# Opioid Addiction

## TABLE OF CONTENTS

1. **Introduction**

2. **Exposure**

3. **Studies Explore Prescription Opioid Dangers**
   - AAP News • Original Publication • March-20-2017

   - Article • Original Publication • April-1-2017

   - Article • Original Publication • April-1-2017

6. **Clues to the Opioid Crisis in Monitoring the Future but Still Looking for Solutions**
   - Commentary • Original Publication • April-1-2017

7. **Risks to Children When Adult Prescription Opioids Are Kept in the House**
   - Journals Blog • Original Publication • March-2-2017

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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Type</th>
<th>Publication Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>Safe Storage of Opioid Pain Relievers Among Adults Living in Households With Children</td>
<td>Article</td>
<td>Original Publication • March-1-2017</td>
</tr>
<tr>
<td>40</td>
<td>Overdose Risk in Young Children of Women Prescribed Opioids</td>
<td>Article</td>
<td>Original Publication • March-1-2017</td>
</tr>
</tbody>
</table>

**Prescribed Use and Misuse**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Type</th>
<th>Publication Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>Study: Prescription Opioid Use in Teens Associated With Future Misuse</td>
<td>AAP News</td>
<td>Original Publication • November-4-2015</td>
</tr>
<tr>
<td>47</td>
<td>Legitimate Opioid Use and Future Risk of Adult Opioid Misuse</td>
<td>AAP Grand Rounds</td>
<td>Original Publication • February-1-2016</td>
</tr>
<tr>
<td>49</td>
<td>Prescription Opioids in Adolescence and Future Opioid Misuse</td>
<td>Article</td>
<td>Original Publication • November-1-2015</td>
</tr>
<tr>
<td>58</td>
<td>Opioids and Operations</td>
<td>Commentary</td>
<td>Original Publication • January-1-2018</td>
</tr>
<tr>
<td>60</td>
<td>Persistent Opioid Use Among Pediatric Patients After Surgery</td>
<td>Article</td>
<td>Original Publication • January-1-2018</td>
</tr>
<tr>
<td>69</td>
<td>Policy Calls for Public Health Approach to Opioid Misuse by Pregnant Women</td>
<td>AAP News</td>
<td>Original Publication • February-20-2017</td>
</tr>
<tr>
<td>71</td>
<td>A Public Health Response to Opioid Use in Pregnancy</td>
<td>From the American Academy of Pediatrics</td>
<td>Original Publication • March-1-2017</td>
</tr>
</tbody>
</table>
TABLE OF CONTENTS

78  Prescription Opioid Epidemic and Infant Outcomes
    Article • Original Publication • May-1-2015

90  Risk Stratification for Opioid Misuse in Children, Adolescents, and Young Adults: A Quality Improvement Project
    Quality Report • Original Publication • January-1-2017

Treatment and Prevention

100 Medication Treatment of Adolescent Opioid Use Disorder in Primary Care
    In Brief • Original Publication • January-1-2018

103 Effective Treatments for Opioid Use Disorder Underused in Youths: AAP News
    AAP News • Original Publication • August-22-2016

105 Medication-Assisted Treatment of Adolescents With Opioid Use Disorders
    From the American Academy of Pediatrics • Original Publication • September-1-2016

109 Recognition and Management of Iatrogenically Induced Opioid Dependence and Withdrawal in Children
    From the American Academy of Pediatrics • Original Publication • January-1-2014

113 A Qualitative Study of Family Experience With Hospitalization for Neonatal Abstinence Syndrome
    Article • Original Publication • October-1-2016

120 Study: Sports Participation May Keep Teens From Using Heroin
    AAP News • Original Publication • July-25-2016

121 The US Opioid Epidemic and Adolescent Sports—A Negative Association Worth Knowing About
    Journals Blog • Original Publication • August-1-2016

122 Nonmedical Prescription Opioid and Heroin Use Among Adolescents Who Engage in Sports and Exercise
    Article • Original Publication • August-1-2016
The opioid epidemic, with devastating effects on individuals, families, and children, is on those of us who have prescribed, and in many cases overprescribed, opioid medications, and the regulatory and professional organizations that, unwittingly, were a primary cause of this national tragedy. Of course, intentions were good, and a reaction to the decades-old problem of undertreating pain in our patients. But, as frequently happens, the pendulum swung too far in the other direction. Spurred on by catch phrases such as “opiophobia” and “pain as the fifth vital sign,” and implicitly encouraged by the 2000 Joint Commission on Accreditation of Healthcare Organizations standards for pain management, healthcare providers wrote prescriptions for opioids at an ever-increasing rate.\(^1\)\(^-\)\(^3\)

