

Colorado's Opioid Solution: Clinicians United to Resolve the Epidemic (CO's CURE)

Colorado Dental Association

2020 Opioid Prescribing and Treatment Guidelines



Developed by Colorado Dental Association in partnership with Colorado Hospital Association, Colorado Medical Society and Colorado Consortium for Prescription Drug Abuse Prevention



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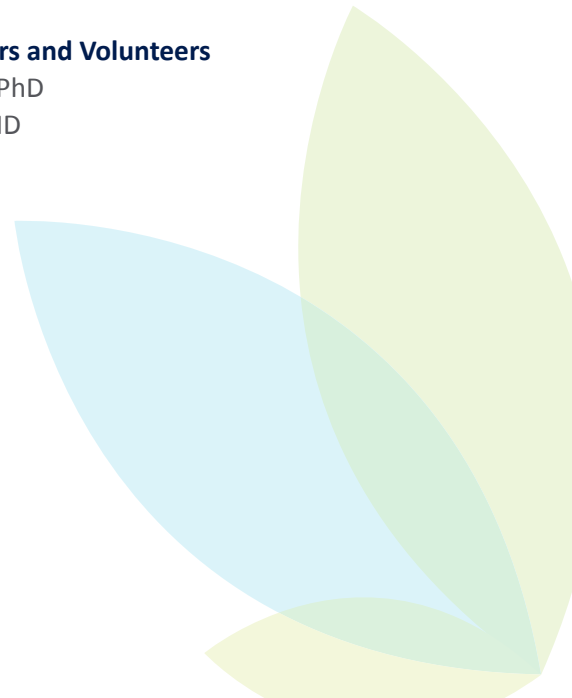


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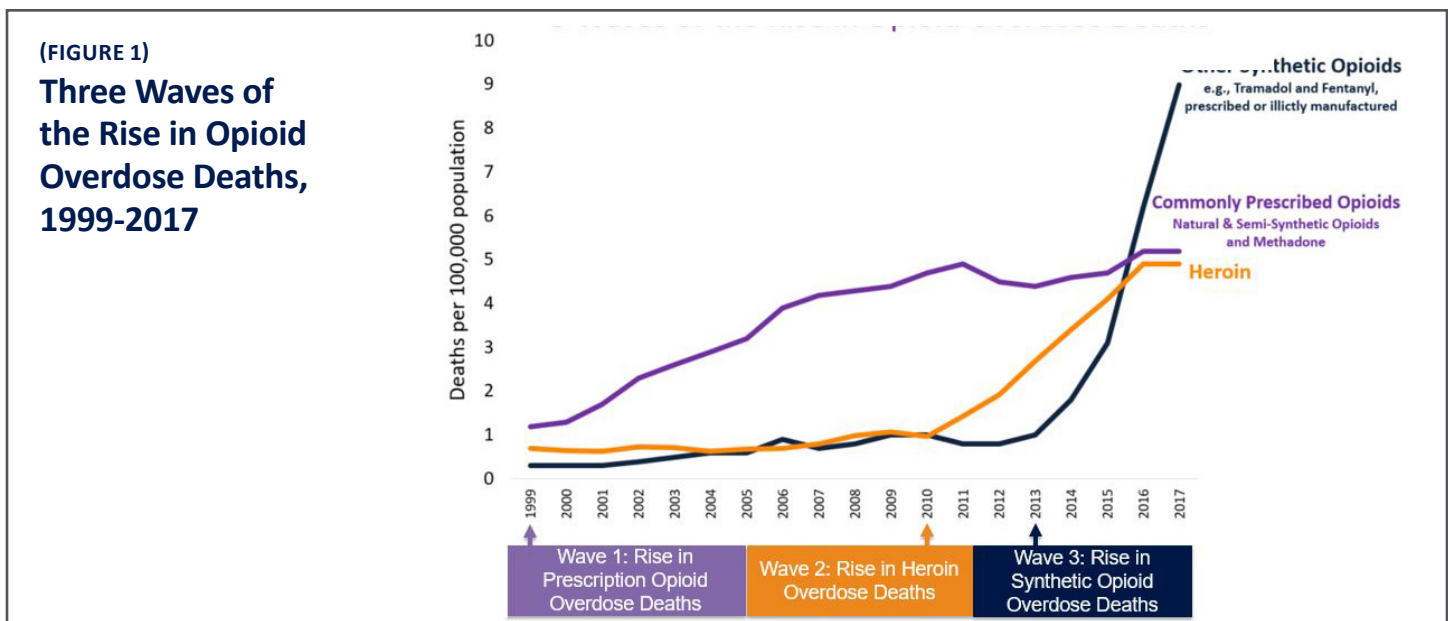
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Introduction

Dentists in Colorado and across the nation continue to face a devastating epidemic of opioid use disorder (OUD) and overdose deaths. Opioids, both prescription and illicit, have become the leading cause of accidental death in the United States for adults 50 years of age or younger.¹ Opioid-related adverse drug events, accidental overdose, physical dependence and the development of OUD have

become an increasingly common part of dental practice. The number of lives impacted by the crisis is astonishing. The Centers for Disease Control and Prevention (CDC) reports that opioid overdose killed nearly 400,000 Americans between 1999 and 2017 (FIGURE 1),² and currently an average of 130 people die every day in the United States of opioid overdose.³



SOURCE: CDC MMWR²

More than 10.3 million people in the United States over the age of 12 years self-reported misusing opioids in 2018, with 9.9 million misusing prescription pain relievers and 808,000 using heroin.⁴ The pharmaceutical use of opioids first skyrocketed between 1990 and 1996; prescriptions for fentanyl rose 1,000%, followed by morphine (49%), oxycodone (15%) and hydromorphone (12%).⁵ The number of prescription opioids sold in the United States increased five-fold between 1999 and 2017, and prescription opioids were involved in 218,000 overdose deaths during this same time.⁵ In 2017, there were 58 opioid prescriptions written for every 100 people in the United States, with an average prescription length of 18 days.⁶

The dire consequences of the widespread availability of prescription opioids in the United States emerged over time. The “lag period” between first exposure to an opioid (either medical or nonmedical) and first treatment admission is, on average, about seven years; the lag period between first exposure and overdose death is between nine and 13 years.^{7,8} In 2017, opioids accounted for 34% of all admissions for substance use disorder (SUD) treatment in people aged 12 years and older.⁹ The economic implications of this epidemic are staggering. The White House Council of Economic Advisers estimates that the full economic cost of the opioid epidemic exceeds one half trillion dollars every year, a figure that represents nearly 3% of the gross domestic product of the United States.¹⁰

Introduction continued

While a number of external factors have contributed to the liberal use of these potentially lethal drugs, the dental community is compelled to acknowledge its role in creating this crisis. Fortunately, clinicians and health care systems also have the power to reverse these grim statistics by reforming their practices with resolve and innovation. Although CO’s CURE acknowledges the value of opioids in certain clinical situations, such as for end-of-life care and the treatment of pain associated with severe trauma, burns and cancer, it advocates using extreme caution in all cases.

