



Opioid Prescribing for Acute Pain Management in Children and Adolescents in Outpatient Settings: Clinical Practice Guideline

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This is the first clinical practice guideline (CPG) from the American Academy of Pediatrics outlining evidence-based approaches to safely prescribing opioids for acute pain in outpatient settings. The central goal is to aid clinicians in understanding when opioids may be indicated to treat acute pain in children and adolescents and how to minimize risks (including opioid use disorder, poisoning, and overdose). The document also seeks to alleviate disparate pain treatment of Black, Hispanic, and American Indian/Alaska Native children and adolescents, who receive pain management that is less adequate and less timely than that provided to white individuals. There may also be disparities in pain treatment based on language, socioeconomic status, geographic location, and other factors, which are discussed.

The document recommends that clinicians treat acute pain using a multimodal approach that includes the appropriate use of nonpharmacologic therapies, nonopioid medications, and, when needed, opioid medications. Opioids should not be prescribed as monotherapy for children or adolescents who have acute pain. When using opioids for acute pain management, clinicians should prescribe immediate-release opioid formulations, start with the lowest age- and weight-appropriate doses, and provide an initial supply of 5 or fewer days, unless the pain is related to trauma or surgery with expected duration of pain longer than 5 days. Clinicians should not prescribe codeine or tramadol for patients younger than 12 years; adolescents 12 to 18 years of age who have obesity, obstructive sleep apnea, or severe lung disease; to treat postsurgical pain after tonsillectomy or adenoidectomy in patients younger than 18 years; or for any breastfeeding patient.

abstract

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The CPG recommends providing opioids when appropriate for treating acutely worsened pain in children and adolescents who have a history of chronic pain; clinicians should partner with other opioid-prescribing clinicians involved in the patient's care and/or a specialist in chronic pain or palliative care to determine an appropriate treatment plan. Caution should be used when treating acute pain in those who are taking sedating medications. The CPG describes potential harms of discontinuing or rapidly tapering opioids in individuals who have been on stable, long-term opioids to treat chronic pain.

The guideline also recommends providing naloxone and information on naloxone, safe storage and disposal of opioids, and direct observation of medication administration. Clinicians are encouraged to help caregivers develop a plan for safe disposal. The CPG contains 12 key action statements based on evidence from randomized controlled trials, high-quality observational studies, and, when studies are lacking or could not feasibly or ethically be conducted, from expert opinion. Each key action statement includes a level of evidence, the benefit-harm relationship, and the strength of recommendation.

I. GREETING

This is the first American Academy of Pediatrics (AAP) clinical practice guideline (CPG) on opioid prescribing in children and adolescents. CPGs provide recommendations to improve patients' care and health outcomes. The process of the AAP for developing these guidelines is meticulous and time intensive. CPG development involves a thorough review of relevant research and close examination of the strength of the studies and other identified documents. The process also considers the benefits and risks of specific practices.

CPGs have traditionally been developed by physicians and researchers, long viewed as the experts in clinical care. Only recently have caregivers and patients been incorporated into this process. Many professional organizations seek the involvement of caregivers and patients in their work; however, it can be challenging to determine how best to engage families, draw on their perspectives and experiences, and authentically involve them in the process. Nonetheless, this task is critical: studies have shown that involving patients and caregivers improves guidelines.¹⁻⁴

The involvement of caregivers and patients can help identify areas that are important to those with lived experiences, highlight real-world barriers to care, increase the legitimacy and trustworthiness of the guideline, improve adherence to clinical recommendations, and disseminate guidelines to communities of interest.

When I was initially approached about participating in this AAP subcommittee, I was both excited and hesitant. I am a caregiver and care partner. Like many, I am an accidental health care advocate because of my family's experience with pediatric pain. My advocacy has spanned 23 years; caring for patients' pain and access to appropriate opioid prescribing have been a large focus of my advocacy. I have witnessed the misapplication of pain treatment guidelines and the unintended harms that families experienced.

I wanted to be part of this subcommittee's work to ensure inclusion of the perspectives of those with lived experiences, and my initial hesitancy to take part was due, in part, to worries about tokenism. Although intentions to include patients and caregivers are often well-meaning, too often, people with lived experience are only symbolically invited and neither fully valued nor truly immersed in the work. As a caregiver and advocate, I am often critical of how the work of medical organizations impacts patients and their families. After witnessing the subcommittee members' work and being genuinely engaged and centered in the CPG development process, I now have immense respect for the process and every member of the subcommittee.

The subcommittee leaders demonstrated thoughtful, dedicated, and compassionate guidance. They ensured inclusivity of all voices and encouraged questions and respectful debate throughout every conversation. They did not shy away from hard discussions. They consistently sought to understand how scenarios might impact children and families and committed to authentically and meaningfully engaging those with lived experiences. I am grateful to this group and feel immense comfort that these are the leaders in caring for our children and youth.

The responsibilities of this subcommittee were substantial. As a result of previous misapplications of other pain management guidelines, there is intense scrutiny on the issue of opioid prescribing nationally. Various interested groups—including patients, caregivers, government entities, politicians, special interest groups, and advocates—are all presently weighing in on this subject. I knew that the subcommittee and our work would be examined by all these stakeholders.

The subcommittee members hold varied expertise related to opioids and represented a broad perspective of views related to prescribing. Subcommittee members respectfully challenged each other, presented concerns, and engaged in fruitful debates that were grounded in the singular focus to improve care of children and families, all

Key Action Statement Table		
Key Action Statement (KAS)	Evidence Quality	Recommendation Strength
KAS 1: Pediatricians and other pediatric health care providers (PHCPs) should treat acute pain using a multimodal approach that includes the appropriate use of nonpharmacologic therapies, nonopioid medications, and, when needed, opioid medications.	B	Strong recommendation
KAS 2: Pediatricians and other PHCPs should NOT prescribe opioids as monotherapy for children and adolescents who have acute pain.	B	Strong recommendation
KAS 3: When prescribing opioids for acute pain in children and adolescents, PHCPs should provide immediate-release opioid formulations, start with the lowest age- and weight-appropriate doses, and provide an initial supply of 5 days or fewer, unless the pain is related to trauma or surgery with an expected duration of pain of more than 5 days.	C	Recommendation
KAS 4.1: When treating acute pain in children and adolescents younger than 12 years, pediatricians and other PHCPs should NOT prescribe codeine or tramadol.	X	Strong recommendation
KAS 4.2: When treating acute pain in adolescents 12–18 years of age who have obesity, obstructive sleep apnea, or severe lung disease, pediatricians and other PHCPs should NOT prescribe codeine or tramadol.	X	Strong recommendation
KAS 4.3: When treating postsurgical pain after tonsillectomy or adenoidectomy in children and adolescents younger than 18 years, pediatricians and other PHCPs should NOT prescribe codeine or tramadol.	X	Strong recommendation
KAS 4.4: When treating acute pain in people of any age who are breastfeeding, pediatricians and other PHCPs should NOT prescribe codeine or tramadol.	X	Strong recommendation
KAS 5: When treating acute pain in children or adolescents who are taking sedating medications, such as benzodiazepines, pediatricians and other PHCPs should use caution when prescribing opioids.	X	Strong recommendation
KAS 6: When prescribing opioids, pediatricians and other PHCPs should provide naloxone and counsel patients and families on the signs of opioid overdose and on how to respond to an overdose.	X	Recommendation
KAS 7: When prescribing opioids, pediatricians and other PHCPs should educate caregivers about safe storage and directly observed administration of medications to children and adolescents.	D	Option
KAS 8: When prescribing opioids, pediatricians and other PHCPs should educate caregivers about safe disposal of unused medications, help caregivers develop a plan to safely dispose of unused medications, and, if possible, offer safe disposal in their practice setting.	A	Strong recommendation
KAS 9: When treating acute, worsened pain in children and adolescents with preexisting chronic pain, pediatricians and other PHCPs should prescribe opioids when indicated and partner with any other opioid-prescribing clinicians involved in the patient's care and with specialists in chronic pain, palliative care, and/or other opioid stewardship programs to determine an appropriate treatment plan.	D	Option
A: Well-designed randomized controlled trials (RCTs) or diagnostic studies on relevant population. B: RCTs or diagnostic studies with minor limitations, overwhelmingly consistent evidence from observational studies. C: Observational studies (case-control and cohort design). D: Expert opinion, case reports, reasoning from first principles. X: Exceptional situations where validating studies cannot be performed and there is a clear preponderance of benefit or harm.		

while minimizing risk. The members' commitment, care, and compassion were evident in every discussion the group engaged in. The discussion of the benefits and risks was nuanced, carefully examining various aspects to ensure that children would not suffer under the misapplication of guidelines, as has happened to adults with pain.

It is with gratitude and respect that the first AAP clinical practice guideline on opioids prescribing in children and adolescents is introduced. The development of this CPG not only adhered to all necessary criteria but also stemmed from the subcommittee's desire and commitment to improve care for all children and families by merging the best clinical recommendations with the human aspects of lived experience.

*With great admiration and appreciation,
Beth Larson-Steckler
Care partner, advocate, Co-Founder Childhood Pancreatitis Foundation*

II. BACKGROUND

Pain is among the most common symptoms that prompt children, adolescents, and families to present for medical care.^{5–7} As a medication class, opioids have long had a beneficial role in the management of some pediatric patients' pain, particularly when that pain is severe. Since the turn of the century, however, rates of opioid use disorder (OUD), poisoning, and overdose have increased dramatically among children and adolescents in the United States.^{8–15} Rates of pediatric opioid prescribing have decreased since a peak in the early 2010s.^{14–16} Against the backdrop of a worsening national opioid-related overdose crisis, some might interpret this change as a positive one. Yet, this widespread decrease in opioid prescribing to pediatric patients likely includes reductions not only in *inappropriate* but also in *appropriate* opioid use to treat severe pain that is not fully responsive to other interventions.^{17–19}

In other words, one potential repercussion of clinicians prescribing fewer opioids is the *undertreatment* of pain. Because pain can adversely impact physical and psychosocial functioning, withholding opioids in situations in which they might be needed could lead to broader negative consequences for some children and adolescents.^{18,20}

It is critical for clinicians to understand when opioids may be indicated and how to safely prescribe them in a manner that minimizes the risk for OUD, poisoning, and overdose. The central goal of this document, the first CPG from the AAP on the subject, is to outline evidence-based approaches to safely prescribing opioids and treating pediatric pain.

An additional goal of this CPG is to ensure equitable treatment of pediatric pain. Studies highlight that Black, Hispanic, and American Indian/Alaska Native (AI/AN) individuals receive both less adequate and less timely pain management than that provided to white individuals—even when they experience similar levels of pain.^{21–25} Contributing factors include implicit bias on the part of treating clinicians, long-standing systemic racism in health care settings, patients' mistrust of clinicians and health systems, cultural differences in experiencing and reporting pain, and language barriers.^{21,26,27}

Additionally, children and adolescents with physical, developmental, or intellectual disabilities may be less likely to receive effective pain management when clinicians do not carefully assess their pain, particularly if a child or adolescent is unable to communicate their pain verbally; this risk is compounded because many scales used for measuring pain were developed for individuals without disabilities.²⁸ Additional disparities may also exist according to socioeconomic status or geographic location, among other factors.²² Inequitable treatment of pain leads to significant distress for children and families, worsened health outcomes, and higher costs of care.²⁹ Throughout, this CPG aims to promote equity with respect to the treatment of pain, including the use of opioids.

This CPG is written for pediatricians and other pediatric health care providers (PHCPs) who prescribe opioids to children and adolescents under age 21 in outpatient settings. The term “pediatricians and other pediatric health care providers” includes pediatric primary care and subspecialty physicians; other specialty physicians (eg, child and adolescent psychiatrists, anesthesiologists, pain specialists, palliative care); and other clinicians who care for children and adolescents with pain, including prescribers (eg, emergency medicine physicians, surgeons, dentists, nurse practitioners, physician assistants, etc) and nonprescribers (eg, assistants, nurses, psychologists, social workers, etc). This CPG focuses on *acute* pain (ie, pain lasting <1 month) rather than subacute (1–3 months),

chronic pain (>3 months), or palliative and end-of-life pain.¹⁹

This CPG makes an evidence-based recommendation to provide opioids when it is appropriate for treating acutely worsened pain in children and adolescents with a history of chronic pain. The CPG also highlights the potential harms of discontinuing or rapidly tapering opioids in individuals who are on stable, prolonged use of opioids to treat chronic pain. These harms include worsening mental health and/or driving individuals to seek opioids through the illicit drug market.^{19,30–32}

This CPG does not directly address opioid prescription in pediatric palliative care and for patients at end-of-life. These children and adolescents often have clinical conditions for which opioids are indicated, often at escalating doses. The CPG does not directly speak to this patient population. This CPG does acknowledge, however, that there are patients on palliative care with chronic pain whose opioid stewardship should be managed in similar ways to other patients with chronic pain.

This CPG acknowledges that illicitly manufactured fentanyl—rather than prescription opioids—is currently the most common cause of poisoning and overdose deaths of children and adolescents.^{10,33,34} Fentanyl-related deaths among adolescents 10 to 19 years of age increased by 182% between 2019 and 2021; 83.9% of adolescent overdose deaths in that time frame involved IMFs.³³ Nonetheless, during the 2000s and early 2010s, it is likely that inappropriate opioid prescribing contributed to the rising rates of negative opioid-related outcomes.^{15,35–39} Indeed, use of prescription pain medication may lead to OUD in a small percentage of individuals and may progress to subsequent use of more potent opioids—including fentanyl.^{35,37,40,41} As many as 5% of adolescents who are exposed to opioids for postoperative analgesia may be at risk for persistent opioid use.³⁹ Thus, the CPG balances the need for effective pain management with opioids, when indicated, with the potential risks of this medication class.

The CPG contains 12 key action statements (KASs). These recommendations are based on evidence from RCTs; high-quality observational studies; and expert opinion, when studies are lacking or could not feasibly or ethically be conducted. The evidence base was amassed from an extensive systematic literature review; where appropriate, this incorporates best practices from other high-quality clinical guidelines and position statements from other professional societies and government agencies. (See Methodology and the accompanying technical report.⁴²)

The subcommittee acknowledges that clinicians and health care systems have contributed—albeit often from a desire to relieve the suffering of patients in pain—to a national opioid-related addiction and overdose crisis through

excessive opioid prescribing. Further, in an overcorrection, clinicians and health care systems have subsequently withheld opioids from some individuals and left pain insufficiently treated—again, often in a genuine attempt to reduce addiction and harm. Throughout, clinicians and health systems have contributed to inequities by race, ethnicity, and other factors. It is the subcommittee’s hope that this CPG leads to optimal treatment of acute pain in children and adolescents and simultaneously helps clinicians to minimize and navigate any risk for opioid-related harms.