In 1991, 76 million prescriptions for opioids were dispensed in the United States. This number increased every year through 2012 when 259 million prescriptions were written, or roughly one bottle of opioid analgesics for every adult in the United States.\(^4\)\(^,\)\(^5\)

Prior to the onset of the current opioid epidemic there had been a general belief, supported by some evidence, that therapeutic use of opioid analgesics rarely led to addiction.\(^1\) While this might be generally true (depending on the definition of “rarely”), the converse is not. The authors of a study published in 2014 reported that 75% of heroin-dependent adults who began abusing opioids during the decade 2000–2010 started by abusing prescription opioids.\(^6\) Concurrent with the increase in prescriptions for opioids has been an increase in heroin use in the United States; between 2007 and 2012 the estimated number of heroin users increased from 373,000 to 680,000, a 76% increase.\(^7\) Most tragically, the rate of death from opioid overdoses tripled between 2000 and 2014, with 28,647 deaths in 2014 attributed to opioid overdoses.\(^6\) In 2015, the number of deaths from opioid overdoses in the United States reached 33,091.\(^9\)

The articles in this collection focus on the manifestations of the opioid epidemic in children and adolescents. Among the many highlights is a study by Patrick et al\(^{10}\) (page 78) documenting an increase in the rate of neonatal abstinence syndrome (NAS) from 6.0/1,000 births in 2009 to 10.7/1,000 births in 2011 among newborns enrolled in the Tennessee Medicaid program. In another study included in the collection, Miech et al\(^{11}\) (page 49) found that legitimate use of prescription opioids before high school graduation was associated with a 33% increased risk of misuse subsequently.

On a more positive note is a report by Veliz et al\(^{12}\) (page 122) that suggests that daily participation in sports and exercise by adolescents may be protective against nonprescription opioid and heroin use.

Overall, there is much food for thought in this collection. The healthcare “industry” helped cause the current opioid epidemic, and it’s up to healthcare professionals to help end it.

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James A Taylor, MD
Editor-in-Chief, AAP Grand Rounds
Most teens abusing prescription opioids previously used them for medical reasons. Doctors wrote about 259 million prescriptions for opioids in 2012, and roughly 1,000 people a day are treated in emergency departments for misusing them, according to the Centers for Disease Control and Prevention (CDC).

Using data from the Monitoring the Future study, researchers from the University of Michigan explored prescription opioid use among high school seniors from 1976-2015. During that time, prevalence of any type of use ranged from 16.5% to 24.1%. Medical use only was most common, ranging from 8.5% to 14.4%, according to the study “Trends in Medical and Nonmedical Use of Prescription Opioids among US Adolescents: 1976-2015” (McCabe SE, et al. Pediatrics. March 20, 2017. https://doi.org/10.1542/peds.2016-2387).

Among those who have used both, the most common pattern was medical use before nonmedical, which ranged from 2.6% to 5.4%.

While males and females had similar rates of nonmedical use of prescription opioids (NUPO), the correlation between medical and nonmedical uses was stronger for males. Researchers said this may be due to accessibility because males tend to get opioids from peers while females often get them from family members. In addition, male nonmedical use tends to be for getting high while females are trying to relieve pain, according to the study.

The authors said physicians should monitor prescription drug use, discuss risks and benefits of prescription opioids with patients and parents, screen for NUPO, substance use and other mental health disorders, and prescribe carefully.

“Prescribing practices that enhance vigilance and monitoring of prescription opioids among adolescents, including education regarding proper disposal when medical use has concluded, warrant further investigation,” they wrote.

The authors of a related commentary (page 27) called for additional ways to curb the opioid crisis.

“Possible interventions include better education of our patients and families when we prescribed these drugs, better drug regulation, development of new affordable approaches to pain management that have lower potential for abuse, and accessible and affordable treatment programs for those already afflicted,” they wrote.

**OPIOID EXPOSURE**

Another study explored the toll of pediatric exposure to prescription opioids using data from U.S. Poison Control Centers.