These guidelines are meant to inform and augment clinical judgment, not replace it. What follows is a compilation of ideas and suggestions that can be implemented by dentists to aid in the prevention of opioid misuse and addiction and in the identification, treatment and support of patients with OUD. It is unlikely that a dental practice can or should attempt to implement each strategy or idea included in these guidelines. Rather, dentists should consider which of these suggestions are most appropriate given their unique practice settings and resources. The suggestions in these guidelines should not be viewed as a substitute for the oversight of legal counsel and compliance leaders.

The Opioid Epidemic in Colorado

Coloradans have been significantly affected by this national public health crisis. Since 2000, Colorado has seen 6,030 overdose deaths from opioids.¹¹ There were 1,635 prescription opioid-related overdose deaths in Colorado from 2013 to 2017, translating to a rate of 5.8 deaths per 100,000 Colorado residents.¹² Heroin-related opioid overdose deaths increased 76% from 2013 to 2017.¹²

Colorado Statistics

In 2017 in the state of Colorado:

- More than 3.7 million opioid prescriptions were dispensed to one million patients at retail locations (**TABLE 1**). These numbers fell slightly from a high of 4.3 million opioid prescriptions for 1.1 million patients in 2015.¹²
- There were 1,012 drug overdose deaths, 57% of which involved an opioid.¹²
- Fifteen percent of opioid-naive patients were prescribed long-acting opioids.¹³
- Ten percent of patient prescription days had overlapping opioid and benzodiazepine prescription use.¹³
- There were 671.3 opioid prescriptions filled per 1,000 residents.¹³
- There were 134.3 treatment admissions for heroin per 100,000 people and 40.6 treatment admissions for pharmaceutical opioids per 100,000 people.¹

(TABLE 1)

Characteristics of Opioid Prescriptions Dispensed, Colorado 2014-2017

Characteristics	2014	2015	2016	2017
Number of Prescriptions Dispensed	4,039,048	4,310,254	4,159,575	3,765,253
Number of Unique Patients	1,085,551	1,131,781	1,102,297	1,027,685
Number of Unique Prescribers	25,011	24,784	28,063	27,676
Number of Unique Pharmacies	941	839	1,039	1,097

Excludes buprenorphine drugs commonly used to treat opioid use disorder

In 2014 NPI was used to identify unique prescribers and pharmacies as DEA numbers were not available until 2015

Data Source: Colorado Prescription Drug Monitoring Program, Colorado Department of Regulatory Agencies Analysis by: Colorado Department of Public Health and Environment, 2018

SOURCE: Colorado Opioid Profile¹²

Introduction continued

(TABLE 2)

High-Risk Prescribing Practices and Patient Behaviors, Colorado 2014-2017

Indicators	2014	2015	2016	2017	2014-2017 % Change
Patients receiving more than 90 MME (%)	10.3	8.9	8.7	8.2	-20.5
Patients with MPEs (rate/100,000 residents)	170.1	124.0	93.6	68.0	-60.0
Patients prescribed LA/ER opioids who were opioid-naïve (%)	18.2	17.6	15.8	15.1	-17.3
Patient prescription days with overlapping opioid prescriptions (%)	22.3	21.5	21.4	20.5	-7.8
Patient prescriptions days with overlapping opioid and benzodiazepine prescriptions (%)	12.1	11.6	11.2	9.9	-18.0

*Schedule II-IV Controlled Substances
Excludes Buprenorphine drugs commonly used for treatment
Annual percentages are based on average of quarterly percentages
Data Source: Vital Statistics Program, CDPHE and the Colorado Prescription Drug Monitoring Program, DORA
Data Analysis by: CDPHE, 2018*

SOURCE: Colorado Opioid Profile¹²

(FIGURE 2)

Number of Drug Poisoning Deaths by Drug Type, 2000–2018



Categories are not mutually exclusive (may total to more than 100% of total drug overdoses) or comprehensive (other drugs not listed).

SOURCE: Colorado Health Institute¹⁴

Introduction continued

While there is considerable variation between counties in Colorado, with some rural counties particularly hard hit, the impact of the opioid crisis is felt in all regions and communities. No county is untouched, and the need to address the effects of the crisis is universal. All Colorado dentists and health care practitioners must work together to turn the tide and resolve the crisis.

The Origins of the Opioid Epidemic

Concerned about potential adverse effects, including addiction and overdose, few physicians prescribed opioids for chronic noncancer pain throughout most of the 20th century.¹⁵ That changed in 1986, however, when pain expert Russell Portenoy published a limited case series of 38 hospital patients that suggested that chronic noncancer pain could be managed safely with high doses of opioids without posing a risk of addiction.¹⁶ Since then, the scientific validity of Portenoy's original work has been called into question; in recent years, the researcher himself has publicly doubted the relative efficacy and safety of long-term opioid use for the treatment of chronic noncancer pain.^{17–20} Portenoy's findings were endorsed by both the American Academy of Pain Medicine and the American Pain Society, which further legitimized his assertions about the safety of opioid medications.²¹ As a result, many pharmaceutical companies began to aggressively market opioids for wider use at increased dosages and in extended-release formulations.

This shift in perspective was reinforced by the Veterans Health Administration, which adopted pain as the “fifth vital sign” in 1999.²² The Joint Commission, a governing body responsible for hospital accreditation, added pain management as a requirement for accreditation in 2000.^{2,15} During the same period, a report by the Institute of Medicine, *Relieving Pain in America*, painted pain management as a “moral imperative, a professional responsibility, and the duty of people in the healing professions.”²³ In addition to these mounting institutional pressures, patient satisfaction surveys increasingly compelled medical providers to place a premium on

pain management. These highly subjective scorecards, which were routinely linked to remuneration, used the management of pain as a marker for patients' satisfaction with the care they received.^{24,25} The rising popularity of patient satisfaction surveys further fueled opioid prescribing, resulting in a 400% rise in U.S. opioid sales from 1999 to 2014.²⁶ Once reserved for the treatment of severe pain, opioid analgesics became routinely prescribed for a wide range of pain complaints.