III. DEFINITION OF TERMS

Addiction

According to the American Society of Addiction Medicine, defined as “a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. [Addiction] is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.”⁴³ The term addiction commonly refers to a moderate or severe substance use disorder and, in the case of opioid addiction, a moderate or severe opioid use disorder (see “opioid use disorder,” below).

Fentanyl

Fentanyl is a synthetic opioid that is commonly used to treat severe pain in the hospital setting, the perioperative period, or attributable to trauma. Fentanyl is approximately 100 times more potent than morphine; hence, when used outside medical settings, small amounts can lead to severe, rapid respiratory depression and death by overdose within minutes.⁴⁴ Medical fentanyl is available by prescription and used for severe, chronic pain management. Illicitly manufactured fentanyl is a common contaminant in counterfeit prescription opioids, which mimic drugs like oxycodone or alprazolam, as well as in drugs like heroin, cocaine, and methamphetamine.

Multimodal Pain Management

The use of more than modality to treat pain. This includes but is not limited to pharmacologic medications targeting different receptors and body sites (eg, topical medications) and nonpharmacologic modalities to treat pain.

Nonmedical Opioid Use

Use of an opioid in a way not intended or prescribed. In isolation, nonmedical opioid use may not constitute a diagnosis of opioid use disorder but may meet criteria for

an opioid use disorder if other symptoms of a disorder are present (see definition below).

Opioids

A class of pain-relieving drugs that include prescription medications as well as illicit heroin. Prescribed opioids include: codeine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, tramadol, and others. Fentanyl that is widely available throughout the United States in the illicit market is, typically, not medical-grade; instead, it is illicitly manufactured (see definition above).

Opioid Dependence

A characteristic set of physiologic changes that occur following prolonged use of opioids, including tolerance and withdrawal. Physiologic dependence by itself is not an opioid use disorder. According to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, tolerance and withdrawal must be accompanied by other symptoms of a substance use disorder (ie, loss of control over use, and/or negative consequences resulting from use) to constitute a diagnosis of opioid use disorder (OUD).⁴⁵

Opioid Use Disorder

A medical condition in which someone uses opioids (either prescription opioids or illicit opioids) in a manner that becomes compulsive, involves loss of control, and continues despite negative consequences, as defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*.⁴⁵ Frequent use of opioids (eg, in the treatment of chronic pain) alone *is not* an OUD; an OUD requires loss of control surrounding use and/or negative consequences resulting from use. (For example, an individual with chronic pain who takes opioids daily for their pain and whose functioning *improves* as a result likely does not have an OUD unless they have lost control over their use or are experiencing negative consequences.)

Overdose

An overdose results from the use of an excessive amount of a drug and can result in serious injury or death. Opioids cause overdose by interrupting the body’s natural drive to breathe. Highly potent opioids such as fentanyl are more likely to cause an overdose than other opioids, particularly if an individual uses them at the same time as other sedating substances and respiratory depressants, such as alcohol or benzodiazepines.

Pain

According to the International Association for the Study of Pain, defined as “an unpleasant sensory and emotional

experience associated with, or resembling that associated with, actual or potential tissue damage.”⁴⁶ Pain is commonly defined as “acute” (lasting less than 1 month), “subacute” (lasting between 1 and 3 months), or “chronic” (lasting more than 3 months).

Pediatricians and Other Pediatric Health Care Providers

For the purpose of this CPG, pediatricians and other PHCPs refers to a qualified medical provider operating within their scope of practice and providing clinical care to children and adolescents. Examples include physicians, nurse practitioners, and physician assistants.⁴⁷

IV. METHODOLOGY

A. Subcommittee Process and Support

Before the start of the CPG process, a task force was convened to explore the need for a CPG on opioid prescription in children. In recognition of the fact that no such guidance currently existed, the task force decided to proceed with development of this CPG.

Staff from the AAP formed a CPG writing subcommittee in 2019, with membership that included 2 chairs; 2 methodologists; a variety of pediatric primary and tertiary care providers; and pediatric experts in pain medicine, emergency medicine, surgery, palliative care medicine, adolescent and addiction medicine, and implementation science. In addition, the subcommittee included a parent representative and a representative from the AAP Partnership for Policy Implementation. Members’ potential conflicts of interest were identified and considered; no conflicts prevented subcommittee members from participating in the CPG development process.

After its formation, the subcommittee defined its scope of work with input from AAP leadership (see box).

After a kickoff meeting in October 2021, the group met virtually monthly throughout the coronavirus disease 2019 pandemic. The group met in-person for a 2-day meeting in November 2022 to review the literature and develop proposed key action statements (KAS). At this meeting, the subcommittee received education on the components of a KAS and an outline of the KAS development process using BridgeWiz (a software platform designed to support and document the KAS development process).^{48,49}

For additional information on the methodology, please see the accompanying technical report.⁴²

B. Scope of the Review

The opioids guideline panel engaged 2 health librarians to assist in searches of PubMed and Embase. The search protocol was developed in the fall of 2021. The initial PubMed query was conducted in March 2022, and an additional search was conducted in June 2023 to identify more recent publications. A subsequent Embase search was completed in July 2022 to identify additional studies published outside the United States.

The literature review was designed to answer 2 overarching PICOT (population, intervention, comparison group, outcome, timeframe) questions. The PICOT framework defines which patients, interventions, comparisons, outcomes, and timeframes are of interest to identify studies for inclusion in the systematic review.⁵⁰

The first PICOT question focused on opioid prescribing to children for acute pain in the outpatient setting, compared with other pharmacologic and nonpharmacologic treatments or different opioids. The question assessed multiple outcomes, including: short-term safety, short-term efficacy and effectiveness, persistent postoperative or postprocedural pain (≥ 2 weeks later), unintentional ingestion, diversion, misuse, excess opioid medication, opioid-related overdose, and incident or recurrent OUD (within 1 year of prescription).

The second PICOT question focused on individual-, family-, or health systems-level interventions that aimed to increase outpatient or ambulatory opioid prescribing safety to children, compared with standard practice. The question’s outcomes were: excess opioids after a prescription or risk of unintentional ingestion, diversion, misuse, opioid-related overdose, or addiction.

See the technical report for detailed information on the PICOT questions, search terms and strategy, review process, and data extraction.⁴²

C. Inclusion and Exclusion Criteria

All studies were required to include children up to 18 years of age. Studies could also include young adults up to 21 years of age, if this population was stratified from older adult participants, as long as children younger than 18 years were also included in the study.

Opioids are a mainstay of medical practice and have long had a role in the management of severe acute pain. With opioid-related overdose deaths reaching unprecedented levels in recent years, patients, families, clinicians, and health systems have been concerned about when and how best to prescribe opioids. Recognizing the need for clear guidance on best approaches to treating pain and prescribing opioids, the American Academy of Pediatrics (AAP) developed this practice guideline to provide an overview of the safety, efficacy, effectiveness, and potential risks (including for unintentional ingestion, diversion, misuse, overdose, and addiction) of opioids for acute pain management. It is primarily directed at clinicians who prescribe opioids to children and adolescents younger than 21 years in outpatient settings.

Studies needed to focus on children with acute pain prescribed an opioid for use in the home setting. Studies were excluded that:

- assessed opioids that were only administered within emergency department, urgent care, or inpatient settings (eg, intranasal fentanyl);
- did not measure an outcome in the home setting;
- assessed opioids administered for management of neonatal opioid withdrawal syndrome; or
- assessed opioids administered for acute episodes of pain related to chronic medical conditions (eg, cancer, palliative care, sickle cell disease).

D. Data Synthesis and Analysis

The evidence tables based on the above PICOT questions and search were presented at the in-person meeting (November 2022). In summary, few RCTs were identified that related to the safety and efficacy of opioids in children with acute pain. Most of the RCTs addressed pain related to surgery or trauma and did not examine opioid prescriptions that originated in an office-based outpatient setting. Similarly, few studies assessed individual-, family-, or health systems-level interventions to increase safe outpatient opioid prescribing. Hence, the RCTs and systematic reviews only covered a small portion of the PICOT questions. As a

result, many of the KASs are based on expert opinion and observational studies.

The subcommittee generated a series of priority KASs at the in-person meeting. At that meeting, participants raised additional, clinically relevant questions that had not been addressed specifically in the original literature review. In response, the methodologists supplemented the original literature search with additional specification terms. The resulting studies were rescreened and rereviewed to identify new, relevant studies.⁴²

Evidence grades for each KAS were determined on the basis of the AAP grading matrix (Fig 1). When the scientific evidence is at least “good” in quality and demonstrates a preponderance of benefits over harms (or vice versa), the KAS provides a “strong recommendation” or “recommendation.” Clinicians should follow a strong recommendation unless there is a clear and compelling rationale for an alternative approach; clinicians are prudent to follow a recommendation but are advised to remain alert to new information and be sensitive to patient preferences.

Integrating evidence quality appraisal with an assessment of the anticipated balance between benefits and harms leads to a designation of a strong recommendation, recommendation, option, or no recommendation. “Option” is a “may” statement that is typically applied when there is a balance between risks and benefits of an intervention or when the evidence is weaker, but there is

Aggregate Evidence Quality	Benefit or Harm Predominates	Benefit and Harm Balanced
Level A Intervention: well designed and conducted trials, meta-analyses on applicable populations Diagnosis: independent gold standard studies of applicable populations	Strong recommendation	Weak recommendation (based on balance of benefit and harm)
Level B Trials or diagnostic studies within minor limitations; consistent findings in from multiple observational studies	Moderate recommendation	
Level C Single or few observational studies or multiple studies with inconsistent findings or major limitations	Weak recommendation (based on low quality evidence)	No recommendation may be made
Level D Expert opinion, case reports, reasoning from first principles		
Level X Exceptional situations in which validating studies cannot be performed, and there is a clear preponderance of benefit or harm	Strong recommendation Moderate recommendation	

FIGURE 1
AAP grading matrix.

still a perceived benefit (eg, the intervention is likely to help but there is lack of evidence support). Compared with “option,” with “no recommendation,” there is lack of support either for or against an intervention.

Once the evidence level was determined, an evidence grade was assigned. AAP policy stipulates that the evidence supporting each KAS be prospectively identified, appraised, and summarized and an explicit link between quality levels and the grade of recommendation be defined.

The evidence supporting the recommendations is graded from “A” to “D,” with “A” being the highest:

- Grade A: consistent level A studies;
- Grade B: consistent level B or extrapolations from level A studies;
- Grade C: level C studies or extrapolations from level B or level C studies;
- Grade D: level D evidence or troublingly inconsistent or inconclusive studies of any level; and
- Level X: not an explicit level of evidence as outlined by the Centre for Evidence-Based Medicine. This level is reserved for interventions that are unethical or impossible to test in a controlled or scientific fashion and for which the preponderance of benefit or harm is overwhelming, precluding rigorous investigation.

A level X was assigned when a KAS reflected existing regulatory body guidance or clinical guidelines (eg, Food and Drug Administration, Centers for Disease Control and Prevention [CDC]). When it was not possible to identify sufficient evidence, recommendations are based on the consensus opinion of the subcommittee members.

V. PREVALENCE OF PEDIATRIC OPIOID PRESCRIBING AND RISK FOR OVERDOSE, POISONING, AND ADDICTION

Opioid prescribing is relatively common in pediatric practice. In 2018, 8.9% of adolescents 15 to 19 years of

age had received at least 1 new prescription for opioid medication in the preceding year.⁵¹ Among children younger than 18 years, approximately 6.7% had filled an opioid prescription from a medical care provider, and 1.2% had filled an opioid prescription from a dental visit.⁵² Surgery was the most common reason a child or adolescent received an opioid prescription, with dentists and surgeons writing 61.4% of opioid prescriptions for children and adolescents younger than 21 years.⁵³

Most children, adolescents, and young adults who receive an opioid prescription do not progress to developing an OUD or experience an overdose.³⁵ One-year prevalence rates for developing an OUD following an opioid prescription in children, adolescents, and young adults range from 0.3% to 5.8%.^{35,37}

Risk factors for OUD or overdose include prescriptions for long-acting opioids, high daily doses, and prescriptions with a duration of 1 week or longer.^{35,36} Additionally, individuals with unaddressed mental health concerns (eg, depression, anxiety, trauma) or prior substance use (eg, nicotine, alcohol, cannabis) are at elevated risk for OUD, poisoning, or overdose.⁵⁴

In the years following appropriate prescription opioid use, the risk of misusing opioids is increased through early adulthood, even for adolescents who have little experience with drugs and who disapprove of illegal drug use.⁴⁰ Additionally, nonmedical prescription opioid use (ie, use of opioids in a manner not directed by a clinician) early in adolescence is associated with heroin use in later adolescence and young adulthood.^{40,41,55} Notably, young children may also be at-risk of prescription opioid poisoning when an adult caregiver receives an opioid prescription.⁵⁶

The risks of prescription opioid use in children must, however, be weighed against the clinical need for appropriate pain management. Pain is a central concern for parents; for example, when a parent learns that their child

KAS 1: <i>Pediatricians and other PHCPs should treat acute pain using a multimodal approach that includes the appropriate use of nonpharmacologic therapies, nonopioid medications, and, when needed, opioid medications. (Evidence quality: B; recommendation strength: strong recommendation.)</i>	
Aggregate Evidence Quality Grade	B
Benefits	Potential for more diverse strategies for pain control, improved patient psychological well-being from understanding both pain and its treatment, improved knowledge of pain management, and enhanced skills for pain management in future episodes.
Risks, harms, costs	Complexity in prescribing and educating. There is a risk from polypharmacy. Variable workforce ability to provide multimodal care. Lack of trust in nonpharmacologic options may delay their effective use. This distrust may result in reliance on ineffective pain control methods and/or delay in effective pain control, which may result in patients feeling not heard or not listened to if their pain is not appropriately addressed.
Benefit-harm assessment	Preponderance of benefits over harms.
Strength of recommendation	Strong recommendation.
Key references	8, 39, 62
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

KAS 2: Pediatricians and other PHCPs should NOT prescribe opioids as monotherapy for children and adolescents who have acute pain (Evidence quality: B; recommendation strength: strong recommendation).

