAMA Pediatr*. 2015;169:996–1002. [PubMed: 26366984]
10. Volkow ND, McLellan AT. Opioid Abuse in Chronic Pain--Misconceptions and Mitigation Strategies. *N Engl J Med*. 2016;374:1253–1263. [PubMed: 27028915]
11. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. *JAMA*. 2016;315:1624–1645. [PubMed: 26977696]
12. Manchikanti L, Fellows B, Ailinani H, et al. Therapeutic use, abuse, and nonmedical use of opioids: a ten-year perspective. *Pain Physician*. 2010;13:401–435. [PubMed: 20859312]

13. Degenhardt L, Charlson F, Mathers B, et al. The global epidemiology and burden of opioid dependence: results from the global burden of disease 2010 study. *Addiction*. 2014;109:1320–1333. [PubMed: 24661272]
14. Vowles KE, McEntee ML, Julnes PS, et al. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. *Pain*. 2015;156:569–576. [PubMed: 25785523]
15. Knipper E, Banta-Green CJ, Jimenez N. Opioid use disorder and misuse: A review of the epidemiology and medical implications for pediatric anesthesiologists. *Paediatr Anaesth*. 2017;27:1070–1076. [PubMed: 29030938]
16. Center for Disease Control and Prevention. Opioid Overdose. Opioid Basics. Commonly Used Terms. Available at: <https://www.cdc.gov/drugoverdose/opioids/terms.html> [accessed] 20 October, 2017
17. Smith SM, Dart RC, Katz NP, et al. Classification and definition of misuse, abuse, and related events in clinical trials: ACTTION systematic review and recommendations. *Pain*. 2013;154:2287–2296. [PubMed: 23792283]
18. O'Connor AB, Turk DC, Dworkin RH, et al. Abuse liability measures for use in analgesic clinical trials in patients with pain: IMMPACT recommendations. *Pain*. 2013;154:2324–2334. [PubMed: 24148704]
19. Center for Behavioral Health Statistics and Quality.(2017). 2016 National Survey on Drug Use and Health: Detailed Tables. Substance Abuse and Mental Health Services Administration, Rockville, MD.
20. Boyd CJ, McCabe SE, Cranford JA, et al. Adolescents' motivations to abuse prescription medications. *Pediatrics*. 2006;118:2472–2480. [PubMed: 17142533]
21. Young A, McCabe SE, Cranford JA, et al. Nonmedical use of prescription opioids among adolescents: subtypes based on motivation for use. *J Addict Dis*. 2012;31:332–341. [PubMed: 23244552]
22. Birnbaum HG, White AG, Schiller M, et al. Societal costs of prescription opioid abuse, dependence, and misuse in the United States. *Pain Med*. 2011;12:657–667. [PubMed: 21392250]
23. Jessell L, Mateu-Gelabert P, Guarino H, et al. Sexual Violence in the Context of Drug Use Among Young Adult Opioid Users in New York City. *J Interpers Violence*. 8 3 ed201510.1177/0886260515596334
24. Gaither JR, Leventhal JM, Ryan SA, et al. National Trends in Hospitalizations for Opioid Poisonings Among Children and Adolescents, 1997 to 2012. *JAMA Pediatr*. 2016;170:1195–1201. [PubMed: 27802492]
25. Curtin SC, Tejada-Vera B, Warner M: Drug overdose deaths among adolescents aged 15–19 in the United States: 1999–2015. NCHS data brief, no 282 Available at: <https://www.cdc.gov/nchs/products/databriefs/db282.htm> [accessed] December, 2017
26. Sites BD, Beach ML, Davis MA. Increases in the use of prescription opioid analgesics and the lack of improvement in disability metrics among users. *Reg Anesth Pain Med*. 2014;39:6–12. [PubMed: 24310049]
27. Manchikanti L, Singh A. Therapeutic opioids: a ten-year perspective on the complexities and complications of the escalating use, abuse, and nonmedical use of opioids. *Pain Physician*. 2008;11:S63–88. [PubMed: 18443641]
28. Centers for Disease C, Prevention. Vital signs: overdoses of prescription opioid pain relievers--- United States, 1999—2008. *MMWR Morb Mortal Wkly Rep*. 2011;60:1487–1492. [PubMed: 22048730]
29. Atluri S, Sudarshan G, Manchikanti L. Assessment of the trends in medical use and misuse of opioid analgesics from 2004 to 2011. *Pain Physician*. 2014;17:E119–128. [PubMed: 24658483]
30. Dart RC, Surratt HL, Cicero TJ, et al. Trends in opioid analgesic abuse and mortality in the United States. *N Engl J Med*. 2015;372:241–248. [PubMed: 25587948]
31. Joranson DE, Ryan KM, Gilson AM, et al. Trends in medical use and abuse of opioid analgesics. *JAMA*. 2000;283:1710–1714. [PubMed: 10755497]
32. Burghardt LC, Ayers JW, Brownstein JS, et al. Adult prescription drug use and pediatric medication exposures and poisonings. *Pediatrics*. 2013;132:18–27. [PubMed: 23733792]