In the United States and Colorado, the prescribing practices of dentists and physicians have played a significant role in the development and continuation of the crisis, contributing to alarming rates of misuse, dependence, addiction and overdose. Despite a growing concern with the opioid prescribing practices of dentists, until now there has been no comprehensive set of guidelines for dentists that addresses opioid stewardship, alternatives to opioids for pain, techniques in harm reduction and treatment of OUD. Clinicians have had to rely on their own discretion when treating pain, striking a balance between oligoanalgesia and overuse of opioids. This set of prescribing and treatment guidelines, created by the Colorado Dental Association (CDA) and the CO's CURE team, provides dentists with evidence-based best practices to inform and improve the clinical care of dental patients.

Introduction continued

CO's CURE

Faced with this enormous public health crisis, Colorado clinicians are taking a stand for the benefit of all. CO's CURE is developing the nation's first set of comprehensive, multispecialty medical guidelines designed to end the opioid epidemic. Within each specialty, there is room for specific nuances of practices, and across all CO's CURE guidelines, there is multispecialty collaboration with input from content experts. Four pillars anchor the clinical guidelines and provide an evidence-based pain and addiction management approach:

1. Limiting opioid usage
2. Using alternatives to opioids (ALTOs) for the treatment of pain
3. Implementing harm reduction strategies
4. Improving treatment and referral of patients with OUD

These pillars were conceived by the Colorado Chapter of the American College of Emergency Physicians (ACEP) and published as part of the *Colorado ACEP 2017 Opioid Prescribing & Treatment Guidelines*. When implemented

in 10 Colorado emergency departments (EDs) as part of the Colorado Opioid Safety Pilot by the Colorado Hospital Association, the approach recommended resulted in a 36% decrease in opioid use and a 31% increase in the use of opioid alternatives for pain management.²⁷ The success experienced in Colorado EDs through these initiatives represents one advance in efforts to address the opioid epidemic in Colorado. To fully resolve the opioid epidemic, Colorado clinicians will need to adopt a more inclusive, coordinated and ambitious approach.

Now is the time for all specialties and clinicians to unite in order to create better treatment paradigms for the benefit of patients and communities across Colorado. The guidelines developed by CO's CURE represent some of the most forward-thinking and comprehensive strategies in the nation. They belong to not one specialty, but to all specialties; rather than divide clinicians into their respective tribes and silos, they unite them in a common cause—to resolve the opioid epidemic in Colorado and beyond.



Limiting Opioid Use in Dental Practice



Limiting Opioid Use in Dental Practice

The majority of patients who develop OUD report that their first exposure to an opioid involved a pain medication that was prescribed to them or diverted from a family member or friend.²⁶ Few would dispute that opioids have a vital role to play in the treatment of pain related to trauma, burn, cancer and many dental and general surgical procedures. And while the majority of the millions of dental patients who are prescribed opioid analgesics do not misuse them or develop OUD, the current epidemic demonstrates that the important minority of patients who do experience profound harm mean that dental and medical clinicians must reevaluate their opioid prescribing practices. The American Dental Association (ADA) has expressed its support of all efforts by dentists to address the opioid epidemic; limiting excessive and inappropriate prescription of opioids in dental practice is a key element of that approach.²⁸

Dentists are among the top prescribers of opioids in the United States and are leading prescribers of opioids to adolescents.²⁹ From 2016 to 2017, dentists comprised 15.8% of all prescribers of opioid medications, second only to internal medicine physicians, and accounted for 8.6% of all dispensed opioid prescriptions in the United States in that time period.³⁰ Recent research suggests that as many as 6% of opioid-naïve patients who receive an opioid prescription may go on to persistent use of opioids.^{31,32} A review of claims data of more than one million commercially insured opioid-naïve patients who filled an opioid prescription between 2005 and 2015 revealed rates of persistent opioid use at one and three years of 6% for patients who received one day of opioid analgesia, 13.5% for persons whose first episode of use was for ≥ 8 days and 29.9% in opioid-naïve patients whose first episode of use was for ≥ 31 days. A review of data for more than 36,000 opioid-naïve surgical patients found that rates of persistent opioid use were 5.9% in patients undergoing minor procedures and 6.5% in patients undergoing major procedures. The fact that these rates are not significantly impacted by the magnitude of the surgical procedure suggests that patient factors heavily influence risk of persistent opioid use. This in turn suggests that careful screening for an elevated risk of developing OUD may help protect vulnerable dental patients.³³ That said, dentists must recognize that virtually any dental patient

who is exposed to opioid analgesia—particularly at higher doses and longer duration—is at risk for dependence and addiction.

While management of dental pain is essential, a growing body of evidence suggests that dentists over rely on opioid analgesia.³⁴ Research finds that, on average, dentists prescribe significantly more opioid pills than their patients use. A 2015 study³⁵ found that median consumption of opioids during the first 24 hours following third molar extraction was reported to be three tablets, and the median total consumption for the seven days following extraction was eight tablets; in contrast, the median quantity of opioids prescribed was 20 pills, with a range between 10 and 40 pills.³⁵ A 2016 study found that more than 40% of U.S. residents are prescribed an opioid following tooth extraction, with the rate of prescription to adolescents (61%) inexplicably higher than that of prescription to adults.³⁶ A study comparing rates of opioid prescribing in dental practice in the United States and the United Kingdom found that the proportion of dental prescriptions written for opioids is 37 times higher in the United States than in the United Kingdom, 22% in the United States vs 0.6% in the U.K.³⁷ The authors acknowledge several key contributors to this difference,³⁸⁻⁴² including that dentists in the United Kingdom are limited by their National Health Service formulary and that codeine is the only opioid they are permitted to prescribe.