Aggregate Evidence Quality Grade	B
Benefits	Minimization of opioid prescribing. Decreased community opioid use, adverse side effects, conversion to chronic use. Opioids, when prescribed in combination with other medications, allow lower doses and may decrease side effects of the other medications. Use of other medications in combination with opioids could potentially decrease opioid side effects.
Risks, harms, cost	Potential for decreased pain control and patient/family satisfaction. Potential for additional appointments or reevaluation.
Benefit-harm assessment	Preponderance of benefits over harms.
Strength of recommendation	Strong recommendation.
Key references	62, 66, 69
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

will undergo surgery, their most common concern is to control the child’s postoperative pain.⁵⁷ Children who undergo multiple invasive procedures are at risk for post-traumatic stress disorder⁵⁸ because pain can be a contributing factor for post-traumatic stress disorder in patients who undergo invasive procedures or surgery.⁵⁹ Injury and trauma can also precipitate severe acute pain that often requires timely, effective pain management. Thus, any clinical intervention that seeks to minimize excess opioid prescribing must be balanced by patient and/or caregiver satisfaction with pain management.⁶⁰ This approach is consistent with the World Health Organization’s Analgesic Ladder.⁶¹

VI. OPTIMIZING NONPHARMACOLOGIC APPROACHES AND NONOPIOID MEDICATIONS FOR PAIN MANAGEMENT

Opioids are an integral part of acute pain management.⁶³ Uniquely among pain medications, opioids have no apparent ceiling effect to the amount of pain they can control. Unfortunately, opioid analgesia is associated with adverse effects that include constipation, pruritus, nausea and vomiting, sedation, respiratory depression, opioid-induced hyperalgesia, opioid tolerance, opioid dependence and addiction, and death.

Because a small percentage of adolescents who are exposed to opioids for postoperative analgesia are at risk for persistent opioid use,³⁹ it is important to optimize opioid prescribing for postoperative and other acute pain conditions.⁶⁴ It is also important to maximize pain management through nonpharmacologic and nonopioid analgesics.⁶⁵

Although opioids are an important tool for acute pain relief, not all acute pain requires opioids. Recent studies and expert consensus suggest that even conditions that have traditionally been thought to require opioids—such as tonsillectomy, third molar surgery, and acute fractures—may have equally effective analgesia with fewer side effects using acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) alone.^{66–69} On the basis of these and other findings, the recently published “Guidelines

for Opioid Prescribing in Children and Adolescents After Surgery” from the American Pediatric Surgical Association highlight that opioids are not necessary following many common pediatric surgeries.⁶²

For a patient with mild-to-moderate pain, the PHCP should start nonopioid medications and treatment. These strategies should be optimized before considering an opioid. If the patient has severe pain or severe pain is anticipated, an opioid can be started at the same time as nonopioid analgesics. The use of opioids should be reassessed regularly and weaned as tolerated.

Children and adolescents with physical, developmental, or intellectual disabilities may express their pain differently from individuals without disabilities and may also be unable to fully verbally communicate their pain experience. PHCPs should take time to carefully assess pain in this population.²⁸ Family members and others who know the child or adolescent well (including other clinicians) can provide additional information to guide pain management. Behavioral pain assessment scales (which commonly incorporate parent and caregiver input) are available to PHCPs and have been validated in individuals with neurocognitive impairment. These are provided in a separate AAP clinical report, “Pain Assessment and Treatment in Children With Significant Impairment of the Central Nervous System.”²⁸

The optimal approach starts with educating patients and their families on nonpharmacologic strategies. It is important that this education describes realistic expectations for patients and their families; this includes not promising the absence of pain but, rather, the goal of keeping pain at a tolerable level. PHCPs should carefully counsel patients and families that some pain may persist even despite effective treatment; this approach can help set patients’ and families’ expectations and help alleviate stress and anxiety, which can, in turn, worsen pain.

Nonpharmacologic analgesic strategies include but are not limited to ice or heat; massage; transcutaneous electrical nerve stimulation; keeping the injured area above heart level to minimize swelling; music therapy; cognitive

behavioral therapy; acupuncture; age-appropriate relaxation or distraction strategies; and complementary therapies, such as reiki, therapeutic touch, and aromatherapy.⁷⁰

Key among nonopioid analgesics are acetaminophen and NSAIDs. Unless there is a specific contraindication to their use (eg, allergy), acetaminophen and NSAIDs should be the primary pharmacologic strategy for the expected duration of healing and can be used around the clock, if needed, when treating acute pain—depending on the severity of pain or clinical situation.⁸

Topical agents (eg, lidocaine, capsaicin, acetaminophen) can also be helpful nonopioid analgesics for certain types of pain. For select patients, regional analgesia may provide opioid sparing analgesia in the postoperative period for acute pain. Patients who have accompanying neuropathic pain may benefit from gabapentinoids and/or antidepressants; those with muscle spasm may benefit from muscle relaxants.

Chronic medical conditions, such as sickle cell disease or cancer—which come with frequent or recurrent episodes of acute pain—should, ideally, be managed by the pediatrician in consultation with a pain management specialist.

When treating pain, PHCPs should carefully consider that data show that Black, Hispanic, and AI/AN individuals are less likely than white individuals to receive timely and effective pain management (including with opioids), even after accounting for the level of pain across a range of pain conditions—many of which result in severe acute pain.^{21–25} Children, adolescents, and families whose primary language is not English may also have difficulties communicating pain to their PHCP. There are likely other disparities in pain treatment by socioeconomic status because multimodal pain treatment often requires the input of an interdisciplinary team that may not be available to individuals who lack health insurance or who cannot afford to pay out-of-pocket for uncovered services. Additionally, geographic disparities likely exist because such

interdisciplinary care may not be available in rural areas.²²

Given that untreated pain is associated with physical impairment and psychological distress, these numerous disparities have critical implications for the child or adolescent’s recovery and functioning. Opioid overuse, as discussed earlier in this CPG, can also potentially contribute to harm, but PHCPs should, regardless, be aware that longstanding, historic disparities in pain treatment exist and are unjust and should work within their health systems to develop pain treatment protocols that ensure equitable pain treatment (see “I. Barriers and Recommendations for Implementation of the CPG’s Recommendations,” which discussed health-system implementation approaches).

Opioids should be reserved for patients who are experiencing moderate-to-severe pain despite the use of the strategies described above.⁸ There are multiple pain scales that can be used to assess pain in children. These include scales for nonverbal children, children of different ages and developmental stages, and children with developmental and intellectual disabilities.⁷¹

To minimize risk to patients and society, opioids should not be used alone for analgesia. There is evidence for equal analgesia with NSAIDs alone for some injuries and procedures (eg, inguinal hernia repair, tonsillectomy, third molar extraction, among other procedures^{62,69}) and equal or superior analgesia—with fewer opioid side effects—with combination therapies of acetaminophen, NSAIDs, and opioids after more painful procedures.⁶⁶ As a result, opioid monotherapy is virtually never appropriate in pediatric care.

VII. SAFE, APPROPRIATE OPIOID PRESCRIBING

Observational studies have shown that many opioid prescriptions are dispensed in patients and contexts associated with elevated risk of overdose. Chua et al assessed prescription claims from a national, commercial insurance

KAS 3: <i>When prescribing opioids for acute pain in children and adolescents, PHCPs should provide immediate-release opioid formulations, start with the lowest age- and weight-appropriate doses, and provide an initial supply of 5 days or fewer, unless the pain is related to trauma or surgery with an expected duration of pain of more than 5 days (Evidence quality: C; recommendation strength: recommendation).</i>	
Aggregate Evidence Quality Grade	C
Benefits	Minimizing amount of surplus opioids in the community. Consistency of guidance in prescribing (equity). Addresses the need for reevaluation and refills and conditions for which long-term use will be needed. Motivates communication. Immediate formulations have lower potential side effects, and lower potential to misuse.
Risks, harms, cost	Risk of inadequate pain management. Potential increased need for frequent refills and/or reevaluations. There is a need for accurate weight for prescribing, and accurate weight may not be available in all settings.
Benefit-harm assessment	Preponderance of benefits over harms.
Strength of recommendation	Recommendation.
Key references	53, 72, 73
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

database and found that 46% of roughly 4 million pediatric opioid prescriptions were high risk because of duration longer than 3 or 7 days, prescription of codeine or tramadol, prescription above ≥ 50 morphine milligram equivalents per day, or a prescription overlapping with benzodiazepine use.⁵³

Additionally, not all opioid prescriptions are needed or fully used. Studies of children and adults who undergo surgery show that many patients do not use all of their prescribed opioids and that prescribing a smaller quantity of opioids postoperatively is associated with reduced opioid use without increased pain scores or refill requests.⁷³⁻⁸⁴ Observational data highlight that factors associated with postoperative use of opioids (which, in some cases, may be clinically warranted) among adolescents may include older age, surgery type (in particular, posterior spinal fusion), and higher patient-reported pain at discharge.⁷⁶

KAS 3 provides best practices for how to prescribe opioids when needed. PHCPs who prescribe opioids to children should offer opioid treatment of pain control when:

- “severe pain” exists (often defined as pain scores of 7–10);
- severe pain is expected to occur and is not expected to respond adequately to nonpharmacologic and non-opioid pain control alone;
- opioids are expected to be an effective method for pain control; and
- the source of pain is known.

Observational studies suggest that the risk of OUD, poisoning, and overdose is minimized when opioids are prescribed at the lowest effective dose for age and weight, and for the shortest duration needed to control pain.^{35,37,39,54}

Opioid doses are typically weight based for children and adolescents < 50 kg (eg, for oxycodone, 0.1 to 0.2 mg/kg

per dose every 4 to 6 hours) and given in fixed doses for those ≥ 50 kg (eg, for oxycodone, 5 to 10 mg every 4 to 6 hours).⁸⁵ For children and adolescents who are obese, PHCPs may consider consulting with a pharmacist to determine the appropriate dose because hydrophilic opioids (eg, oxycodone, morphine) should initially be dosed based on ideal body weight, whereas lipophilic opioids (eg, methadone) should initially be dosed based on total body weight.

In many states, laws limit the maximum number of days an initial opioid prescription can be dispensed (eg, 3, 5, or 7 days). Typically, a duration of 5 days or fewer is sufficient for many types of acute pain; if refills are needed to provide coverage for a longer duration of pain treatment, PHCPs can discuss this with families during follow-up. PHCPs might consider longer durations for some types of pain (eg, following surgeries known to be associated with prolonged pain), but these are likely to be relatively uncommon in general outpatient pediatric practices. Additionally, PHCPs should avoid treating acute pain with long-acting opioid formulations; instead, they should use immediate-release formulations, which are associated with a lower risk of OUD and overdose.^{35,36}

A recent analysis of commercial health insurance administrative claims found that mandated use of PDMPs at the state level was associated with a reduction in opioid prescriptions to adolescents and young adults as well as decreased opioid-related overdoses.⁸⁶ If a PHCP notes concerning findings within the prescription drug monitoring program, they should initiate a conversation with the patient and family rather than immediately making a determination not to prescribe opioids. For example, a patient who has filled opioid prescriptions at multiple different pharmacies may have done so because opioid supplies ran low or may have multiple prescribers if their access to care has been inconsistent or changed because of insurance.

KAS 4.1: <i>When treating acute pain in children and adolescents younger than 12 years, pediatricians and other PHCPs should NOT prescribe codeine or tramadol (Evidence quality: X; recommendation strength: strong recommendation).</i>	
Aggregate Evidence Quality Grade	X
Benefits	Avoiding inadequate pain control, respiratory depression, and death attributable to genetically variable codeine metabolism. Alignment of health care with federal guidelines.
Risks, harms, costs	Inadequate pain control, increased cost (given low cost of codeine), lack of provider familiarity with alternative pain medications, more difficult to prescribe medications that are scheduled differently from codeine.
Benefit-harm assessment	Preponderance of benefits over harms.
Role of patient and parent preferences	For patients who had been previously managed well with limited side effects or have no access to other medications, the guideline group considered that tramadol or codeine may need to be used, but this need should be diminishing in frequency over time.
Strength of recommendation	Strong recommendation
Key references	90 – 94
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

KAS 4.2: <i>When treating acute pain in adolescents 12 to 18 years of age who have obesity, obstructive sleep apnea, or severe lung disease, pediatricians and other PHCPs should NOT prescribe codeine or tramadol (Evidence quality: X; recommendation strength: Strong recommendation).</i>	
Aggregate Evidence Quality Grade	X
Benefits	Avoiding inadequate pain control, respiratory depression, and death attributable to genetically variable codeine metabolism. Codeine may have inadequate pain control for some patients (eg, depending on codeine metabolism). Alignment of health care with federal guidelines.
Risks, harms, costs	Inadequate pain control, increased cost (given low cost of codeine), lack of provider familiarity with alternative pain medications, more difficult to prescribe medications that are scheduled differently from codeine.
Benefit-harm assessment	Preponderance of benefits over harms.
Role of patient and parent preferences	For patients who had been previously managed well with limited side effects or have no access to other medications, the guideline group considered that tramadol or codeine may need to be used, but this need should be diminishing in frequency over time.
Strength of recommendation	Strong recommendation.
Key references	90, 93, 95
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

As with any medication, PHCPs should counsel parents on the potential adverse effects of opioids, including constipation; pruritis; nausea and vomiting; sedation; respiratory suppression; and/or the possibility of tolerance, dependence, addiction, or death. Voepel-Lewis et al showed that parents who were given such risk information improved their decisions to appropriately hold pain medications if adverse effects occurred, without any detriment to pain management.⁷²

In addition, the subcommittee recommends that all patients and caregivers of patients with pain or expected pain be provided with written educational and instructional materials on nonpharmacologic therapies and nonopioid and opioid medications. Evidence indicates that providing these materials improves pain control and reduces opioid prescribing.^{60,87-89} Educating patients and families on multimodal, nonpharmacologic approaches to pain control, risks of opioid use, and existing data surrounding pain duration and severity can facilitate shared decision-making and temper expectations if patients and families specifically request opioid prescriptions to manage and treat pain.