Jakob D. Allen, a Marcel J. Casavant, MD, b,c,1 Henry A. Spiller, MS, D.ABAT, b,c Thiphalak Chounthirath, MS, a Nichole L. Hodges, PhD, a Gary A. Smith, MD, DrPH a, c

OBJECTIVES: This study analyzes and compares exposures to prescription opioids among children and adolescents younger than 20 years old in the United States.

METHODS: Data from the National Poison Data System for 2000 through 2015 were analyzed.

RESULTS: Poison control centers received reports of 188,468 prescription opioid exposures among children aged <20 years old from 2000 through 2015. The annual number and rate of exposures increased early in the study period, but declined after 2009, except for buprenorphine exposures, which increased during the last 3 study years. Hydrocodone accounted for the largest proportion of exposures (28.7%), and 47.1% of children exposed to buprenorphine were admitted to a health care facility (HCF). The odds of being admitted to an HCF were higher for teenagers than for children aged 0 to 5 years (odds ratio [OR]: 2.86; 95% confidence interval [CI]: 2.78–2.94) or children aged 6 to 12 years (OR: 6.62; 95% CI: 6.06–7.02). Teenagers also had greater odds of serious medical outcomes than did children aged 0 to 5 years (OR: 3.03; 95% CI: 2.92–3.15) or children aged 6 to 12 years (OR: 4.59; 95% CI: 4.21–5.00). The rate of prescription opioid–related suspected suicides among teenagers increased by 52.7% during the study period.

CONCLUSIONS: Prescription opioid–related HCF admissions and serious medical outcomes were higher among teenagers. Contrary to trends for other prescription opioids, exposures to buprenorphine have increased in recent years; children aged 0 to 5 years accounted for almost 90% of buprenorphine exposures. These findings indicate that additional prevention efforts are needed.

WHAT’S KNOWN ON THIS SUBJECT: Previous reports have shown that opioids are heavily prescribed to the general population in the United States and have the highest overdose rate among all prescription drugs. Analgesics are the third most commonly implicated substances in poison center pediatric exposures.

WHAT THIS STUDY ADDS: From 2000 through 2015, 188,468 pediatric opioid exposures were reported to US poison control centers. Health care facility admission occurred in 8.7% and 21.5% of exposures among 0- to 5-year-olds and teenagers, respectively. Serious outcomes were more frequent among teenagers.

# Supplemental Information

**SUPPLEMENTAL TABLE 4** AAPCC Generic Codes for Prescription Opioids and Opioid Groupings Used in This Study

<table>
<thead>
<tr>
<th>Type of Opioid and Generic Code(s)</th>
<th>Substance Name</th>
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</thead>
<tbody>
<tr>
<td>Buprenorphine 0200625</td>
<td>Buprenorphine</td>
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<tr>
<td>Fentanyl 0200628</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>Hydromorphone 0200630</td>
<td>Hydromorphone</td>
</tr>
<tr>
<td>Meperidine 0037707</td>
<td>Meperidine</td>
</tr>
<tr>
<td>Methadone 0037703</td>
<td>Methadone</td>
</tr>
<tr>
<td>Morphine 0037704</td>
<td>Morphine</td>
</tr>
<tr>
<td>Oxymorphone 0200632</td>
<td>Oxymorphone</td>
</tr>
<tr>
<td>Tramadol 0201131</td>
<td>Tramadol</td>
</tr>
<tr>
<td>Codeine 0037701</td>
<td>Codeine</td>
</tr>
<tr>
<td>Acetylsalicylic acid with codeine</td>
<td>Acetylsalicylic acid with codeine</td>
</tr>
<tr>
<td>Acetaminophen with codeine</td>
<td>Acetaminophen with codeine</td>
</tr>
<tr>
<td>Hydrocodone 0200629</td>
<td>Hydrocodone alone or in combination</td>
</tr>
<tr>
<td>Acetaminophen with hydrocodone</td>
<td>Acetaminophen with hydrocodone</td>
</tr>
<tr>
<td>Oxycodone 0037705</td>
<td>Oxycodone alone or in combination</td>
</tr>
<tr>
<td>Acetylsalicylic acid with oxycodone</td>
<td>Acetylsalicylic acid with oxycodone</td>
</tr>
<tr>
<td>Acetaminophen with oxycodone</td>
<td>Acetaminophen with oxycodone</td>
</tr>
<tr>
<td>Propoxyphene 0041718</td>
<td>Acetylsalicylic acid with propoxyphene</td>
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<tr>
<td>Acetaminophen with propoxyphene</td>
<td>Acetaminophen with propoxyphene</td>
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<tr>
<td>Propoxyphene 0072702</td>
<td>Acetylsalicylic acid with propoxyphene</td>
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<tr>
<td>Other 0041707</td>
<td>Acetylsalicylic acid with other narcotics or narcotic analogs</td>
</tr>
<tr>
<td>Acetaminophen with other narcotics or narcotic analogs</td>
<td>Acetaminophen with other narcotics or narcotic analogs</td>
</tr>
<tr>
<td>Butorphanol 0200626</td>
<td>Butorphanol</td>
</tr>
<tr>
<td>Tapentadol 0200633</td>
<td>Tapentadol</td>
</tr>
<tr>
<td>Other 0037708</td>
<td>Other or unknown narcotics</td>
</tr>
</tbody>
</table>