Because of the pain associated with many dental surgical procedures, dental specialists play a pivotal role in changing dental opioid prescribing.⁴³ Studies of patients undergoing common general surgical procedures find that, on average, general surgeons prescribe twice the quantity of opioid pills their patients report actually using.^{32,44-47} While there are fewer studies examining the mismatch between dental opioid prescribing and what patients actually require, a 2016 study of patients undergoing tooth extraction similarly found that more than half of opioid pills went unused.^{35,48-50} A review of opioid prescribing by dentists between 2011 and 2015 found that as much as half of dental opioid prescribing exceeds the doses and/or durations recommended by national guidelines.⁵¹ Over prescription of opioids contributes to

Limiting Opioid Use in Dental Practice continued

an enormous reservoir of unused opioids that is ripe for later misuse and diversion.^{35,50} This reservoir of unused and undiscarded opioids poses a grave threat to public health, as nonmedical use and diversion are a prime driver of the opioid epidemic. Researchers estimate that as much as 23% of opioids prescribed by medical and dental professionals are used nonmedically.⁴⁹

While many dentists have made strides in curtailing opioid prescribing, there remain opportunities for further reform. A large study of opioid prescribing practices across specialties found that dental opioid prescribing fell from 2007 to 2012 by 6%,^{52,53} a reduction surpassed only by ED physicians.⁵² In the five years that followed, dentists were leaders in reducing their rates of opioid prescription, writing nearly half a million fewer opioid prescriptions in 2017 compared to 2012, dropping from 18.5 million in 2012 to 18.1 million in 2017.⁵⁴ Dentists are encouraged to build on the impressive progress these data represent.

Until recently, no dental opioid discharge prescribing guidelines have been available, a deficit that has forced dentists and dental specialists to rely on customary prescribing practices learned in training.^{55,56} As a result, there is wide variability among individual dentists in opioid prescribing patterns. A retrospective study of opioid prescribing after third molar extraction in 2.7 million Medicaid claims found an approximately three-fold difference between the 10th and 90th percentile in the oral morphine equivalents prescribed.³⁶ Small studies of the impact of opioid prescribing guidelines on dental prescribing practice finds that adherence to guidelines reduces both overall opioid prescribing and interprescriber variability.⁵⁵ While the ADA has yet to formulate opioid prescribing guidelines, states and academic dental researchers are beginning this important work based on what patients report actually consuming after common dental procedures. Research in general surgical patients finds no correlation between patient satisfaction or pain relief and the quantity or duration of opioid prescriptions they receive, suggesting that dentists, like general surgeons, may curtail their opioid prescribing without sacrificing analgesia or patient satisfaction.⁵⁷

Across all specialties, a commonsense first step to addressing the opioid epidemic is to prescribe opioids more judiciously. Dentists have a vital role to play in ending the crisis by screening patients, using alternatives to opioids and multimodal analgesia, prescribing opioids conservatively and providing counsel on the risks of opioid analgesia.

Practice Recommendations

1. Opioids are dangerous drugs with significant potential for misuse and addiction, numerous side effects, rapid development of tolerance, debilitating withdrawal symptoms and lethality in overdose. Dentists are encouraged to reserve opioids for the treatment of pain that has not responded to multimodal nonopioid therapy and for patients in whom nonopioid therapy is contraindicated or anticipated to be ineffective.

- a. Opioids are among the three broad categories of medications with potential for misuse, dependence and addiction, the other two being central nervous system (CNS) depressants and stimulants. Opioids act by attaching to opioid receptors on nerve cells in the brain, spinal cord, gastrointestinal (GI) tract and other organs, triggering a spike in dopamine that not only reduces the perception of pain but can also manufacture a powerful sense of well-being and pleasure by affecting the brain's limbic reward system.
- b. When used repeatedly, opioids induce tolerance, as exposure to opioids leads to loss of receptor activity and higher doses are required over time to produce the same effect.^{58,59} This mechanism also contributes to the high risk of overdose following a period of abstinence.⁶⁰ Tolerance can be lost in times of abstinence, and exposure to a previously "safe" dose can lead to disastrous results.⁶¹
- c. The effects of opioids are mediated by specific subtype opioid receptors (μ , δ and κ) that are also activated by endogenous endorphins and enkephalins. The production of endogenous opioids is inhibited by the repeated administration of outside opioids, which accounts for the discomfort that ensues when the drugs are discontinued.

Limiting Opioid Use in Dental Practice continued

- d. Opioid therapy is associated with a number of common and sometimes serious side effects, including sedation, respiratory depression, constipation, nausea and vomiting, impaired judgment and coma (TABLE 3).^{27,62} These complications, which often necessitate additional medical care, can prevent patients from performing daily tasks and remaining active in the workforce.
- e. In addition, opioids can impair immune responses, impact NK and T-cell function and promote angiogenesis. There is evidence that for some malignancies, opioids may act directly on tumor cells to promote growth and metastasis.
- f. Genetic variation, particularly in the cytochrome P450 2D6 (CYP2D6) enzyme, creates significant patient variability in the metabolism of many opioids.^{63–65} This variability leads to increased rates of opioid-related adverse effects for some patients and undertreatment of pain for others.
- g. Opioid-induced hyperalgesia (OIH) is a paradoxical phenomenon of increased sensitivity to noxious stimuli associated with long-term opioid use. Evidence suggests that even short-term exposure to opioids may produce OIH.^{66,67}
- h. Given the risks associated with opioid use, the risk-to-benefit ratio does not support the use of opioids in low-severity pain management if nonopioid alternatives are viable options, especially given that nonopioid analgesics, including acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), have been shown to be as or more effective than opioid medications in managing pain.^{33,68–71}

(TABLE 3)

Common and Serious Side Effects of Opioid Analgesia

Common Side Effects	Serious Side Effect of Chronic Opioid Use
<ul style="list-style-type: none"> • Nausea/vomiting • Constipation • Pruritus • Euphoria • Respiratory depression, particularly with the simultaneous use of alcohol, benzodiazepines, antihistamines, muscle relaxants or barbiturates • Lightheadedness • Dry mouth 	<ul style="list-style-type: none"> • Cardiac abnormalities, including prolonged QTc and torsades de pointes • Sudden cardiac death with the concomitant use of benzodiazepines and methadone • Hormonal disruptions, including decreased testosterone in males • Decreased luteinizing hormone, follicle-stimulating hormone, and fertility in women • Musculoskeletal compromise, including an increased risk of osteoporosis • Immunosuppression • Inhibition of cellular immunity via delta and kappa receptors • Hyperalgesia (i.e., upregulation of receptors and increased tolerance) • Sleep disturbances (e.g., shortened deep sleep cycle) • Delayed or inhibited gastric emptying, increased sphincter tone, and blockade of peristalsis

SOURCE: Martin PR, Hubbard JR. Substance-related disorders. In: Ebert MH, Loosen PT, Nurcombe B: Current Diagnosis & Treatment in Psychiatry. New York: McGraw Hill; 2000:233-259.⁶²

Limiting Opioid Use in Dental Practice continued

2. It is recommended that dental pain be addressed through clinical intervention rather than via opioid analgesia.

- a. Dentists best serve patients in pain by performing definitive treatment.
- b. Dentists are encouraged to refer patients without insurance or with financial constraints to low-cost or free dental care. Pain may prompt patients to self-medicate with illicitly obtained pain relievers.
 - i. The CDA supports Colorado dental charities and nonprofit dental clinics throughout the state. These organizations offer dental care on a sliding-fee scale to individuals who are unable to afford treatment. Several of these organizations have financial and residency requirements. Others are established to help a certain portion of the population (e.g., children, people experiencing homelessness and people with disabilities).
 - ii. The CDA maintains a directory of clinics that provide low-cost dental care in Colorado (<https://cdaonline.org/welcome/lowcostcare/>).
- c. It is advised that patients with acute dental pain be managed with nonopioid analgesia until they receive definitive care. Nerve blocks with long-acting local anesthetics and/or scheduled acetaminophen/NSAID are preferred to brief courses of opioid analgesia. (See Alternatives to Opioids for the Treatment of Pain section for more information.)