On April 20, 2017, the US Food and Drug Administration (FDA) assigned its strongest warning, a contraindication,

restricting the use of codeine and tramadol medicines in children younger than 12 years.⁹⁰ The contraindication includes the use of either codeine or tramadol to treat pain, including pain occurring after surgery, such as tonsillectomy or adenoidectomy.⁹¹⁻⁹³ Single-ingredient codeine medications and all tramadol-containing products are FDA approved *only* for use in adults. With respect to children 12 to 18 years of age, given the extensive FDA warnings and contraindications against codeine and tramadol, it may be easiest for PHCPs to generally avoid these medications in those younger than 18 years.

Unfortunately, even after this contraindication was issued, codeine and tramadol prescriptions have remained common.⁵³ This continued prescribing may stem from PHCPs' belief that, because these opioids are lower potency than others (eg, oxycodone, hydrocodone, morphine), they are safer and less likely to contribute to addiction or overdose. Contraindication was based on the medications' serious risks, however, including slowed or difficult breathing and death; these risks are greatest in children younger than 12 years. Adverse event reports submitted to the FDA Adverse Event Reporting System include deaths in children younger than 18 years even

KAS 4.3: <i>When treating postsurgical pain after tonsillectomy or adenoidectomy in children and adolescents younger than 18 years, pediatricians and other PHCPs should NOT prescribe codeine or tramadol (Evidence quality: X; recommendation strength: Strong recommendation).</i>	
Aggregate Evidence Quality Grade	X
Benefits	Avoiding death and respiratory depression. Codeine may have inadequate pain control for some patients (eg, depending on codeine metabolism). Alignment of health care with federal guidelines.
Risks, harms, costs	Lack of provider familiarity with alternative pain medications, more difficult to prescribe medications that are scheduled differently from codeine, medications may be more difficult to access at a pharmacy.
Benefit-harm assessment	Preponderance of benefits over harms.
Strength of recommendation	Strong recommendation.
Key references	90, 91, 96, 97
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

KAS 4.4: <i>When treating acute pain in people of any age who are breastfeeding, pediatricians and other PHCPs should NOT prescribe codeine or tramadol (Evidence quality: X; recommendation strength: Strong recommendation).</i>	
Aggregate Evidence Quality Grade	X
Benefits	Eliminating the potential for codeine and tramadol to be transmitted through human milk.
Risks, harms, costs	Inadequate pain control. For patients requiring an opioid, they would require a stronger opioid. Lack of provider familiarity with alternative pain medications, more difficult to prescribe medications that are scheduled differently from codeine.
Benefit-harm assessment	Preponderance of benefits over harms.
Strength of recommendation	Strong recommendation.
Key references	90, 104, 105
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

after a single dose of these medications.⁹⁰ In a 2015 randomized control trial, Friedrichsdorf et al demonstrated that, among children 4 to 15 years of age undergoing tonsillectomy, oversedation was common with codeine regimens, and itching was common among tramadol regimens.⁹⁴

Building on the FDA contraindication noted above, an FDA warning was added to drug labels of codeine and tramadol in 2018. (Codeine is an opioid and prodrug that is used to treat mild to moderate pain in adults; tramadol is an opioid with serotonin and norepinephrine reuptake inhibitor activity that is used to treat moderate to severe pain in adults.) The FDA warning recommends against their use in adolescents between 12 and 18 years of age with obesity or who are at risk for breathing issues, such as those with obstructive sleep apnea or underlying severe lung disease.⁹⁰ Cytochrome P450 isoenzyme 2D6 (CYP2D6) genotype plays a role in adverse events, as ultra-rapid metabolizers of substrates of CYP2D6 convert codeine in the individual's body too quickly into potentially dangerously high levels of morphine (the active form of codeine), which contributes to life-threatening or fatal respiratory depression.^{93,95}

As noted above, the FDA contraindicates the use of codeine or tramadol to treat pain after a child has a tonsillectomy or adenoidectomy.⁹⁰⁻⁹² Between 1969 and 2016, there were 9 reported cases of respiratory depression

related to tramadol use, including 3 fatalities.⁹⁰ The American Academy of Otolaryngology–Head and Neck Surgery also recommends against tramadol following these procedures.⁹⁷

In the United States each year, nearly 300 000 cases of tonsillectomy and adenoidectomy are performed in children younger than 15 years.⁹⁸ Pain is the leading cause of morbidity following these procedures. This pain can lead to decreased oral intake and dehydration and, potentially, bleeding complications from dry mucous membranes.

Several studies have demonstrated that nonopioid medications provide safe and effective analgesia for patients undergoing tonsillectomy or adenoidectomy.^{91,96} Liu and Ulualp reviewed records for more than 500 children younger than 18 years who received alternating doses of acetaminophen and ibuprofen post-tonsillectomy.⁹⁹ They found that this regimen was associated with effective pain control in most children and was not associated with increased bleeding rates.¹⁰⁰

Other clinical trial data suggest, however, that bleeding may be slightly increased with administration of NSAIDs in the post-tonsillectomy setting; thus, acetaminophen may be the preferred first-line medication in some clinical settings.¹⁰¹ Nonpharmacologic pain management strategies can also be employed, such as distraction, acupuncture, and cold or heat application.^{102,103} When opioids are needed for severe pain following tonsillectomy or adenoidectomy not fully

KAS 5: <i>When treating acute pain in children or adolescents who are taking sedating medications, such as benzodiazepines, pediatricians and other PHCPs should use caution when prescribing opioids (Evidence quality: X; recommendation strength: Strong recommendation).</i>	
Aggregate Evidence Quality Grade	X
Benefits	Prevention of avoidable respiratory depression; decreased risk of death; avoidance of oversedation.
Risks, harms, cost	Potential for increased pain, decreased sleep quality and quantity, impact on mental health.
Benefit-harm assessment	Preponderance of benefits over harms.
Intentional vagueness	There are other medications that interact with opioids; this list is not intended to be inclusive but, rather, to highlight medications with severe potential for adverse events.
Strength of recommendation	Strong recommendation.
Key references	19, 36, 113, 114
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

KAS 6: <i>When prescribing opioids, pediatricians and other PHCPs should provide naloxone and counsel patients and families on the signs of opioid overdose and on how to respond to an overdose (Evidence quality: X; recommendation strength: Recommendation).</i>	
Aggregate Evidence Quality Grade	X
Benefits	Potential to destigmatize opioid use. A universal recommendation may decrease disparities for patients who get opioid prescription on availability. Increased potential for patients to stay alive and to reverse an overdose. Comfort using medication given the option to reverse; increased reversal agents in the community.
Risks, harms, cost	Costs of medication. Inconvenience of prescribing and/or obtaining naloxone. Potential for precipitation of pain crisis or withdrawal, increased fear of opioids. Potential community shortage of naloxone.
Benefit-harm assessment	Preponderance of benefits over harms.
Strength of recommendation	Recommendation.
Key references	19, 121 – 124
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

responsive to nonopioid medications (or if medication allergies preclude the use of acetaminophen or NSAIDs), pediatricians and other PHCPs should consider opioids other than codeine or tramadol, including, for example, oxycodone or hydrocodone.

Active metabolites of both codeine and tramadol can be found in human milk.^{106–108} Numerous cases of excessive sleepiness and breathing issues have been documented among breastfed infants who are exposed to these medications through human milk.¹⁰⁹ For this reason, the FDA issued a warning that breastfeeding is not recommended when taking codeine or tramadol.⁹⁰ The risks of central nervous system depression to the breastfeeding parent and the breastfed infant have been acknowledged by the American College of Obstetricians and Gynecologists and in AAP recommendations for managing neonatal opioid withdrawal syndrome.^{105,110,111} Some have called into question the need to avoid codeine during breastfeeding, but given current FDA recommendations, this CPG also recommends that breastfeeding people should avoid codeine.¹¹²

VIII. MINIMIZING RISK FOR POISONING AND OVERDOSE

Along with the risks of medication error or adverse effects of opioids, there is notable risk for poisoning and overdose through unintentional or intentional ingestion; this risk exists when a child or adolescent is prescribed an opioid, as well as when a household contact is prescribed one.^{10,115–118} PHCPs who prescribe opioids should, therefore, incorporate strategies to reduce this risk. Additionally, PHCPs should be aware

that poisonings and overdoses disproportionately impact Hispanic and AI/AN individuals and should work with their health systems to ensure equitable provision of these strategies. This section focuses on key prevention strategies, including necessary considerations to minimize the risk for opioid poisoning and/or overdose for children and their families.

As noted, there is an increased risk of opioid overdose when adolescents and adults are coprescribed opioids and benzodiazepines or other sedating and/or respiratory depressant medications.^{36,119,120} Concomitant use of opioids and sedating medications can lead to significant sedation, respiratory depression, and death. This danger drove the FDA to add a boxed warning to the drug labeling of opioids and benzodiazepines in 2016, alerting clinicians to the danger of coprescribing these medication classes.¹¹⁴ Further, in 2022, the CDC recommended that clinicians who care for adults should use caution when coprescribing opioids and benzodiazepines.¹⁹

In rare pediatric cases, concomitant prescribing may be appropriate. Clinicians should, however, exercise caution and also coprescribe naloxone when coprescribing opioids and sedating medications to children and adolescents. Notably, the FDA has clarified that individuals (including adolescents) who have an OUD and may need buprenorphine or methadone (opioid agonists that are used in the treatment of OUD) should, nonetheless, receive these medications even if they are already receiving benzodiazepines but that care should be used when coprescribing these medications.¹¹⁴

Recognizing Opioid Overdose

Opioid overdose is life threatening and requires immediate emergency attention. Recognizing the signs of opioid overdose is essential to saving lives.

Call 911 immediately—and if available, provide naloxone—if a person exhibits ANY of the following symptoms:

- Their face is extremely pale and/or feels clammy to the touch.
- Their body goes limp.
- Their fingernails or lips have a purple or blue color.
- They start vomiting or making gurgling noises.
- They cannot be awakened or are unable to speak.
- Their breathing or heartbeat slows or stops.

KAS 7: <i>When prescribing opioids, pediatricians and other PHCPs should educate caregivers about safe storage and directly observed administration of medications to children and adolescents (Evidence quality: D; recommendation strength: Option).</i>	
Aggregate Evidence Quality Grade	D
Benefits	Education may lead to safer storage; reduced risks of unintentional ingestion, misuse, overdose, and diversion. Appropriate dosing and monitoring of medications may allow for detection of diversion.
Risks, harms, cost	Patients may worry about having the medication in their homes. Safe storage options may be unavailable and/or cost prohibitive, generating financial considerations and tradeoffs.
Benefit-harm assessment	Preponderance of benefits.
Strength of recommendation	Option
Key references	135 – 138
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

Naloxone is an opioid antagonist that is highly effective at reversing opioid overdoses. In pharmacies and community settings, naloxone is most commonly available as a 4-mg nasal spray, a dose that is typically large enough to reverse an opioid-related overdose, including overdose attributable to illicit fentanyl.^{125,126} It should be noted that this dose and formulation is different from that commonly used in hospital settings.

Despite its lifesaving benefits and safety profile, naloxone remains underprescribed.¹²⁷ In 2020, the FDA recommended that health care professionals who prescribe opioids should discuss naloxone with all patients receiving such a prescription.¹²¹ The FDA further recommended that health care professionals consider prescribing naloxone to patients who are at risk for opioid overdose (eg, patients with a history of opioid overdose or substance use disorder; those taking benzodiazepines or other sedating medications) and patients who live with others who are at risk for poisoning or overdose, including children. The 2022 CDC guidelines for prescribing opioids to adults also recommended that providers offer naloxone when prescribing opioids and educate patients on overdose prevention and naloxone use.¹⁹

In line with FDA and CDC guidance, the subcommittee recommends that naloxone be provided to children who are prescribed opioids. PHCPs who are unfamiliar with

naloxone can receive training to expand their understanding; the CDC provides such training resources.¹²⁸ The AAP's HealthyChildren.org site also has useful resources to which providers can refer parents.¹²⁹

As discussed earlier in this CPG, PHCPs should counsel patients and caregivers about the benefits and potential adverse effects of opioids when prescribing to children and adolescents. Such interventions may improve caregiver knowledge and safe opioid administration.¹²² In addition, it is essential that PHCPs counsel children, adolescents, and their families on the signs of an opioid overdose (see Box¹²³) and instruct families on how to respond to an opioid overdose, including calling for emergency services and administering naloxone.^{124,130–133}

Some families may encounter challenges in obtaining naloxone because of cost. Therefore, clinicians should work to ensure that families can obtain naloxone, including by prescription or through a state standing order, by direct provision to the patient, or from community health resources. To increase access to naloxone, the FDA approved the nasal spray formulation for over-the-counter (OTC) availability in 2023.¹³⁴ Beginning in August 2023, it has increasingly become available in community pharmacies for OTC purchase. However, the cost is \$45 for a kit with 2 nasal sprays, which may be prohibitive for many families; thus, PHCPs should continue to help

KAS 8: <i>When prescribing opioids, pediatricians and other PHCPs should educate caregivers about safe disposal of unused medications, help caregivers develop a plan to safely dispose of unused medications, and, if possible, offer safe disposal in their practice setting (Evidence quality: A; recommendation strength: Strong recommendation).</i>	
Aggregate Evidence Quality Grade	A
Benefits	Education may lead to safer disposal. It may result in a reduced risk of unintentional ingestion, misuse, overdose, and diversion; as well as reduce community opioid availability and future inappropriate use.
Risks, harms, cost	Premature disposal of medications; potential environmental impact; cost of disposal or disposal programs. Patients may be reluctant to agree to return medications; there may be inconvenience and stigma of using a disposal program.
Benefit-harm assessment	Preponderance of benefits over harms.
Strength of recommendation	Strong recommendation.
Key references	142 – 147
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

families obtain naloxone with little or no out-of-pocket cost (eg, through a prescription covered by insurance with little or no copay or through free distribution in the community).

Although prescription opioids are commonly found in homes where children live, they are often improperly stored.^{137,139} Additionally, adolescents who are prescribed opioids often report that they have unsupervised access to these medications.¹⁴⁰ Safe medication storage is an important strategy to prevent poisonings in children; it is especially critical for opioids, which can be life threatening if young children ingest them, even in small amounts. Additionally, safe storage may prevent adolescents from diverting and engaging in nonmedical use of opioids. Caregivers should be educated on storage of opioids in a secure (ie, locked) location that is inaccessible to children and adolescents.