Sean Esteban McCabe, PhD, Brady T. West, PhD, Phil Veliz, PhD, Vita V. McCabe, MD, Sarah A. Stoddard, PhD, Carol J. Boyd, PhD

OBJECTIVES: Most US studies of national trends in medical and nonmedical use of prescription opioids have focused on adults. Given the limited understanding in these trends among adolescents, we examine national trends in the medical and nonmedical use of prescription opioids among high school seniors between 1976 and 2015.

METHODS: The data used for the study come from the Monitoring the Future study of adolescents. Forty cohorts of nationally representative samples of high school seniors (modal age 18) were used to examine self-reported medical and nonmedical use of prescription opioids.

RESULTS: Lifetime prevalence of medical use of prescription opioids peaked in both 1989 and 2002 and remained stable until a recent decline from 2013 through 2015. Lifetime nonmedical use of prescription opioids was less prevalent and highly correlated with medical use of prescription opioids over this 40-year period. Adolescents who reported both medical and nonmedical use of prescription opioids were more likely to indicate medical use of prescription opioids before initiating nonmedical use.

CONCLUSIONS: Prescription opioid exposure is common among US adolescents. Long-term trends indicate that one-fourth of high school seniors self-reported medical or nonmedical use of prescription opioids. Medical and nonmedical use of prescription opioids has declined recently and remained highly correlated over the past 4 decades. Sociodemographic differences and risky patterns involving medical and nonmedical use of prescription opioids should be taken into consideration in clinical practice to improve opioid analgesic prescribing and reduce adverse consequences associated with prescription opioid use among adolescents.

WHAT’S KNOWN ON THIS SUBJECT: Opioid analgesic prescribing has increased in the United States over the past 4 decades. To date, studies examining national trends in medical and nonmedical use of prescription opioids have focused primarily on adults and relied on separate data sources.

WHAT THIS STUDY ADDS: Medical use of prescription opioids was highly correlated with nonmedical use over the past 4 decades, especially among male adolescents. Adolescents reporting both medical and nonmedical use of prescription opioids were more likely to initiate medical before nonmedical use.
and this pattern may be driven by the one-third of adolescents who report NUPO involving leftover opioid medications from their own previous prescriptions.22,27,28

The medical use of prescription opioids was generally more prevalent among female adolescents, whereas NUPO differed little by sex. Although sex differences in medical use of prescription opioids have been documented,13,14,21,29 the current study extended previous research by examining long-term trends. The medical use of prescription opioids was found to be highly correlated with NUPO across the 40 cross-sectional samples among high school seniors, consistent with previous findings among adults.1,3–7 Notably, we found that the correlation was much stronger for male than female adolescents.

Based on past research, there are several possible reasons why medical use of prescription opioids is more highly correlated with NUPO among male adolescents than female adolescents. First, NUPO is directly related to the availability of prescription opioids, and several previous studies have shown sex differences in the diversion associated with NUPO among adolescents.30–33 For instance, male nonmedical users are more likely to obtain prescription opioids from their peers, whereas female nonmedical users are more likely to obtain prescription opioids from family members.31,32 The higher rate of peer-to-peer diversion among male adolescents may increase the risk of NUPO when medical availability increases.