3. It is recommended that Colorado dentists review the information contained in the Colorado Prescription Drug Monitoring Program (PDMP) prior to prescribing an opioid in order to inform decision-making around opioid therapy. Dentists are required to register with the PDMP and may incur fines for failure to do so; more importantly, failure to register for and consistently use the PDMP undermines the utility of this valuable resource.

- a. Per House Bill (HB) 14-1283, all Colorado-licensed prescribing practitioners with Drug Enforcement Administration (DEA) registrations are required to create an account with the Colorado PDMP.⁷²
 - i. The Colorado Dental Board has fines starting at \$1,250 that may be imposed on dentists who fail to complete the PDMP registration.⁷³
 - ii. As of July 2019, approximately 1,000 (20%) of the 4,500 dentists with active licenses in Colorado with a DEA license had not created a PDMP account. In addition, nearly 1,500 dentists (30%) who have a PDMP account have not logged on for more than two years.⁷⁴
 - iii. Dentists can register at <https://www.colorado.gov/dora-pdmp> with a dental license number and other pieces of identifying information. For questions about the PDMP registration process, contact the PDMP help desk at 855-263-6403 or visit <https://www.colorado.gov/pacific/dora/PDMP>.
- b. PDMPs provide records of controlled substances dispensed to individual patients and may inform prescribing, coordination of care and addiction screening or referral. Information from a PDMP can identify patients with multiple preexisting opioid prescriptions from various providers (“doctor shopping”) and identify those already using other controlled medications on a chronic basis.⁷⁵
- c. The ADA recommends that dentists register with and use PDMPs to promote the appropriate use of opioids and deter misuse and diversion.⁷⁶ The American Association of Oral and Maxillofacial Surgeons (AAOMS) advises that accessing PDMPs is a key element of responsible prescribing of opioids.⁷⁷

Limiting Opioid Use in Dental Practice continued

- d. The Journal of the American Dental Association (JADA) has published a comprehensive guide to use of the PDMP, *The prescription monitoring program data: What it can tell you.*
 - e. Colorado law requires dentists to check the PDMP prior to issuing a second (or subsequent) prescription for an opioid.
 - f. PDMPs have been found to significantly reduce both the frequency and quantity of dental opioid prescribing.⁷⁸
 - i. A cross-sectional study of patients prescribed opioids at a dental urgent care in New York state before and after legislation of mandatory PDMP use found a decrease in rates of opioid prescribing from 30% to 9.6% as well as a 78% reduction in total quantity of pills prescribed.⁷⁸
 - ii. Drug monitoring programs have been shown to influence opioid prescribing practices, especially in the case of lost or long-term prescriptions.⁷⁹
 - iii. PDMP data can guide policy and professional reform by providing information on prescribing patterns in a state. A review of PDMP data in South Carolina found that a notable minority of dental patients had incidents of multiple preexisting opioid prescriptions, a factor implicated in patient misuse, overdose and diversion. In rare cases, the PDMP can identify fraudulent prescribers.⁸⁰
 - g. PDMP data may prompt a referral to an addiction medicine specialist, consultation with a pain management specialist and/or referral to harm reduction services.
 - h. Information from the PDMP may not necessarily preclude the use of opioids for treatment of acute or postoperative dental pain, but it is advised that such information be incorporated in analysis of the risks and benefits of opioid therapy.
 - i. In the case of on-call coverage, it is recommended that the on-call dentist check the PDMP for any requests for additional opioid prescriptions by a patient, even if it is the on-call dentist's first prescription for the patient.
 - j. Dentists are discouraged from dispensing controlled substances directly from their clinics. In addition to the increased responsibility of complying with complicated regulatory requirements in place for direct dispensing, opioid dispensing that is not captured by the PDMP undermines the power and utility of this vital program.
- 4. Prior to prescribing an opioid, it is suggested that dentists perform a rapid risk assessment to screen for potential for misuse and addiction and obtain a complete medical history to identify medical comorbidities that increase the risk of opioid-related adverse events.**
- a. Dentists are reminded that any patient may be at risk of opioid misuse and addiction. Multiple organizations and agencies, including the ADA, CDC and Colorado Department of Regulatory Agencies (DORA), advocate using a validated screening instrument to evaluate for factors that might predispose patients to addiction and misuse. The following screening tools may help dentists identify high-risk patients:⁸¹
 - i. Opioid Risk Tool
 - ii. NIDA Quick Screen
 - iii. Screener and Opioid Assessment for Patients with Pain – Revised (SOAPP-R)
 - iv. Pain Medication Questionnaire (PMQ)
 - b. The ADA recommends that dentists obtain a substance-use history prior to prescribing an opioid. While more than three-quarters of dentists use patient history forms that inquire about illicit drug use—an increase from 64% in 2010—relatively few dentists practice active risk mitigation when prescribing opioids.^{80,82} A 2015 survey of dentists found that two-thirds of dentists did not feel that screening for SUD is compatible with their professional role.⁸² More recent dental school graduates were more likely to view SUD screening and risk mitigation as within the scope of dental practice.⁹
 - c. While screening instruments are imperfectly sensitive, evidence strongly suggests that clinical impression alone fails to identify patients at elevated risk for misuse and addiction.⁸³

Limiting Opioid Use in Dental Practice continued

- d. The stigma surrounding SUD causes many patients to conceal their condition. An empathic, nonjudgmental approach to the patient interview increases the likelihood of obtaining a full, accurate patient history.
- e. In addition to incorporating the patient’s substance use history, it is recommended that screening for elevated risk of misuse or OUD also assess for the following risk factors.^{84,85}

High-risk criteria include:

Personal or family history of SUD (alcohol, tobacco, illicit drugs, prescription drugs)
Age between 16 and 45
History of or current behavioral health disorder (<i>e.g., depression, anxiety, attention deficit disorder, bipolar disorder, schizophrenia</i>)
History of past trauma, physical or sexual abuse or other adverse childhood events

- f. In addition to screening for risk of misuse and OUD, dentists are encouraged to assess a patient’s medical history for comorbid health conditions that increase the risk of opioid-related adverse effects and exercise caution when prescribing opioids to those at increased risk for adverse drug reactions, particularly respiratory depression and accidental overdose.