National efforts, such as the CDC's Up and Away campaign, emphasize the importance of safe medication storage and provide resources for families.¹³⁵ Safe storage education¹³⁸ and the provision of medication lock boxes have demonstrated improvement in reported caregiver medication storage practices.^{136,141} PHCPs should counsel caregivers on these strategies. They should also recommend that caregivers directly observe the administration of opioids to children and adolescents to ensure that medications are taken as prescribed¹⁰ because doing so may prevent unintentional poisoning, diversion, and nonmedical opioid use.

Data highlight that adolescents who engage in nonmedical prescription opioid use (ie, use of an opioid medication in a manner not recommended by a PHCP) most commonly obtained leftover opioids from their own prescription or that of a family member or friend.¹⁴⁸ Up to 78% of parents and caregivers do not report safe disposal of their child's opioid prescription.¹⁴³ Pairing opioid disposal education with safe disposal methods increases the likelihood that a parent or caregiver will dispose of their children's leftover opioids promptly after use and decreases planned retention of unused opioids.^{149,150}

PHCPs should not only educate families about the need for safe disposal but also recommend ways to safely dispose of unused opioids.¹⁴⁷ Additionally, health care facilities and pharmacies are encouraged to leverage on-site resources and infrastructure to facilitate safe disposal in the same location where families receive an opioid prescription.

The FDA now requires opioid manufacturers to make available prepaid return-mail envelopes at outpatient pharmacies so patients can send back unused medication with no charge.¹⁵¹ Prescription opioids can also be safely disposed of via a Drug Enforcement Administration-registered receptacle,¹⁵² takeback events,¹⁴⁴ mail-in programs,¹⁴² or through the use of an envelope containing drug-deactivating chemicals.^{145,146} The FDA recommends take-back programs as being the preferred method for disposal, followed by flushing.¹⁵³ The FDA maintains a list of medications that can be flushed down the toilet; many commonly used prescription opioids are on this list.¹⁵⁴ However, given the potential impact of this practice on the environment and water supplies, flushing medications should only be used when take-back or other disposal options are unavailable.

IX. MANAGING ACUTE PAIN IN INDIVIDUALS WITH PREEXISTING CHRONIC PAIN AND/OR ON LONG-TERM OPIOID THERAPY

Chronic pain is common in children and adolescents.^{155,161,162} Frequent headaches occur in up to 15% of adolescents, and functional abdominal pain occurs in 13.5% of children and adolescents.¹⁵⁵ Low back pain and widespread muscular pain are also common in adolescents, as are other conditions that may be marked by chronic pain, such as occurs with endometriosis.¹⁵⁵ Some chronic conditions that PHCPs commonly encounter (eg, headache, migraine, abdominal pain) should generally not be treated with opioids; in these cases, opioid treatment might mask a more serious underlying diagnosis, and non-opioid medications are often more effective at providing symptomatic relief. Hence, in general, these pain syndromes should not be treated with opioids.

KAS 9: *When treating acute, worsened pain in children and adolescents with preexisting chronic pain, pediatricians and other PHCPs should prescribe opioids when indicated and partner with any other opioid-prescribing clinicians involved in the patient's care and with specialists in chronic pain, palliative care, and/or other opioid stewardship programs to determine an appropriate treatment plan (Evidence quality: D; recommendation strength: Option).*

Aggregate Evidence Quality Grade	D
Benefits	Improved pain management, mental health outcomes, trust in health system. Reduced stigma, avoidance of biases, promotion of collaboration in pain management.
Risks, harms, cost	Risk of overtreatment, oversedation, and overprescribing. Potential for misprescribing or incorrect prescribing.
Benefit-harm assessment	Preponderance of benefits over harms.
Strength of recommendation	Option
Key references	31, 155 – 160
For details on the derivation of the recommendation strength, see Methodology, Data Synthesis and Analysis, above.	

Nonetheless, some patients with chronic pain from these conditions may already be prescribed opioids that they are using daily or near-daily to control their pain. Other pediatric patients may receive frequent opioid prescriptions for the management of pain from chronic diseases, such as sickle cell disease, osteogenesis imperfecta, or epidermolysis bullosa, or in relation to a physical disability associated with pain.

Some of these children and adolescents may need surgery (either related or unrelated to their underlying condition), experience trauma, or have worsened acute pain during their treatment of chronic pain. As a result, some patients who are already on opioids may require additional support for severe, worsened pain. It is often more difficult to provide this group of patients with adequate analgesia compared with those without preexisting chronic pain. Not only are children and adolescents with chronic pain more likely to require higher doses of opioids to manage acutely worsened pain, but they also may have central sensitization to pain and nociception that make them likely to experience increased pain from surgery or trauma. Individuals with developmental or intellectual disabilities may be unable to fully verbally communicate their pain.²⁸

In each of these cases, PHCPs should manage pain in close coordination with family members, caregivers, and other clinicians who know the child or adolescent well and can provide further information on the extent of pain the child or adolescent is likely experiencing.

It is important to maintain these patients' baseline opioid dosing and add additional opioids that are appropriate to the degree of injury. Hence, when treating children and adolescents with chronic pain and who are on long-term, stable treatment with opioids, PHCPs should *not* discontinue or rapidly taper opioids.^{163,164}

Difficulties in providing adequate analgesia occur whether the patient is already on opioid analgesia.¹⁵⁶ As noted above, patients with chronic pain may require more analgesics, whether they are already taking opioids. They may also need to use them for a longer period of time than would be expected for patients without chronic pain.

For patients who have already been prescribed opioids, it is important that PHCPs contact the prescribing clinician so that they are aware of the need for additional use and any needed prescriptions. In some cases, individuals prescribed long-term opioids may have an "agreement" that prevents them from seeking opioids from other providers, thus making clear communication with their primary opioid provider critical to ensure that children and adolescents are not unfairly punished for seeking acute pain management from a different clinician.

In the perioperative context, patients should also continue taking any nonopioid analgesics (eg, antidepressants, antiepileptic medications used for pain management). If this is not possible (such as when, for example, the patient

is *nil per os*), substitution of an intravenous form or a similarly acting medication should be made when needed. N-methyl-D-aspartate antagonists (such as ketamine) and mixed opioid agonist or N-methyl-D-aspartate antagonists (such as methadone) may improve the effectiveness of opioids in perioperative pain management by minimizing or reversing opioid tolerance.¹⁶⁰

Regional analgesia, if possible, can be a powerful technique to provide profound analgesia for chronic pain patients. When no regional block is available, intravenous lidocaine and cyclooxygenase inhibitors (such as acetaminophen, ibuprofen, or ketorolac) may be useful in improving analgesia. Finally, nonpharmacologic pain management can also provide additional analgesia. Although such interventions are often not the province of many outpatient PHCPs, PHCPs are often called on to provide recommendations for pain management and can recommend that specialists consider these options.

One specific instance potentially requiring daily opioid agonists is in the care of adolescents with an OUD who receive buprenorphine or methadone.¹⁶⁵ In general, it is important to discuss pain management goals when working with a patient with OUD. Although, as discussed earlier in this CPG, opioids are not needed for most common procedures and injuries, some patients with an OUD may nonetheless require opioids. Patients on buprenorphine may be able to use increased doses to manage their pain. Alternatively, individuals on buprenorphine or methadone can receive short-acting opioid medications that are administered in addition to their medications for OUD.¹⁶⁶

Patients with OUD who are on oral naltrexone (an opioid antagonist) who may need opioids postoperatively should discontinue the medication 48 to 72 hours before planned surgery; patients on long-acting injectable naltrexone may consider switching to the oral formulation at least 1 month before surgery and then discontinue the medication 48 to 72 hours before planned surgery.¹⁶⁷ Some individuals with OUD may wish to avoid opioids entirely.¹⁵⁷

Regardless, close collaboration of PHCPs with addiction treatment providers can be critical to developing an ideal pain management plan. Throughout, the goal should be to support ongoing OUD treatment and recovery, while also ensuring appropriate pain control (including the use of opioids, after a careful consideration with patients and families about the relative benefits and risks).

In summary, patients who have been on long-term opioids deserve special consideration. In some cases, their care may be complex enough that it is appropriate for PHCPs to consult with a pediatric pain medicine specialist.¹⁵⁶ Throughout, when treating children and adolescents with chronic pain and on long-term, stable treatment with opioids, pediatricians and other PHCPs should *not* discontinue or rapidly taper opioids. It is critical that PHCPs

distinguish between frequent prescription opioid use, which for many individuals with chronic pain involves controlled, stable opioid doses and results in improved function, and an opioid use disorder, which is defined by loss of control surrounding opioid use and worsened daily functioning.⁴⁵ Where they exist, opioid stewardship programs with collaboration with pharmacists and other health care providers can also help with challenges and barriers. Discontinuation and tapers of individuals on stable, long-term opioid doses are associated with adverse outcomes, including untreated pain, worsened mental health, suicide, and reliance on illicit opioids for pain management (eg, illicitly manufactured fentanyl, heroin).^{31,32,110,158,159,168}

X. BARRIERS AND RECOMMENDATIONS FOR IMPLEMENTATION OF THE CPG'S RECOMMENDATIONS

Successfully and sustainably implementing this CPG into practice requires careful consideration of barriers and facilitators. Common barriers to implementation at the practice- and provider-levels include insufficient training, time, and resources; resistance to change; and implicit bias. Evidence indicates that clinical decision support (CDS) can be delivered through electronic health record (EHR) systems to overcome some of the barriers related to knowledge, time, and resources. EHR systems designed to automate opioid prescriptions have been successfully used to improve opioid prescribing practices by automating age- and weight-appropriate dosing and setting a default number of doses and/or days in the prescription based on the specific clinical scenario.^{88,169}

Additionally, CDS can ensure the appropriate use of opioid and nonopioid medications, as well as encourage the coprescription of naloxone.¹⁷⁰ CDS can be leveraged to prevent nonrecommended practices, such as codeine and tramadol prescribing; routine prescribing of opioids with benzodiazepines; and discontinuation of opioids in patients who are on long-term opioid treatment of chronic pain.

It is important to emphasize that well-designed EHR systems may not be able to overcome the well-documented disparities in opioid prescribing and dosing that are related to implicit bias.^{25,26} The subcommittee strongly recommends that practices and providers monitor opioid metrics by health equity measures, such as race and ethnicity, preferred language, and insurance status. Practices and providers should intervene when disparities are identified. Implicit bias training and engagement of communities experiencing disparities are key improvement strategies.¹⁷¹

There is a lack of RCTs comparing the efficacy of opioids to nonopioids in managing pain outside of the orthopedic and postoperative tonsillectomy populations. For this reason, it is important that implementation strategies consider local setting- and condition-specific

pathways, provider feedback, and monitoring and reporting of balancing measures to providers and caregivers.

Local pathways can include setting- and condition-specific guidance on when to prescribe opioids, which specific opioids and formulations to prescribe, how much to prescribe, which nonopioid medications to prescribe, and what nonpharmacologic therapies to recommend. Provider and institutional comparative feedback has been successfully used to reduce opioid prescribing.^{60,88,172,173} Balancing measures—such as phone calls, refills, emergency department return visits, readmissions, and pain control at home—should be monitored and reported.^{60,87,88,169,170,174}

The subcommittee recommends that all patients and caregivers of patients with pain or expected pain be provided with educational and instructional materials on nonpharmacologic therapies and nonopioid and opioid medications. Evidence indicates that providing these materials improves pain control and reduces opioid prescribing.^{60,87-89}

Brief scenario-tailored education has, however, been shown to be more effective than routine education in improving the safe disposal of opioids and caregiver recognition and response to excess sedation.^{122,149,150} Additionally, direct provision of disposal bags has been shown to be superior to education in improving the safe disposal of opioid medications.^{147,149} Finally, policy-level facilitators can support the successful implementation of this CPG into practice. At the local and state levels, policy makers can promote the provision of safe disposal locations and boxes. At the federal level, the recent FDA approval of naloxone nasal spray for OTC, nonprescription may improve the accessibility of this medication; education by providers regarding its use and recommendations that families obtain it will still be essential, however.^{134,175}

XI. EVIDENCE GAPS AND FUTURE RESEARCH DIRECTIONS

The evidence base is growing rapidly for best approaches to treat pediatric pain and prevent OUD, poisoning, and overdose, and the guidelines in this CPG are based on the highest quality research available at the time of writing. Nonetheless, there are significant gaps and an urgent need for future research on a range of topics relevant to pediatricians and other PHCPs.

These gaps and opportunities are described in detail in the accompanying technical report; some of the most important considerations are listed below.

- **High-quality clinical trials to establish the ideal dosing and duration of treatment with opioids.** Clinical trials to date have examined a relatively small number of the currently available, approved opioid medications in pediatric populations. How opioids (eg, oxycodone, hydrocodone, morphine, etc) compare

regarding efficacy (ie, pain control), tolerability (ie, medication side effects), and safety (ie, risk of OUD, poisoning, and overdose) is poorly understood, with the result that opioid choice is often a matter of clinician preference or common institutional practices. The ideal dose, dosing schedule, and duration of treatment also requires better understanding. Throughout, clinical endpoints (eg, at what pain level can opioids be safely stopped or tapered) should be developed with guidance from patients and family members.

- **High-quality clinical trials of opioids, nonopioid medications, and nonpharmacologic approaches.** There are a very small number of randomized controlled trials that compare opioid and nonopioid medications, such as NSAIDs and acetaminophen. More studies are needed to more clearly guide multimodal approaches to pain management. These studies should include an examination of how nonopioid medications (not only oral NSAIDs and acetaminophen, but also other oral and nonoral medications, including topical treatments) and nonpharmacologic treatments should be best combined to avoid or minimize opioid use. In examining these questions, researchers should study a range of conditions; studies to date have often focused on narrowly defined pain conditions, such as pain following a specific procedure or injury.
- **Studies in outpatient settings, particularly primary care.** Clinical trials of pediatric pain are commonly conducted in postoperative settings or in emergency departments or other inpatient hospital wards. Data on managing pain in outpatient settings, in which cases patients and family members monitor pain symptoms at home (rather than a clinician at the bedside), are scarce. Additionally, many studies use restrictive selection criteria, often excluding children with comorbidities, such as disabilities or mental health conditions. Because some of these children and adolescents may experience more severe distress from pain and have the greatest need for support, studies that include them in outpatient settings are greatly needed.
- **Clinical trials of pharmacogenetic and other genetic or molecular information to guide opioid prescribing.** Increasingly, precision medicine—in which treatment is optimized through the use of personalized information, including genetic and molecular profiling—is likely to help guide pain management decisions. Pharmacogenetics, for example, could guide decisions about which opioid formulation, dose, and dosing schedule is likely to be most appropriate for an individual patient based on their likely response to the medication. Genetic data (including, for example, polygenic risk scores) might also help identify an individual's likely risk of experiencing an adverse reaction to an opioid or of developing an OUD. Further studies,

however, are needed to understand how such information might impact clinical outcomes and how pediatricians and PHCPs should incorporate it into pain management decisions and counseling of patients and families.