33. Groenewald CB, Rabbitts JA, Gebert JT, et al. Trends in opioid prescriptions among children and adolescents in the United States: a nationally representative study from 1996 to 2012. *Pain*. 2016;157:1021–1027. [PubMed: 26716995]
34. Mazer-Amirshahi M, Mullins PM, Rasooly IR, et al. Trends in prescription opioid use in pediatric emergency department patients. *Pediatr Emerg Care*. 2014;30:230–235. [PubMed: 24651218]
35. Kaiser SV, Asteria-Penalzoa R, Vittinghoff E, et al. National patterns of codeine prescriptions for children in the emergency department. *Pediatrics*. 2014;133:e1139–1147. [PubMed: 24753533]
36. Chumpitazi CE, Rees CA, Camp EA, et al. Decreased Opioid Prescribing in a Pediatric Emergency Department After the Rescheduling of Hydrocodone. *J Emerg Med*. 2017;52:547–553. [PubMed: 27727038]
37. McCabe SE, West BT, Veliz P, et al. Trends in Medical and Nonmedical Use of Prescription Opioids Among US Adolescents: 1976–2015. *Pediatrics*. 2017;139.
38. Pezalla EJ, Rosen D, Erensen JG, et al. Secular trends in opioid prescribing in the USA. *J Pain Res*. 2017;10:383–387. [PubMed: 28243142]
39. Guy GP Jr., Zhang K, Bohm MK, et al. Vital Signs: Changes in Opioid Prescribing in the United States, 2006–2015. *MMWR Morb Mortal Wkly Rep*. 2017;66:697–704. [PubMed: 28683056]
40. Walco GA, Gove N, Phillips J, et al. Opioid Analgesics Administered for Pain in the Inpatient Pediatric Setting. *J Pain*. 2017;18:1270–1276. [PubMed: 28652205]
41. Fredheim OM, Log T, Olsen W, et al. Prescriptions of opioids to children and adolescents; a study from a national prescription database in Norway. *Paediatr Anaesth*. 2010;20:537–544. [PubMed: 20609118]
42. The Danish Health Data Authority Health Analysis, Medicinal Product Statistics & Health Data Program. Available at: <http://www.medstat.dk/en> [accessed] November, 2017
43. Chai G, Governale L, McMahon AW, et al. Trends of outpatient prescription drug utilization in US children, 2002–2010. *Pediatrics*. 2012;130:23–31. [PubMed: 22711728]
44. McCabe SE, Boyd CJ, Young A. Medical and nonmedical use of prescription drugs among secondary school students. *J Adolesc Health*. 2007;40:76–83. [PubMed: 17185209]
45. Johnston LD, O'Malley PM, Miech RA, et al. Monitoring the Future national survey results on drug use, 1975–2015: Overview, key findings on adolescent drug use. Ann Arbor: Institute for Social Research. The University of Michigan 2016;
46. Miech R, Johnston L, O'Malley PM, et al. Prescription Opioids in Adolescence and Future Opioid Misuse. *Pediatrics*. 2015;136:e1169–1177. [PubMed: 26504126]
47. Hooten WM, Brummett CM, Sullivan MD, et al. A Conceptual Framework for Understanding Unintended Prolonged Opioid Use. *Mayo Clin Proc*. 2017;92:1822–1830. [PubMed: 29108841]
48. Hooten WM, St Sauver JL, McGree ME, et al. Incidence and Risk Factors for Progression From Short-term to Episodic or Long-term Opioid Prescribing: A Population-Based Study. *Mayo Clin Proc*. 2015;90:850–856. [PubMed: 26141327]
49. Harbaugh CM, Lee JS, Hu HM, et al. Persistent Opioid Use Among Pediatric Patients After Surgery. *Pediatrics* 2017;10.1542/peds.2017–2439
50. Whiteside LK, Russo J, Wang J, et al. Predictors of Sustained Prescription Opioid Use After Admission for Trauma in Adolescents. *J Adolesc Health*. 2016;58:92–97. [PubMed: 26476855]
51. Grant DR, Schoenleber SJ, McCarthy AM, et al. Are We Prescribing Our Patients Too Much Pain Medication? Best Predictors of Narcotic Usage After Spinal Surgery for Scoliosis. *J Bone Joint Surg Am*. 2016;98:1555–1562. [PubMed: 27655983]
52. Abou-Karam M, Dube S, Kvann HS, et al. Parental Report of Morphine Use at Home after Pediatric Surgery. *J Pediatr*. 2015;167:599–604 e591–592. [PubMed: 26205183]
53. Yaster M, Gao S, Vozzo PT, et al. Physicians Dispense More Opioid Than Needed to Treat Same Day Surgery Pain, a Prospective Pediatric Cohort Study. *Anesthesia and Analgesia*. 2016;122.
54. Voepel-Lewis T, Wagner D, Tait AR. Leftover prescription opioids after minor procedures: an unwitting source for accidental overdose in children. *JAMA Pediatr*. 2015;169:497–498. [PubMed: 25798880]