Medical comorbidities and patient factors that increase risk of opioid-related adverse drug events:

Pulmonary comorbidities (chronic obstructive pulmonary disease [COPD], obstructive or central sleep apnea)	Cardiac comorbidities (congestive heart failure)
Organ dysfunction (<i>e.g., renal or hepatic</i>)	Age greater than 65
Prior SUD diagnosis (including alcohol use disorder) ⁸⁶	Current or past tobacco smoker
Obesity (BMI ≥ 30 kg/m ²)	Use of supplemental oxygen
Receiving chronic opioid therapy (COT) for pain	Use of benzodiazepines, gabapentinoids or other sedatives ⁸⁶

- g. A full understanding of a patient’s current medications is essential to assessing risk of opioid-related adverse events. It is advisable to ask patients specifically about current or past opioid, benzodiazepine, or sedative/hypnotic use prior to prescribing an opioid.
- h. Dentists are encouraged to obtain medical records from a patient’s primary care provider when there is a concern that that patient is not able to provide a full, accurate medical history.
- i. Patients receiving chronic opioid therapy (COT) for pain and patients receiving buprenorphine or methadone for treatment of OUD require careful management. Dentists are encouraged to coordinate care with the patient’s COT or medication for addiction treatment (MAT) provider to optimize dental outcomes and minimize the risk of adverse events. **(SEE TABLE 10, MANAGING ACUTE AND PERIOPERATIVE DENTAL PAIN IN PATIENTS RECEIVING MAT, IN THE ALTERNATIVES TO OPIOIDS FOR THE TREATMENT OF PAIN SECTION.)**

Limiting Opioid Use in Dental Practice continued

5. Dentists are encouraged to educate patients and families or caregivers about the potential risks and side effects of opioids and the alternative pharmacologic and nonpharmacologic therapies available for managing pain. It is recommended that all patients who receive opioids be educated about their side effects and potential for addiction.

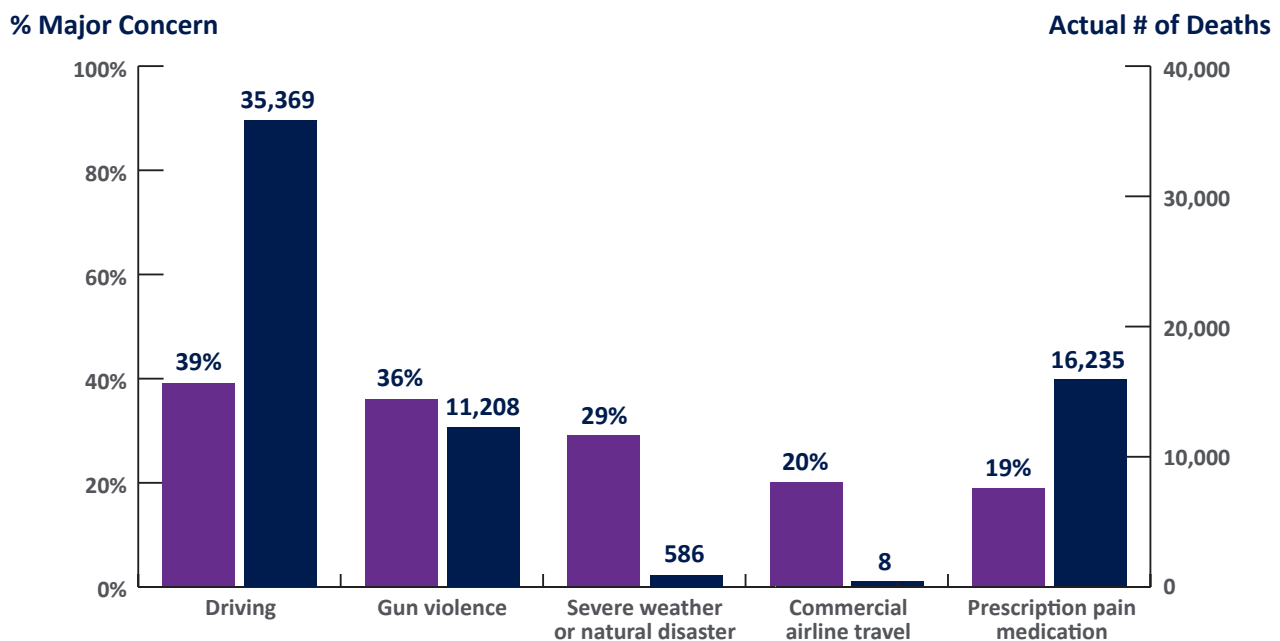
- a. Evidence suggests (FIGURE 3) that patients are often not aware of the risks associated with opioid medications or that there may be equally effective pharmacologic and nonpharmacologic alternatives to opioids available for treatment of pain.
- b. The ADA *Mouth Healthy* patient-facing materials are a valuable resource dentists can use to educate patients and families on the risk of opioid analgesia.

- c. Other materials for patients and families include:
 - i. [Managing Pain After Dental Care](#) (Michigan OPEN [Opioid Prescribing Engagement Network])
 - ii. [Learn the Facts: Opioids and Dental Pain Management](#) (Michigan OPEN)
 - iii. [Opioids and Wisdom Tooth Removal](#)
 - iv. [Patient Guide to Over-the-Counter Medications](#)
- d. When prescribing these agents, it is always appropriate to initiate a detailed discussion about the significant risks of adverse effects and addiction associated with opioids (TABLE 3).
- e. Dentists are advised to counsel their patients that while a prior history of SUD, other behavioral health conditions and younger age all increase this potential, an opioid-naïve patient with no risk factors can develop misuse, dependence or addiction.^{87,88}
- f. It is recommended that dentists inform their patients that they may request nonopioid therapy, even for severe pain.

(FIGURE 6)

Public Perception of Opioid Risk

Fewer than one in five Americans consider prescription pain medication to be a serious safety threat.