Second, male nonmedical users are more likely to use prescription opioids nonmedically to get high, whereas female nonmedical users are more likely to use for physical pain relief.20,32,34 The higher rate of non-pain relief motives among male adolescents could partially account for the stronger correlation between medical use of prescription opioids and NUPO. The findings of the current study reinforce the need

![Figure 2](image-url)
March is National Poison Prevention Month to raise awareness about what we can do to help families keep their children safe from preventable ingestions and toxic exposures. To help celebrate this important preventive health month, we are early releasing two studies that will officially appear in our March issue focused on two aspects of adults having opioid pain relievers in the home with young children. The first deals with issues of safe storage and the second with overdose risk in children who gain access to these medications.

The first study on safe storage of opioids by McDonald et al. (10.1542/peds.2016-2161) focuses on survey results of a national sample of adults who self-reported the need for opioid pain relievers (OPRs) and had children less than 18 years living at home with them. Questions were asked regarding safe storage of these medications (meaning having them latched or locked away). Sadly, just under a third of the 681 adults who were surveyed and had young children in their home practiced safe storage and just over 10% used safe storage with older children at home. So are there factors to differentiate those families who practiced safe versus unsafe storage? There are, and they involve a number of issues ranging from efficacy of the medication to relieve their pain to awareness of concerns were their children to access those medications. Better education of adults who take prescription opioids is needed—so feel free to share this study with colleagues who care for the parents of your patients since they may want to remind families along with you of the importance of keeping all prescription medications secure from young ones in the home.

The second study by Finkelstein et al. (10.1542/peds.2016-2887) looks at 20 years of opioid overdoses in children in homes where prescription opioids were present. The authors share the results of a population-based nested case-control study performed in Ontario involving children 10 years of age or less living in a home where either an opioid or non-steroidal anti-inflammatory medication (serving as control cases) had been prescribed and whether children were hospitalized or died from an opioid overdose. Over twenty years, just over 100 children in Ontario died of an opioid overdose with half being less than 2 years of age. The odds of these children having a mother prescribed an opioid or an antidepressant was far greater than those who had not had them prescribed. This study combined with the first provides a sobering dose of concern and should lead to all of us working with adult clinicians and pharmacists to come together and work to limit the amount of drug administered by prescription, make sure the drug is well–stored at home away from children, and when done using it, we should also review how to properly dispose of these medications in an environmental and safe way so that children cannot discover these drugs in the trash where they can have easy access to them thinking they might look like candy. If you need more info on how to properly dispose of expired or used medications whether they are opioid or not, check with your local pharmacist so you can provide the expertise needed (if you don’t have it already) to prevent the overdoses from unsafe storage and discarding of opioid and other medications in the home of your patients.
Legitimate Opioid Use and Future Risk of Adult Opioid Misuse

Investigators from multiple institutions utilized data from the Monitoring the Future Study (MFS) to evaluate the association between legitimate opioid use by 12th grade and opioid misuse after high school. MFS is a survey conducted annually since 1975 of the behaviors, attitudes, and values of a nationally representative sample of US 12th graders. A random sample of 12th graders who have completed the baseline survey are selected yearly to complete follow-up surveys that include questions about opioid misuse. This study uses information from MFS participants who completed a baseline survey between 1990 and 2012 and follow-up surveys for the first 3 years after high school, corresponding to participant ages of 19–23.

The predictor variable was legitimate opioid use by 12th grade as determined by response to the baseline survey question “Have you ever taken any narcotics other than heroin because a doctor told you to use them?” The outcome variable was any opioid misuse in the past 12 months determined by participant response to the follow-up survey question about whether they had “taken narcotics other than heroin on your own – that is, without a doctor telling you to take them.” The risk of legitimate use of opioids by 12th grade leading to future misuse was assessed 2 ways using regression analyses. First, the risk was assessed after controlling for potential confounders. In addition, study participants were categorized by risk of future misuse into 8 strata, based on characteristics known to predict opioid misuse (such as marijuana use, cigarette smoking, barbiturate and sedative use, binge drinking, and attitudes toward marijuana use). The independent effect of legitimate opioid use as a risk of future misuse was then estimated among participants in each strata.

There were 6,220 participants included in analysis who completed at least 1 follow-up survey (71% response rate). A history of prescription opioid use by 12th grade was independently associated with a 33% increase in the risk of future opioid misuse (RR = 1.33; 95% CI, 1.04–1.70). In the second analysis, participants with baseline risk scores of 1.75%–3% (strata 2) and 3%–5% (strata 3) who were legitimately exposed to opioids by 12th grade were 3- and 2-fold, respectively, more likely to have future misuse than those in the same strata who were not exposed. Legitimate use of opioids by 12th grade was not significantly associated with future misuse among participants in any other strata.