- **Studies of the cumulative impact of opioid exposure during childhood and adolescence.** A large body of research has identified brain structure and function changes occurring in association with frequent or heavy use of potentially addictive substances (eg, nicotine, alcohol, and cannabis). Treating pain is a clinical priority, and opioids should be used for severe acute pain that otherwise would be insufficiently controlled. Nonetheless, in a small percentage of individuals, opioids can precipitate an OUD. Relatively little is known about the biological and psychological consequences of short- and long-term opioid exposure—and repeated treatment episodes—during critical periods of child and adolescent development; such information would help pediatricians and PHCPs counsel patients and families about potential risk.
- **Examination of institutional policies that enhance or hinder appropriate opioid prescribing practices.** There is significant institutional variability in analgesic use. Although this CPG was focused on outpatient settings, as an example of such variability, a recent study of opioid prescribing for critically ill infants found that in the US Northeast, in 2 hospitals, fewer than one-half of infants received an opioid during their hospitalization, but in 3 other hospitals, more than 80% of infants received an opioid, and such variability was not fully explained by differences in clinical need.¹⁷⁶ Policies at the state, local, and health-system levels all impact opioid prescribing. Some policies likely improve appropriate opioid prescribing in the aggregate (eg, limiting initial opioid prescriptions to several days and prohibiting excessively long durations of opioids). However, such policies might also prevent some individuals from receiving opioids for longer periods of time when they may be needed (eg, pain management after an especially painful surgical procedure, or in the treatment of chronic pain) and could result in children and adolescents experiencing uncontrolled pain and distress. Studies are needed to understand how such prescribing policies—which are often designed with adult populations in mind—might help or hurt pediatric populations. Such studies could guide future clinical practice guidelines and the development of evidence-based prescribing policies at state, local, and health-system levels. Within health care systems (including outpatient clinics and hospitals), quality improvement incentives are also likely to guide pediatricians' and PHCPs' prescribing practices through the use of direct feedback and monitoring and reporting of balancing measures.

Despite the need for these studies, the evidence base and understanding of current best clinical practices was sufficiently strong to support the key action statements in this CPG. Still, pain research in children and adolescents has lagged behind that for adults, and clinical trials and high-quality observational studies addressing the knowledge gaps raised above are urgently needed. Throughout, particularly as researchers conduct clinical trials and assess the impact of institutional policies, researchers must be vigilant and identify instances of undertreated pain and ensure that children and adolescents are not treated differently on the basis of race, ethnicity, or other sociodemographic factors.

XII. CONCLUSIONS

Clinicians' approaches to pain management have changed dramatically in the last 2 decades. At the turn of the century, prevailing narratives on pain treatment supported the liberal use of opioids. Common narratives included, for example, that pain is "the fifth vital sign," and that individuals who are in pain cannot develop an addiction when prescribed an opioid.

As prescription opioids increasingly became involved in US overdose deaths, the proverbial pendulum swung widely, and many clinicians and health systems inflexibly began refusing to offer opioids for pain—even in cases when these prescriptions were likely indicated.

This CPG acknowledges that these narratives and practices have harmed children and families across the country; the document seeks to provide a sensible path forward. Pain should be treated using multimodal approaches that include opioids when appropriate. This treatment should adhere to best practices to minimize the risk for OUD, poisoning, and overdose.

This CPG also acknowledges the longstanding inequities that have impacted the treatment of pediatric pain for many individuals, particularly communities of color. These disparities have negative health and mental health impacts on families. PHCPs should monitor health equity measures (ie, race, ethnicity, preferred language, insurance status) and intervene whenever disparities are identified.

PHCPs are experts at treating medical conditions with social and behavioral considerations. Because of this, PHCPs are exceptionally well-positioned to balance the benefits of effective pain management with the potential risks of prescribing opioids when they are indicated. This subcommittee strongly believes that it is time for the pediatric workforce to promote rational and equitable pain management. It is the subcommittee's sincere hope that this CPG will help PHCPs optimize the care of children, adolescents, and families across the United States.

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ABBREVIATIONS

AI/AN: American Indian/Alaska Native
CDC: Centers for Disease Control and Prevention
CDS: clinical decision support
CPG: clinical practice guideline
EHR: electronic health record
FDA: US Food and Drug Administration
KAS: key action statement
NSAID: nonsteroidal anti-inflammatory drug
OUD: opioid use disorder
PHCP: pediatric health care providers
RCT: randomized controlled trial

The guidance in this report does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

All clinical practice guidelines from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

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REFERENCES

1. Archambault PM. WikiBuild: a new application to support patient and health care professional involvement in the development of patient support tools. *J Med Internet Res*. 2011;13(4):e114
2. Bryant EA, Scott AM, Thomas R. Patient and public involvement in the development of clinical practice guidelines: a scoping review protocol. *BMJ Open*. 2020;10(10):e037327
3. Gilligan T, Salmi L, Enzinger A. Patient-clinician communication is a joint creation: working together toward well-being. *Am Soc Clin Oncol Educ Book*. 2018;38:532–539
4. Serrano-Aguilar P, Trujillo-Martin MM, Pérez de la Rosa A, et al; Spanish SLE CPG Development Group. Patient participation in a clinical guideline development for systemic lupus erythematosus. *Patient Educ Couns*. 2015;98(9):1156–1163
5. Feldman DE, Nahin RL. National estimates of chronic musculoskeletal pain and its treatment in children, adolescents, and young adults in the United States: data from the 2007-2015 National Ambulatory Medical Care Survey. *J Pediatr*. 2021;233:212–219.e1
6. Anderson JL, Oliveira J E Silva L, Funni SA, Bellolio F, Jeffery MM. Epidemiology of paediatric pain-related visits to emergency departments in the USA: a cross-sectional study. *BMJ Open*. 2021;11(8):e046497
7. Groenewald CB, Wright DR, Palermo TM. Health care expenditures associated with pediatric pain-related conditions in the United States. *Pain*. 2015;156(5):951–957
8. Yaster M, Reid AL, Cohen MN, Monitto CL. Opioids in the management of acute pediatric pain: an update in a time of crisis. *Clin J Pain*. 2019;35(6):487–496
9. Yaster M, McNaull PP, Davis PJ. The opioid epidemic in pediatrics: a 2020 update. *Curr Opin Anaesthesiol*. 2020;33(3):327–334
10. Gaither JR, Shabanova V, Leventhal JM. US national trends in pediatric deaths from prescription and illicit opioids, 1999-2016. *JAMA Netw Open*. 2018;1(8):e186558
11. Gaw CE, Curry AE, Osterhoudt KC, Wood JN, Corwin DJ. Characteristics of fatal poisonings among infants and young children in the United States. *Pediatrics*. 2023;151(4):e2022059016
12. Friedman J, Hadland SE. The overdose crisis among U.S. adolescents. *N Engl J Med*. 2024;390(2):97–100
13. Hadland SE, Wharam JF, Schuster MA, Zhang F, Samet JH, Larochelle MR. Trends in receipt of buprenorphine and naltrexone for opioid use disorder among adolescents and young adults, 2001-2014. *JAMA Pediatr*. 2017;171(8):747–755
14. Hudgins JD, Porter JJ, Monuteaux MC, Bourgeois FT. Trends in opioid prescribing for adolescents and young adults in ambulatory care settings. *Pediatrics*. 2019;143(6):e20181578
15. Renny MH, Yin HS, Jent V, Hadland SE, Cerdá M. Temporal trends in opioid prescribing practices in children, adolescents, and younger adults in the US from 2006 to 2018. *JAMA Pediatr*. 2021;175(10):1043–1052
16. Sutherland TN, Wunsch H, Newcomb C, Hadland SE, Gaskins L, Neuman MD. Trends in routine opioid dispensing after common pediatric surgeries in the United States: 2014–2019. *Pediatrics*. 2022;149(5):e2021054729
17. Kertesz SG, Gordon AJ, Satel SL. Opioid prescription control: when the corrective goes too far. Available at: <https://www.healthaffairs.org/content/forefront/opioid-prescription-control-corrective-goes-too-far>. Accessed October 15, 2023
18. Krane EJ. The opioid debate-PRO: opioids have an important role in pain management in children. *Clin J Pain*. 2019;35(6):468–472
19. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC clinical practice guideline for prescribing opioids for pain—United States, 2022. *MMWR Recomm Rep*. 2022;71(3):1–95

20. Mikkelsen HT, Haraldstad K, Helseth S, Skarstein S, Småstuen MC, Rohde G. Pain and health-related quality of life in adolescents and the mediating role of self-esteem and self-efficacy: a cross-sectional study including adolescents and parents. *BMC Psychol*. 2021;9(1):128
21. Goyal MK, Kuppermann N, Cleary SD, Teach SJ, Chamberlain JM. Racial disparities in pain management of children with appendicitis in emergency departments. *JAMA Pediatr*. 2015;169(11):996–1002
22. US Department of Health and Human Services. Pain Management Best Practices InterAgency Task Force report: updates, gaps, inconsistencies, and recommendations. Available at: <https://www.hhs.gov/ash/advisory-committees/pain/reports/index.html>. Accessed October 15, 2023
23. Lee P, Le Saux M, Siegel R, et al. Racial and ethnic disparities in the management of acute pain in US emergency departments: meta-analysis and systematic review. *Am J Emerg Med*. 2019; 37(9):1770–1777
24. Groenewald CB, Rabbitts JA, Hansen EE, Palermo TM. Racial differences in opioid prescribing for children in the United States. *Pain*. 2018;159(10):2050–2057
25. Goyal MK, Johnson TJ, Chamberlain JM, et al; Pediatric Emergency Care Applied Research Network (PECARN). Racial and ethnic differences in emergency department pain management of children with fractures. *Pediatrics*. 2020;145(5): e20193370
26. Morden NE, Chyn D, Wood A, Meara E. Racial inequality in prescription opioid receipt—role of individual health systems. *N Engl J Med*. 2021;385(4):342–351
27. Raphael JL, Oyeku SO. Implicit bias in pediatrics: an emerging focus in health equity research. *Pediatrics*. 2020;145(5): e20200512
28. Hauer J, Houtrow AJ; American Academy of Pediatrics, Section on Hospice and Palliative Medicine, Council on Children With Disabilities. Pain assessment and treatment in children with significant impairment of the central nervous system. *Pediatrics*. 2017;139(6):e20171002
29. American Medical Association, Pain Care Task Force. Addressing obstacles to evidence-informed pain care. *AMA J Ethics*. 2020; 22(1):E709–E717
30. Dowell D, Compton WM, Giroir BP. Patient-centered reduction or discontinuation of long-term opioid analgesics: the HHS guide for clinicians. *JAMA*. 2019;322(19):1855–1856
31. Agnoli A, Xing G, Tancredi DJ, Magnan E, Jerant A, Fenton JJ. Association of dose tapering with overdose or mental health crisis among patients prescribed long-term opioids. 2021;326(5): 411–419
32. US Food and Drug Administration. FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering. Available at: [https://www.fda.gov/drugs/fda-drug-safety-podcasts/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes#:~:text=On%20April%209%2C%202019%20FDA,%2C%20psychological%20distress%2C%20and%20suicide](https://www.fda.gov/drugs/fda-drug-safety-podcasts/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes#:~:text=On%20April%209%2C%202019%20FDA,%2C%20psychological%20distress%2C%20and%20suicide.). Accessed October 15, 2023
33. Tanz LJ, Dinwiddie AT, Mattson CL, O'Donnell J, Davis NL. Drug overdose deaths among persons aged 10-19 years—United States, July 2019-December 2021. *MMWR Morb Mortal Wkly Rep*. 2022;71(50):1576–1582
34. Friedman J, Godvin M, Shover CL, Gone JP, Hansen H, Schriger DL. Trends in drug overdose deaths among US adolescents, January 2010 to June 2021. *JAMA*. 2022;327(14):1398–1400
35. Hadland SE, Bagley SM, Gai MJ, et al. Opioid use disorder and overdose among youth following an initial opioid prescription. *Addiction*. 2021;116(10):2790–2800
36. Chua KP, Brummett CM, Conti RM, Bohnert A. Association of opioid prescribing patterns with prescription opioid overdose in adolescents and young adults. *JAMA Pediatr*. 2020;174(2): 141–148
37. Schroeder AR, Dehghan M, Newman TB, Bentley JP, Park KT. Association of opioid prescriptions from dental clinicians for US adolescents and young adults with subsequent opioid use and abuse. *JAMA Intern Med*. 2019;179(2):145–152
38. Hadland SE, Rivera-Aguirre A, Marshall BDL, Cerdá M. Association of pharmaceutical industry marketing of opioid products with mortality from opioid-related overdoses. *JAMA Netw Open*. 2019;2(1):e186007
39. Harbaugh CM, Lee JS, Hu HM, et al. Persistent opioid use among pediatric patients after surgery. *Pediatrics*. 2018;141(1): e20172439
40. Miech R, Johnston L, O'Malley PM, Keyes KM, Heard K. Prescription opioids in adolescence and future opioid misuse. *Pediatrics*. 2015;136(5):e1169–e1177
41. Cerdá M, Santaella J, Marshall BD, Kim JH, Martins SS. Nonmedical prescription opioid use in childhood and early adolescence predicts transitions to heroin use in young adulthood: a national study. *J Pediatr*. 2015;167(3):605–612.e1–2
42. Raman SR, Smith MJ. Evidence for the use of opioid medication for pediatric acute pain in the outpatient setting: technical report. *Pediatrics*. 2024;154(4):e2024068753
43. American Academy of Pain Medicine; American Pain Society; American Society of Addiction Medicine. Public policy statement on the rights and responsibilities of health care professionals in the use of opioids for the treatment of pain: a consensus document from the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine. *Pain Med*. 2004;5(3):301–302
44. Johnson-Arbor K. What is fentanyl? Available at: <https://www.poison.org/articles/what-is-fentanyl>. Accessed October 15, 2023
45. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. American Psychiatric Association; 2022
46. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. *Pain*. 2020;161(9):1976–1982
47. Hampl SE, Hassink SG, Skinner AC, et al. Clinical practice guideline for the evaluation and treatment of children and adolescents with obesity. *Pediatrics*. 2023;151(2):e2022060640