SOURCE: What Americans believe about opioid prescription painkiller use. Presented at the: National Safety Council — Opioid Painkiller Media Briefing; 2015. <https://www.nsc.org/Portals/0/Documents/NewsDocuments/031115-PublicOpinion-Poll.pdf>. Accessed December 16, 2019.⁸⁹

Limiting Opioid Use in Dental Practice continued

6. If the decision is made to prescribe an opioid, dentists are advised to use the lowest effective opioid dose for the shortest possible duration.

- a. Receiving higher intensity and/or longer duration opioid therapy for acute pain has been associated with an increased risk of opioid-related adverse effects, long-term disability and long-term opioid use.^{90–92} There is significant evidence that higher doses of opioid therapy are associated with higher incidence of sedation, respiratory depression and overdose death in a range of settings.^{93,94}
- b. Per the AAOMS, “When indicated for acute breakthrough pain, consider short-acting opioid analgesics. If opioid analgesics are considered, start with the lowest effective dose and the shortest duration possible.”⁷⁷
- c. For patients with acute dental pain or postprocedural pain, initial opioid prescriptions of a three-day supply or shorter will generally be sufficient.
- d. It is recommended that an initial prescription to an opioid-naive patient not exceed 50 morphine milligram equivalents (MME)/day, as risk of overdose in an opioid-naive patient outweighs potential benefit at higher dosages.
- e. In Colorado, Senate Bill (SB) 18-022 Clinical Practice for Opioid Prescribing limits first-time opioid prescriptions for acute noncancer pain to seven days, with the ability to add a discretionary second (or subsequent) seven-day fill only after the PDMP has been checked.
- f. The ADA in a 2018 policy statement supported statutory limits on opioid dosage and duration of no more than seven days for the treatment of acute pain, consistent with the CDC evidence-based guidelines.⁵⁴
- g. For acute pain outlasting initial opioid prescription, it is recommended that dentists reevaluate patients in person to assess for complications. Prior to prescribing additional opioids, it is advised that the working diagnosis and management approach be reconsidered; as part of this review, consider rescreening patients with a risk assessment tool. Dentists are encouraged to complete additional patient education prior to prescribing additional opioids.

h. Unused opioids create the possibility of intentional or unintentional opioid diversion.^{48,95} By one estimate, 23% of prescription opioids are used nonmedically.⁴⁹ In addition to minimizing risk to the patient, minimizing the durations and doses of opioid prescription protects others from the harms associated with misuse of diverted opioids.

7. If opioids are required, dentists are advised to prescribe immediate-release formulations. The initiation of long-acting and extended-release formulations for treatment of acute pain is strongly discouraged.

- a. Long-acting and extended-release opioids are indicated only for chronic pain and it is advised they not be used for the treatment of acute or intermittent symptoms.⁹⁶
- b. These agents are especially dangerous in opioid-naive patients, even at recommended dosages, as they are associated with increased risk of overdose.
- c. Long-term opioid use is nearly 4.5 times higher in those started on long-acting opioids compared to immediate-release.³¹
- d. The AAOMS recommends that oral and maxillofacial surgeons avoid initiating treatment with long-acting and extended-release opioid analgesics.⁷⁷
- e. Discontinuation of long-acting and extended-release opioids in patients who take these medications regularly for chronic pain is not recommended. The baseline opioid requirements of patients on COT must be met prior to addressing acute pain.
- f. Dentists are cautioned that tramadol is not a “safe” opioid. Widely viewed as a less potent opioid, clinicians often prescribe tramadol in an attempt to avoid “stronger” medications. While tramadol is a Schedule IV drug—a factor that may help reinforce this view—wide variations in the pharmacogenetics of tramadol metabolism can result in significant individual differences in adverse and analgesic effects,⁹⁷ including seizures and dangerous drug interactions not seen with other opioids. It is important to note that tramadol carries a risk of persistent opioid use that is equal to or greater than that of other opioids.^{31,98}

Limiting Opioid Use in Dental Practice continued

(TABLE 4)

Examples of Long- and Short-Acting Opioids

NOTE: Opioid products with a single ingredient (e.g., oxycodone) are favored over combination formulations (e.g., oxycodone/acetaminophen), as patients are encouraged to take nonopioid analgesics (e.g., acetaminophen, NSAID) consistently prior to resorting to an opioid. Use of monoproducts allows acetaminophen or NSAID to be taken preferentially and used as a first-line agent with a lower risk of suprathreshold dosing or accidental poisoning. Combination products are indicated by asterisk (*) below.

Short-acting opioids include but are not limited to the following agents:

- HYDROCODONE — immediate release (e.g., Vicodin,* Lorcet,* Lortab,* Norco*)
- HYDROMORPHONE — immediate release (e.g., Dilaudid)
- MORPHINE — immediate release
- OXYCODONE — immediate release (e.g., Percocet,* Percodan,* Roxicodone)
- OXYMORPHONE — immediate release (e.g., Opana)
- TRAMADOL — immediate release (e.g., Ultracet,* Ultram); note caution stated in point 7f, above
- TAPENTADOL — immediate release (e.g., Nucynta)

It is recommended that long-acting and extended-release formulations not be prescribed for acute pain. Examples include but are not limited to the following agents:

- FENTANYL — transdermal (e.g., Duragesic)
- HYDROCODONE — extended release (e.g., Hysingla ER, Zohydro ER)
- HYDROMORPHONE — extended release (e.g., Exalgo)
- METHADONE (e.g., Dolophine)
- MORPHINE — sustained release (e.g., MS Contin, Avinza, Kadian)
- OXYCODONE — sustained release (e.g., OxyContin)
- OXYMORPHONE — extended release (e.g., Opana ER)
- TRAMADOL — extended release (e.g., Ultram ER); note caution stated in point 7f, above
- TAPENTADOL — extended release (e.g., Nucynta ER)

** denotes combination product*

Limiting Opioid Use in Dental Practice continued

8. Dentists are advised to avoid prescribing opioids to patients already taking benzodiazepines, gabapentinoids, barbiturates or other CNS depressants. If an opioid is prescribed, it is recommended that patients be counseled on the increased risk of respiratory depression, adverse drug reactions and death with concurrent use.