The authors conclude that legitimate opioid use by 12th grade predicts future opioid misuse among patients who otherwise have little drug experience and who disapprove of illegal drug use.

Persistent Opioid Use Among Pediatric Patients After Surgery

Calista M. Harbaugh, MD, a Jay S. Lee, MD, b Hsou Mei Hu, PhD, c Sean Esteban McCabe, PhD, c Terri Voepel-Lewis, PhD, RN, d Michael J. Englesbe, MD, e Chad M. Brummett, MD, e Jennifer F. Waljee, MD, MPH, MS f

BACKGROUND: Despite efforts to reduce nonmedical opioid misuse, little is known about the development of persistent opioid use after surgery among adolescents and young adults. We hypothesized that there is an increased incidence of prolonged opioid refills among adolescents and young adults who received prescription opioids after surgery compared with nonsurgical patients.

METHODS: We performed a retrospective cohort study by using commercial claims from the Truven Health Marketscan research databases from January 1, 2010, to December 31, 2014. We included opioid-naïve patients ages 13 to 21 years who underwent 1 of 13 operations. A random sample of 3% of nonsurgical patients who matched eligibility criteria was included as a comparison. Our primary outcome was persistent opioid use, which was defined as ≥1 opioid prescription refill between 90 and 180 days after the surgical procedure.

RESULTS: Among eligible patients, 60.5% filled a postoperative opioid prescription (88,637 patients). Persistent opioid use was found in 4.8% of patients (2.7%–15.2% across procedures) compared with 0.1% of those in the nonsurgical group. Cholecystectomy (adjusted odds ratio 1.13; 95% confidence interval, 1.00–1.26) and colectomy (adjusted odds ratio 2.33; 95% confidence interval, 1.01–5.34) were associated with the highest risk of persistent opioid use. Independent risk factors included older age, female sex, previous substance use disorder, chronic pain, and preoperative opioid fill.

CONCLUSIONS: Persistent opioid use after surgery is a concern among adolescents and young adults and may represent an important pathway to prescription opioid misuse. Identifying safe, evidence-based practices for pain management is a top priority, particularly among at-risk patients.

WHAT’S KNOWN ON THIS SUBJECT: Opioid-related morbidity and mortality among US adolescents and young adults continues to rise. Postoperative opioid prescriptions vary widely and are often in excess among children and adults. Postoperative care is an important risk factor for prolonged opioid use among adults.

WHAT THIS STUDY ADDS: This study is the first to investigate persistent opioid use among adolescents and young adults after surgery. This study highlights the need for safe prescribing and monitoring habits in the postoperative setting to prevent long-term addiction, misuse, and adverse effects.

Risk Stratification for Opioid Misuse in Children, Adolescents, and Young Adults: A Quality Improvement Project

Rachel Thienprayoon, MD, MSCS, Kelly Porter, MSN, APRN, CNP, Michelle Tate, RN, Marshall Ashby, MHS, MBA, Mark Meyer, MD

BACKGROUND: The Pediatric Palliative and Comfort Care Team (PACT) at Cincinnati Children’s Hospital Medical Center (CCHMC) provides opioids to a large population of patients in the ambulatory setting. Before this project, PACT had no reliable system to risk stratify patients for opioid misuse.

METHODS: The global aim was safe opioid prescribing by the palliative care team. The specific, measurable, achievable, realistic, and timely aim was as follows: “In patients who present for follow up with PACT, we will use the “opioid bundle” to increase risk stratification for opioid misuse from 0% to 90% over 5 months.” The opioid bundle includes a urine drug screen, Ohio Automated Rx Reporting System report, pill count, and screening history for drug abuse and mental health disorders. The setting was multiple CCHMC ambulatory clinics. Participants included all PACT members.

RESULTS: Since implementing the new system, we have increased risk stratification for opioid misuse among outpatients from 0% to >90%. Results have been sustained for 12 months. Key processes have become reliable: obtaining informed consent and controlled substance agreements for all new patients and obtaining the opioid bundle to enable risk stratification in a consistent and timely fashion. A total of 34% of patients have been stratified as high risk, and an additional 27% have been stratified as moderate risk.