48. Michel G. *BridgeWiz*. 1.0 ed [software]. Yale Center for Medical Informatics; 2012
49. Shiffman RN, Michel G, Rosenfeld RM, Davidson C. Building better guidelines with BRIDGE-Wiz: development and evaluation of a software assistant to promote clarity, transparency, and implementability. *J Am Med Inform Assoc*. 2012;19(1):94–101
50. Velentgas P, Dreyer NA, Nourjah P, Smith SR, Torchia MM, eds. Developing a protocol for observational comparative effectiveness research: a user's guide. Available at: <https://www.govinfo.gov/content/pkg/GOVPUB-HE20-PURL-gpo37130/pdf/GOVPUB-HE20-PURL-gpo37130.pdf>. Accessed October 15, 2023
51. Centers for Disease Control and Prevention. 2019 Annual surveillance report of drug related risks and outcomes—United States. Available at: <https://www.cdc.gov/drugoverdose/pdf/pubs/2019-cdc-drug-surveillance-report.pdf>. Accessed October 15, 2023
52. Banks J, Hill C, Chi DL. Plan type and opioid prescriptions for children in Medicaid. *Med Care*. 2021;59(5):386–392
53. Chua KP, Brummett CM, Conti RM, Bohnert AS. Opioid prescribing to US children and young adults in 2019. *Pediatrics*. 2021;148(3):e2021051539
54. Cranfield E, Ashcroft E, Forget P. Mortality by opioid poisoning in children and teenagers and opioid prescriptions. *BMC Pediatr*. 2021;21(1):569
55. Kelley-Quon LI, Cho J, Strong DR, et al. Association of nonmedical prescription opioid use with subsequent heroin use initiation in adolescents. *JAMA Pediatr*. 2019;173(9):e191750
56. Finkelstein Y, Macdonald EM, Gonzalez A, Sivilotti MLA, Mamdani MM, Juurlink DN; Canadian Drug Safety and Effectiveness Research Network. Overdose risk in young children of women prescribed opioids. *Pediatrics*. 2017;139(3):e20162887
57. Wisselo TL, Stuart C, Muris P. Providing parents with information before anaesthesia: what do they really want to know? *Paediatr Anaesth*. 2004;14(4):299–307
58. Hobbie WL, Stuber M, Meeske K, et al. Symptoms of post-traumatic stress in young adult survivors of childhood cancer. *J Clin Oncol*. 2000;18(24):4060–4066
59. El-Gabalawy R, Sommer JL, Pietrzak R, et al. Post-traumatic stress in the postoperative period: current status and future directions. *Can J Anaesth*. 2019;66(11):1385–1395
60. Kelley-Quon LI, Ourshalimian S, Lee J, et al. Multi-institutional quality improvement project to minimize opioid prescribing in children after appendectomy using NSQIP pediatric. *J Am Coll Surg*. 2022;234(3):290–298
61. World Health Organization. *WHO Guidelines for the Pharmacological and Radiotherapeutic Management of Cancer Pain*. World Health Organization; 2018
62. Kelley-Quon LI, Kirkpatrick MG, Ricca RL, et al. Guidelines for opioid prescribing in children and adolescents after surgery: an expert panel opinion. *JAMA Surg*. 2021;156(1):76–90
63. Cravero JP, Agarwal R, Berde C, et al. The Society for Pediatric Anesthesia recommendations for the use of opioids in children during the perioperative period. *Paediatr Anaesth*. 2019;29(6):547–571
64. Ferland CE, Vega E, Ingelmo PM. Acute pain management in children: challenges and recent improvements. *Curr Opin Anaesthesiol*. 2018;31(3):327–332
65. Nicholas TAV, Robinson R. Multimodal analgesia in the era of the opioid epidemic. *Surg Clin North Am*. 2022;102(1):105–115
66. Farr BJ, Ranstrom L, Mooney DP. Eliminating opiate prescribing for children after nonperforated appendectomy. *J Am Coll Surg*. 2020;230(6):944–946
67. Poonai N, Bhullar G, Lin K, et al. Oral administration of morphine versus ibuprofen to manage postfracture pain in children: a randomized trial. *CMAJ*. 2014;186(18):1358–1363
68. Kelly LE, Sommer DD, Ramakrishna J, et al. Morphine or ibuprofen for posttonsillectomy analgesia: a randomized trial. *Pediatrics*. 2015;135(2):307–313
69. Carrasco-Labra A, Polk DE, Urquhart O, et al. Evidence-based clinical practice guideline for the pharmacologic management of acute dental pain in children: a report from the American Dental Association Science and Research Institute, the University of Pittsburgh School of Dental Medicine, and the Center for Integrative Global Oral Health at the University of Pennsylvania. *J Am Dent Assoc*. 2023;154(9):814–825.e2
70. Rusy LM, Weisman SJ. Complementary therapies for acute pediatric pain management. *Pediatr Clin North Am*. 2000;47(3):589–599
71. Fox MA, Ayyangar R, Parten R, Haapala HJ, Schilling SG, Kalpakjian CZ. Self-report of pain in young people and adults with spastic cerebral palsy: interrater reliability of the revised Face, Legs, Activity, Cry, and Consolability (r-FLACC) scale ratings. *Dev Med Child Neurol*. 2019;61(1):69–74
72. Voepel-Lewis T, Zikmund-Fisher BJ, Smith EL, Redman RW, Zyzanski S, Tait AR. Parents' analgesic trade-off dilemmas: how analgesic knowledge influences their decisions to give opioids. *Clin J Pain*. 2016;32(3):187–195
73. Hill MV, Stucke RS, McMahon ML, Beeman JL, Barth RJ, Jr. An educational intervention decreases opioid prescribing after general surgical operations. *Ann Surg*. 2018;267(3):468–472
74. Hill MV, McMahon ML, Stucke RS, Barth RJ, Jr. Wide variation and excessive dosage of opioid prescriptions for common general surgical procedures. *Ann Surg*. 2017;265(4):709–714
75. Howard R, Waljee J, Brummett C, Englesbe M, Lee J. Reduction in opioid prescribing through evidence-based prescribing guidelines. *JAMA Surg*. 2018;153(3):285–287
76. Odegard M, Ourshalimian S, Hijaz D, et al. Factors associated with postoperative opioid use in adolescents. *J Pediatr Surg*. 2024;59(4):709–717
77. Overton HN, Hanna MN, Bruhn WE, et al; Opioids After Surgery Workgroup. Opioid prescribing guidelines for common surgical procedures: an expert panel consensus. *J Am Coll Surg*. 2018;227:411–418
78. Monitto CL, Hsu A, Gao S, et al. Opioid prescribing for the treatment of acute pain in children on hospital discharge. *Anesth Analg*. 2017;125(6):2113–2122
79. Hunsberger JB, Hsu A, Yaster M, et al. Physicians prescribe more opioid than needed to treat pain in children after

- outpatient urological procedures: an observational cohort study. *Anesth Analg*. 2020;131(3):866–875
80. 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(5):497–498
 81. Feinberg AE, Chesney TR, Srikandarajah S, et al; Best Practice in Surgery Group. Opioid use after discharge in postoperative patients: a systematic review. *Ann Surg*. 2018;267(6):1056–1062
 82. Garren BR, Lawrence MB, McNaull PP, et al. Opioid-prescribing patterns, storage, handling, and disposal in postoperative pediatric urology patients. *J Pediatr Urol*. 2019;15(3):260.e1–260–e7
 83. Bicket MC, Long JJ, Pronovost PJ, et al. Prescription opioid analgesics commonly unused after surgery: a systematic review. *JAMA Surg*. 2017;152(11):1066–1071
 84. Bicket MC, White E, Pronovost PJ, et al. Opioid oversupply after joint and spine surgery: a prospective cohort study. *Anesth Analg*. 2019;128(2):358–364
 85. Berde CB, Sethna NF. Analgesics for the treatment of pain in children. *N Engl J Med*. 2002;347(14):1094–1103
 86. Toce MS, Michelson KA, Hudgins JD, et al. Association of prescription drug monitoring programs with opioid prescribing and overdose in adolescents and young adults. *Ann Emerg Med*. 2023;81(4):429–437
 87. Harbaugh CM, Vargas G, Sloss KR, et al. Association of opioid quantity and caregiver education with pain control after pediatric tonsillectomy. *Otolaryngol Head Neck Surg*. 2020;162(5):746–753
 88. Bryl AW, Demartinis N, Etkin M, Hollenbach KA, Huang J, Shah S. Reducing opioid doses prescribed from a pediatric emergency department. *Pediatrics*. 2021;147(4):e20201180
 89. Bailey L, Sun J, Courtney M, Murphy P. Improving postoperative tonsillectomy pain management in children—a double blinded randomised control trial of a patient analgesia information sheet. *Int J Pediatr Otorhinolaryngol*. 2015;79(5):732–739
 90. US Food and Drug Administration. FDA Drug Safety Communication: FDA restricts use of prescription codeine pain and cough medicines and tramadol pain medicines in children; recommends against use in breastfeeding women. Available at: <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-restricts-use-prescription-codeine-pain-and-cough-medicines-and>. Accessed October 15, 2023
 91. Kelly LE, Rieder M, van den Anker J, et al. More codeine fatalities after tonsillectomy in North American children. *Pediatrics*. 2012;129(5):e1343–e1347
 92. Khetani JD, Madadi P, Sommer DD, et al. Apnea and oxygen desaturations in children treated with opioids after adenotonsillectomy for obstructive sleep apnea syndrome: a prospective pilot study. *Paediatr Drugs*. 2012;14(6):411–415
 93. Orliaguet G, Hamza J, Couloigner V, et al. A case of respiratory depression in a child with ultrarapid CYP2D6 metabolism after tramadol. *Pediatrics*. 2015;135(3):e753–e755
 94. Friedrichsdorf SJ, Postier AC, Foster LP, et al. Tramadol versus codeine/acetaminophen after pediatric tonsillectomy: a prospective, double-blinded, randomized controlled trial. *J Opioid Manag*. 2015;11(4):283–294
 95. Ciszkowski C, Madadi P, Phillips MS, et al. Codeine, ultrarapid-metabolism genotype, and postoperative death. *N Engl J Med*. 2009;361(8):827–828
 96. Moir MS, Bair E, Shinnick P, Messner A. Acetaminophen versus acetaminophen with codeine after pediatric tonsillectomy. *Laryngoscope*. 2000;110(11):1824–1827
 97. Mitchell RB, Archer SM, Ishman SL, et al. Clinical practice guideline: tonsillectomy in children (update). *Otolaryngol Head Neck Surg*. 2019;160(1_suppl):S1–S42
 98. Hall MJ, Schwartzman A, Zhang J, Liu X. Ambulatory surgery data from hospitals and ambulatory surgery centers: United States, 2010. *Natl Health Stat Report*. 2017(102):1–15
 99. Liu C, Ulualp SO. Outcomes of an alternating ibuprofen and acetaminophen regimen for pain relief after tonsillectomy in children. *Ann Otol Rhinol Laryngol*. 2015;124(10):777–781
 100. Giordano T, Durkin A, Simi A, et al. High-dose celecoxib for pain after pediatric tonsillectomy: a randomized controlled trial. *Otolaryngol Head Neck Surg*. 2023;168(2):218–226
 101. Diercks GR, Comins J, Bennett K, et al. Comparison of ibuprofen versus acetaminophen and severe bleeding risk after pediatric tonsillectomy: a noninferiority randomized clinical trial. *JAMA Otolaryngol Head Neck Surg*. 2019;145(6):494–500
 102. Helgadottir HL, Wilson ME. A randomized controlled trial of the effectiveness of educating parents about distraction to decrease postoperative pain in children at home after tonsillectomy. *Pain Manag Nurs*. 2014;15(3):632–640
 103. Dorkham MC, Chalkiadis GA, von Ungern Sternberg BS, Davidson AJ. Effective postoperative pain management in children after ambulatory surgery with a focus on tonsillectomy: barriers and possible solutions. *Paediatr Anaesth*. 2013;24(3):239–248
 104. Martin E, Vickers B, Landau R, et al. ABM clinical protocol #28, peripartum analgesia and anesthesia for the breastfeeding mother. *Breastfeed Med*. 2018;13(3):164–171
 105. American College of Obstetricians and Gynecologists, Committee on Clinical Consensus—Obstetrics. Pharmacologic stepwise multimodal approach for postpartum pain management: ACOG Clinical Consensus No. 1. *Obstet Gynecol*. 2021;138(3):507–1368
 106. Halder S, Russell R, Quinlan J. Codeine and breast-feeding mothers. *Int J Obstet Anesth*. 2015;24(1):5–7
 107. Sachs H; Committee on Drugs. The transfer of drugs and therapeutics into human breast milk: an update on selected topics. *Pediatrics*. 2013;132(3):e796–e809
 108. Bloor M, Paech MJ, Kaye R. Tramadol in pregnancy and lactation. *Int J Obstet Anesth*. 2012;21(2):163–167
 109. Koren G, Cairns J, Chitayat D, Gaedigk A, Leeder SJ. Pharmacogenetics of morphine poisoning in a breastfed neonate of a codeine-prescribed mother. *Lancet*. 2006;368(9536):704
 110. Mark TL, Parish W. Opioid medication discontinuation and risk of adverse opioid-related health care events. *J Subst Abuse Treat*. 2019;103:58–63