55. McCabe SE, West BT, Boyd CJ. Leftover prescription opioids and nonmedical use among high school seniors: a multi-cohort national study. *J Adolesc Health*. 2013;52:480–485. [PubMed: 23298996]
56. McCabe SE, Boyd CJ. Sources of prescription drugs for illicit use. *Addict Behav*. 2005;30:1342–1350. [PubMed: 16022931]
57. Schechter NL, Walco GA. The Potential Impact on Children of the CDC Guideline for Prescribing Opioids for Chronic Pain: Above All, Do No Harm. *JAMA Pediatr*. 2016;170:425–426. [PubMed: 26977702]
58. Washington State Health Care Authority. Opioid Clinical Policy—Medicaid. Available at: <https://www.hca.wa.gov/billers-providers/programs-and-services/opioids> [accessed] December, 2017
59. Chen LH, Hedegaard H, Warner M. Drug-poisoning Deaths Involving Opioid Analgesics: United States, 1999–2011. *NCHS Data Brief*. 2014;1–8.
60. Partnership for Drug-Free Kids (formerly known as The Partnership at DrugFree.org). (2013). 2012 Partnership Attitude Tracking Study. Teens and Parents. Available at: <https://drugfree.org/wp-content/uploads/2013/04/PATS-2012-FULL-REPORT2.pdf> [accessed] December, 2017
61. McDonald EM, Kennedy-Hendricks A, McGinty EE, et al. Safe Storage of Opioid Pain Relievers Among Adults Living in Households With Children. *Pediatrics*. 2017;139.
62. Centers for Disease Control and Prevention: What States Need to Know about PDMPs. Available at: <https://www.cdc.gov/drugoverdose/pdmp/states.html> [accessed] December, 2017
63. Reifler LM, Droz D, Bailey JE, et al. Do prescription monitoring programs impact state trends in opioid abuse/misuse? *Pain Med*. 2012;13:434–442. [PubMed: 22299725]
64. Freeman PR, Goodin A, Troske S, et al. Kentucky House Bill 1 Impact Evaluation: Executive summary pre-pared for the Kentucky Cabinet for Health and Family Services [Internet]. Frankfort, KY: Institute for Pharmaceutical Outcomes and Policy, Department of Pharmacy Practice and Science, College of Pharmacy, University of Kentucky; Lexington, KY; 2015
65. Brown R, Riley MR, Ulrich L, et al. Impact of New York prescription drug monitoring program, I-STOP, on statewide overdose morbidity. *Drug Alcohol Depend*. 2017;178:348–354. [PubMed: 28692945]
66. Wen H, Schackman BR, Aden B, et al. States With Prescription Drug Monitoring Mandates Saw A Reduction In Opioids Prescribed To Medicaid Enrollees. *Health Aff (Millwood)*. 2017;36:733–741. [PubMed: 28373340]

Table 1.

Terms used in this manuscript.

Opioid use	Legitimate opioid use as prescribed by a health care provider.
Opioid misuse	Use of prescription opioids (e.g. oxycodone, morphine, tramadol) in manner or dose other than prescribed by a healthcare practitioner, whether harmful or not.
Opioid use disorder	Misuse of prescription opioids (e.g. oxycodone, hydrocodone) and/or use of illegal opioids (e.g. heroin, carfentanil) resulting in significant impairment or distress; a DSM-5 diagnostic code. Opioid use disorder also includes the terms “opioid addiction”, “opioid abuse”, and “opioid dependence” [*] .
Opioid overdose	Use resulting in injury to the body (poisoning) when opioids are taken in excessive amounts, whether fatal or not.

^{*} American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.