CONCLUSIONS: A system to ensure safe opioid prescribing practices to all patients is critical for providers. Identifying key processes and executing them reliably has enabled the palliative care team at CCHMC to risk stratify >90% of patients receiving opioids in the ambulatory setting for opioid misuse.

Prescription drug abuse is a national epidemic. In 2012, 4.9 million Americans admitted to the misuse of pain relievers, making them the second most commonly used illicit substance in the United States. The Centers for Disease Control and Prevention estimate that 44 people die in the United States every day from overdose of prescription painkillers. Palliative care physicians are often responsible for managing pain and other symptoms in patients with cancer and life-limiting diagnoses. Because opioids are the cornerstone of treatment of cancer-related pain, potential patient misuse of prescription medications and national regulatory responses should be of particular concern to palliative care physicians and oncologists. But general pediatricians, pediatric surgeons, and pediatric dentists may also be responsible for providing.
Medication Treatment of Adolescent Opioid Use Disorder in Primary Care

Brittany L. Carney, MS,* Scott E. Hadland, MD, MPH, MS,† Sarah M. Bagley, MD, MSc‡
*Department of Internal Medicine/Pediatrics, Boston Medical Center, Boston, MA
†Department of Pediatrics, Boston University School of Medicine, Boston, MA

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Electronic Code of Federal Regulations, 42 CFR 8.12 - Federal Opioid Treatment Standards. § Part 8—Medication Assisted Treatment for Opioid Use Disorders. Available at: https://www.ecfr.gov/cgi-bin/text-idx?SID=25e371ab03b3ad92db009353a71&mcdiv=pt42.1.8&mcrg=dk5


Since 2000, a threefold increase in unintentional opioid poisonings among adolescents has followed a dramatic increase in adult opioid-related deaths. In 2016, 1 in 11 high school seniors reported past-year nonprescription use of opioids. Despite these increases, only 8.5% of adolescents received addiction treatment.

In September 2016, the American Academy of Pediatrics (AAP) released a policy statement recommending that pediatricians offer medication for the treatment of severe opioid use disorder (OUD). There are 3 medications approved for OUD treatment: buprenorphine, naltrexone, and methadone. Buprenorphine and methadone are opioid agonists that decrease cravings for opioids and treat withdrawal symptoms. In addition, both provide opioid blockade, which means that if an individual uses another opioid after taking their medication, euphoric effects are blocked. Naltrexone, an opioid antagonist, blocks the opioid receptor, preventing the effects of opioid use. It may also reduce cravings for opioids. Head-to-head clinical trials of these medications in adolescents are lacking; observational data from adults suggest that of these medications, methadone may be the most effective for retention in treatment.

MEDIICATIONS

Buprenorphine is taken daily via sublingual tablets or films and can be prescribed in pediatric primary care. The film is a dissolving strip absorbed through the buccal mucosa or tongue. Buprenorphine has 2 formulations: 1) combined with naloxone (buprenorphine/naloxone) and 2) a formulation without naloxone. Pediatricians should prescribe the combined formulation. Naloxone is not absorbed systemically, but if misused and injected, naloxone blocks opioid receptor, triggering uncomfortable withdrawal symptoms that discourage misuse. Pregnant females are generally prescribed buprenorphine only due to concerns about fetal naloxone exposure. Per federal regulations, providers must complete an 8-hour online or in-person course to receive a US Drug Enforcement Agency waiver before prescribing buprenorphine. As of 2016, nurse practitioners and physician assistants can also obtain waivers. Multiple organizations, including the AAP, have endorsed an adolescent-focused version of the course for pediatricians (http://www.aap.org/mat).

Naltrexone is available in a daily oral tablet or a monthly depot injection. No special certification is required to prescribe naltrexone. Many practitioners initially prescribe tablets for 1 week to ensure tolerability before transitioning to monthly injection. Because naltrexone is an opioid antagonist, it can precipitate sudden withdrawal symptoms in a patient who recently used opioids. Therefore, clinicians should only administer naltrexone 3 to 6 days after the most recent use of short-acting opioids (eg, most short-acting prescription opioids or heroin) and 7 to 10 days after the most recent use of long-acting opioids (eg, most long-acting prescription opioids, buprenorphine, or methadone). It is important to check the