111. Patrick SW, Barfield WD, Poindexter BB; Committee on Fetus and Newborn, Committee on Substance Use and Prevention. Neonatal opioid withdrawal syndrome. *Pediatrics*. 2020;146(5):e2020029074
112. Zipursky J, Juurlink DN. The implausibility of neonatal opioid toxicity from breastfeeding. *Clin Pharmacol Ther*. 2020;108(5):964–970
113. US Food and Drug Administration. FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. Available at: <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-warns-about-serious-risks-and-death-when-combining-opioid-pain-or>. Accessed October 15, 2023
114. US Food and Drug Administration. FDA drug safety communication: FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressants: careful medication management can reduce risks. Available at: <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-urges-caution-about-withholding-opioid-addiction-medications>. Accessed October 15, 2023
115. Chung CP, Callahan ST, Cooper WO, et al. Outpatient opioid prescriptions for children and opioid-related adverse events. *Pediatrics*. 2018;142(2):e20172156
116. Lovegrove MC, Mathew J, Hampp C, Governale L, Wysowski DK, Budnitz DS. Emergency hospitalizations for unsupervised prescription medication ingestions by young children. *Pediatrics*. 2014;134(4):e1009–e1016
117. Tadros A, Layperson SM, Davis SM, Bozeman R, Davidov DM. Emergency department visits by pediatric patients for poisoning by prescription opioids. *Am J Drug Alcohol Abuse*. 2016;42(5):550–555
118. Allen JD, Casavant MJ, Spiller HA, Chounthirath T, Hodges NL, Smith GA. Prescription opioid exposures among children and adolescents in the United States: 2000-2015. *Pediatrics*. 2017;139(4):e20163382
119. Chou R, Hartung D, Turner J, et al; Opioid Treatments for Chronic Pain. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *BMJ*. 2015;350:h2698
120. Park TW, Saitz R, Ganoczy D, Ilgen MA, Bohnert AS. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case cohort study. *BMJ*. 2015;350:h2698
121. US Food and Drug Administration. FDA recommends health care professionals discuss naloxone with all patients when prescribing opioid pain relievers or medicines to treat opioid use disorder. Available at: <https://www.fda.gov/drugs/fda-drug-safety-podcasts/fda-recommends-health-care-professionals-discuss-naloxone-all-patients-when-prescribing-opioid-pain#:~:text=For%20all%20patients%20who%20are,benzodiazepines%20or%20other%20medicines%20that>. Accessed October 15, 2023
122. Voepel-Lewis T, Malviya S, Grant JA, et al. Effect of a brief scenario-tailored educational program on parents' risk knowledge, perceptions, and decisions to administer prescribed opioids: a randomized controlled trial. *Pain*. 2021;162(3):976–985
123. Substance Abuse and Mental Health Administration. Opioid Overdose. Substance Abuse and Mental Health Administration; 2024. Available at: <https://www.samhsa.gov/medications-substance-use-disorders/medications-counseling-related-conditions/opioid-overdose>. Accessed September 3, 2024
124. American Academy of Pediatrics. The opioid epidemic: how to protect your family. Available at: <https://www.healthychildren.org/English/ages-stages/teen/substance-abuse/Pages/The-Opioid-Epidemic.aspx>. Accessed October 15, 2023
125. Centers for Disease Control and Prevention. Lifesaving naloxone. Available at: <https://www.cdc.gov/stopoverdose/naloxone/index.html>. Accessed October 15, 2023
126. Payne ER, Stancliff S, Rowe K, Christie JA, Dailey MW. Comparison of administration of 8-milligram and 4-milligram intranasal naloxone by law enforcement during response to suspected opioid overdose—New York, March 2022–August 2023. *MMWR Morb Mortal Wkly Rep*. 2024;73(5):110–113
127. Guy GP, Jr, Haegerich TM, Evans ME, Losby JL, Young R, Jones CM. Vital signs: pharmacy-based naloxone dispensing—United States, 2012-2018. *MMWR Morb Mortal Wkly Rep*. 2019;68(31):679–686
128. Centers for Disease Control and Prevention. Naloxone training. Available at: <https://www.cdc.gov/opioids/naloxone/training/index.htm>. Accessed October 15, 2023
129. American Academy of Pediatrics (AAP). Talk to your teen about drugs – and keep talking. Available at: <https://www.healthychildren.org/English/agesstages/teen/substanceabuse/Pages/default.aspx>.
130. Hadland SE, Agarwal R. What to know about fentanyl & using naloxone for opioid overdose. Available at: <https://www.healthychildren.org/English/ages-stages/teen/substance-abuse/Pages/what-parents-need-to-know-about-naloxone-foropioid-overdose.aspx>. Accessed October 15, 2023
131. American Academy of Pediatrics. Resources to address the opioid epidemic. Available at: <https://www.aap.org/en/patient-care/substance-use-and-prevention/resources-toaddress-the-opioid-epidemic/>. Accessed October 15, 2023
132. Centers for Disease Control and Prevention. Lifesaving naloxone from pharmacies. Available at: <https://www.cdc.gov/vitalsigns/naloxone/index.html#:~:text=Many%20states%20have%20laws%20that,done%2C%20particularly%20in%20rural%20counties>. Accessed October 15, 2023
133. American Academy of Pediatrics. Medication safety tips for families. Available at: <https://www.healthychildren.org/English/safety-prevention/at-home/medication-safety/Pages/Medication-Safety-Tips.aspx>. Accessed October 15, 2023
134. US Food and Drug Administration. FDA approves first over-the-counter naloxone nasal spray. Available at: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-over-counter-naloxone-nasal-spray>. Accessed October 15, 2023
135. Centers for Disease Control and Prevention. PROTECT initiative: advancing children's medication safety. Available at: <https://www.cdc.gov/medication-safety/protect/index.html>. Accessed October 15, 2023

136. Webb AC, Jorge EA, Omairi I, Nichols MH, Monroe KW. Self-reported usage of safety equipment provided through a community partnership approach to injury prevention in the pediatric emergency department. *Pediatr Emerg Care*. 2022;38(7):e1391–e1395
137. McDonald EM, Kennedy-Hendricks A, McGinty EE, Shields WC, Barry CL, Gielen AC. Safe storage of opioid pain relievers among adults living in households with children. *Pediatrics*. 2017; 139(3):e20162161
138. Sloss KR, Vargas G, Brummett CM, et al. Association of caregiver-reported education with locked storage and disposal of prescription opioids after children's surgery. *J Pediatr Surg*. 2020;55(11):2442–2447
139. Garbutt JM, Kulka K, Dodd S, Sterkel R, Plax K. Opioids in adolescents' homes: prevalence, caregiver attitudes, and risk reduction opportunities. *Acad Pediatr*. 2019;19(1):103–108
140. Ross-Durow PL, McCabe SE, Boyd CJ. Adolescents' access to their own prescription medications in the home. *J Adolesc Health*. 2013;53(2):260–264
141. Webb AC, Nichols MH, Shah N, Monroe KW. Effect of lock boxes and education on safe storage of medications. *Inj Epidemiol*. 2020;7(suppl 1):21
142. Adler AC, Yamani AN, Sutton CD, Guffey DM, Chandrakantan A. Mail-back envelopes for retrieval of opioids after pediatric surgery. *Pediatrics*. 2020;145(3):e20192449
143. Odegard MN, Ourshalimian S, Hijaz D, et al. Factors associated with safe prescription opioid disposal after surgery in adolescents. *J Surg Res*. 2022;279:42–51
144. Gray JA, Hagemeyer NE. Prescription drug abuse and DEA-sanctioned drug take-back events: characteristics and outcomes in rural Appalachia. *Arch Intern Med*. 2012;172(15):1186–1187
145. US Department of Justice. Drug disposal information. Available at: https://www.deadiversion.usdoj.gov/drug_disposal/drug_disposal.html. Accessed October 15, 2023
146. US Food and Drug Administration. Where and how to dispose of unused medicines. Available at: <https://www.fda.gov/consumers/consumer-updates/where-and-how-dispose-unused-medicines>. Accessed October 15, 2023
147. Lawrence AE, Carsel AJ, Leonhart KL, et al. Effect of drug disposal bag provision on proper disposal of unused opioids by families of pediatric surgical patients: a randomized clinical trial. *JAMA Pediatr*. 2019;173(8):e191695
148. Substance Abuse and Mental Health Services Administration. 2017 National Survey on Drug Use and Health (NSDUH-2017-DS0001). Available at: <https://www.samhsa.gov/data/release/2017-national-survey-drug-use-and-health-nsduh-releases>. Accessed October 15, 2023
149. Voepel-Lewis T, Farley FA, Grant J, et al. Behavioral intervention and disposal of leftover opioids: a randomized trial. *Pediatrics*. 2020;145(1):e20191431
150. Voepel-Lewis T, Veliz P, Heinze J, et al. Enhancing risk perception may be insufficient to curtail prescription opioid use and misuse among youth after surgery: a randomized controlled trial. *Patient Educ Couns*. 2022;105(7):2217–2224
151. US Food and Drug Administration. FDA moves forward with mail-back envelopes for opioid analgesics dispensed in outpatient settings. Available at: <https://www.fda.gov/newsevents/pressannouncements/fda-moves-forward-mail-back-envelopes-opioid-analgesics-dispensed-outpatient-settings>. Accessed October 15, 2023
152. Gray J, Hagemeyer N, Brooks B, Alamian A. Prescription disposal practices: a 2-year ecological study of drug drop box donations in Appalachia. *Am J Public Health*. 2015;105(9):e89–e94
153. US Food and Drug Administration. Disposal of unused medicines: what you should know. Available at: <https://www.fda.gov/drugs/safe-disposal-medicines/disposal-unused-medicines-what-you-should-know>. Accessed October 15, 2023
154. US Food and Drug Administration. Drug disposal: FDA's flush list for certain medicines. Available at: <https://www.fda.gov/drugs/disposal-unused-medicines-what-you-should-know/drug-disposal-fdas-flush-list-certain-medicines#FlushList>. Accessed October 15, 2023
155. King S, Chambers C, Huguet A, et al. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. *Pain*. 2011;152(12):2729–2738
156. D'souza G, Walia A, Agarwal R. Error traps in the perioperative care of children with chronic pain. *Paediatr Anaesth*. 2023;33(7):520–525
157. Kitzman JM, Mesheriakova VV, Borucki AN, Agarwal R. Substance use disorders in adolescents and young adults: history and perioperative considerations from the Society for Pediatric Pain Medicine [published online ahead of print July 14, 2023]. *Anesth Analg*. doi: 10.1213/ANE.0000000000006623
158. US Department of Health and Human Services, Working Group on Patient-Centered Reduction or Discontinuation of Long-term Opioid Analgesics. HHS guide for clinicians on the appropriate dosage reduction or discontinuation of long-term opioid analgesics. Available at: https://www.hhs.gov/system/files/Dosage_Reduction_Discontinuation.pdf. Accessed October 15, 2023
159. James JR, Scott JM, Klein JW, et al. Mortality after discontinuation of primary care-based chronic opioid therapy for pain: a retrospective cohort study. *J Gen Intern Med*. 2019;34:2749–2755
160. Mao J. NMDA and opioid receptors: their interactions in antinociception, tolerance and neuroplasticity. *Brain Res Brain Res Rev*. 1999;30(3):289–304
161. Farrant B, Denny S, Vroegop P, Fenaughty J, Clark TC. Prevalence, severity and impact of chronic pain among a representative cross-sectional study of New Zealand high school students. *J Paediatr Child Health*. 2023;59(1):144–152
162. Chuck Rich RL, Jr, Agnello RN, Franklin G. Chronic pain across the ages. *Prim Care*. 2022;49(3):439–453
163. Macintyre PE, Roberts LJ, Huxtable CA. Management of opioid-tolerant patients with acute pain: approaching the challenges. *Drugs*. 2020;80:9–21
164. Aroke EN, McMullan SP, Woodfin KO, Richey R, Doss J, Wilbanks BA. A practical approach to acute postoperative pain management in chronic pain patients. *J Perianesth Nurs*. 2020;35(6):564–573
165. Committee on Substance Use and Prevention. Medication-assisted treatment of adolescents with opioid use disorders. *Pediatrics*. 2016;138(3):e20161893

166. De Aquino JP, Parida S, Avila-Quintero VJ, et al. Opioid-induced analgesia among persons with opioid use disorder receiving methadone or buprenorphine: a systematic review of experimental pain studies. *Drug Alcohol Depend.* 2021;228:109097
167. Vickers AP, Jolly A. Naltrexone and problems in pain management. *BMJ.* 2006;332(7534):132–133
168. Gordon KS, Manhapra A, Crystal S, et al. All-cause mortality among males living with and without HIV initiating long-term opioid therapy, and its association with opioid dose, opioid interruption and other factors. *Drug Alcohol Depend.* 2020;216:108291
169. Chua KP, Thorne MC, Ng S, Donahue M, Brummett CM. Association between default number of opioid doses in electronic health record systems and opioid prescribing to adolescents and young adults undergoing tonsillectomy. *JAMA Netw Open.* 2022;5(6):e2219701
170. Baxter KJ, Short HL, Wetzel M, Steinberg RS, Heiss KF, Raval MV. Decreased opioid prescribing in children using an enhanced recovery protocol. *J Pediatr Surg.* 2019;54(6):1104–1107
171. Lion KC, Faro EZ, Coker TR. All quality improvement is health equity work: designing improvement to reduce disparities. *Pediatrics.* 2022;149(suppl 3):e2020045948E
172. Liebschutz JM, Xuan Z, Shanahan CW, et al. Improving adherence to long-term opioid therapy guidelines to reduce opioid misuse in primary care: a cluster-randomized clinical trial. *JAMA Intern Med.* 2017;177(9):1265–1272
173. Rolfzen ML, Wick A, Mascha EJ, et al. Best practice alerts informed by inpatient opioid intake to reduce opioid prescribing after surgery (PRIOR): a cluster randomized multiple crossover trial. *Anesthesiology.* 2023;139(2):186–196
174. Piper KN, Baxter KJ, Wetzel M, et al; Pediatric Surgical Research Collaborative. Provider education decreases opioid prescribing after pediatric umbilical hernia repair. *J Pediatr Surg.* 2020;55(7):1319–1323
175. US Food and Drug Administration. FDA approves second over-the-counter naloxone nasal spray product. Available at: <https://www.fda.gov/news-events/press-announcements/fda-approves-second-over-counter-naloxone-nasal-spray-product>. Accessed October 15, 2023
176. Keane OA, Ourshalimian S, Lakshmanan A, et al. Institutional and regional variation in opioid prescribing for hospitalized infants in the US. *JAMA Netw Open.* 2024;7(3):e240555