- a. Patients taking opioids and benzodiazepines concurrently have 10 times the risk of fatal overdose compared to those taking opioids alone.¹⁰⁰
- b. Per the AAOMS, clinicians are encouraged to “limit the prescriptions of opioid analgesics to patients currently taking benzodiazepines and/or other opioids because of the risk factors for respiratory depression.”⁷⁷
- c. The risk of adverse events may also be increased by concurrent use of other medications with CNS depressant properties, including but not limited to nonbenzodiazepine sedative-hypnotics, muscle relaxants, gabapentinoids, sedating antidepressants, antipsychotics and antihistamines.^{57,94,101}
- d. For some patients these combinations are unavoidable, as routine discontinuation of long-standing medications is not possible given the risks of withdrawal or the worsening of an underlying condition for which these medications are prescribed. In these cases, dentists are strongly advised to maximize use of nonopioid multimodal analgesia.
 - i. It is recommended that patients receiving concurrent prescriptions for CNS depressants and opioids also be prescribed naloxone (**SEE HARM REDUCTION SECTION**).

9. Dentists are advised to educate dental patients who receive prescriptions for opioids on the risks and proper use of opioids as well as the safe storage and disposal of unused medications.

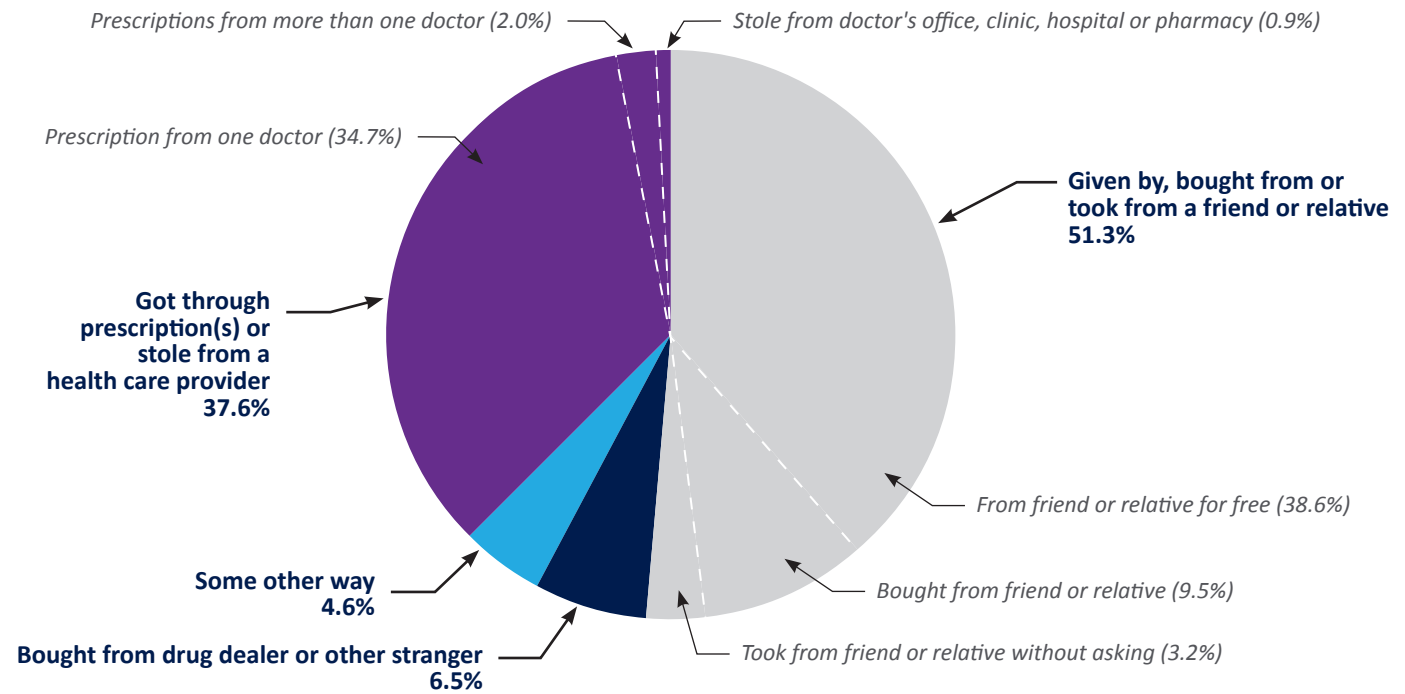
- a. It is recommended that patients be instructed on how to take opioids correctly, including the planned medication, doses and schedule. Clear and concise patient instructions reduce the risk of opioid-related adverse events. It is suggested that patient instructions include the following directions:
 - i. Take the minimum quantity of opioid necessary to achieve tolerable levels of pain and meaningful functional improvement. Take opioids on an “as-needed” rather than scheduled basis.
 - ii. Reduce the dose and/or frequency of opioid analgesic as pain and function improve.
 - iii. Avoid agents that may potentiate the sedative effect of opioids, including sleeping medications, sedatives and alcohol.
 - iv. Avoid driving or operating heavy machinery while taking opioids.
 - v. Seek help at first sign of any adverse effects or signs of tolerance, dependence or addiction.
- b. It is recommended that patients be instructed in proper storage of medication to safeguard against diversion.
 - i. Patients may be educated that over half of the opioids prescribed from dental surgeries are not used, creating opportunities for diversion of these medications and that more than half of people who misuse opioids receive them from friends and/or family.^{35,48,50}
 - ii. Patients may be educated that it is safest to store opioids in a locked location. If that is not possible, patients are advised to store opioid medications in a place out of reach of children and not easily accessed by visitors or other household members. (Experts advise against storing opioids in medicine cabinets.)

Limiting Opioid Use in Dental Practice continued

(TABLE 4)

Where Pain Relievers Were Obtained for Most Recent Misuse Among People Aged 12 or Older Who Misused Pain Relievers in the Past Year: 2018

9.9 Million People Aged 12 or Older Who Misused Pain Relievers in the Past Year



NOTE: Respondents with unknown data for the source for most recent misuse or who reported some other way but did not specify a valid way were excluded.

SOURCE: SAMHSA NSDUH 2018¹⁰²

c. Once the acute pain phase has ended and medication is no longer required, it is critical that patients promptly dispose of unused opioids. Dentists are encouraged to provide patients with the following information:

- i. Patients should not retain unused opioids for potential later use.
- ii. Unused medication should be discarded through a safe disposal program. Many hospitals, pharmacies and police departments in Colorado have take-back programs, and the DEA sponsors national take-back days <https://takebackday.dea.gov/>.
- iii. An interactive map of collection box locations can be found at www.takemededback.org.
- iv. All but one of the counties in Colorado offer safe disposal sites for controlled substances, and the number of these facilities is increasing rapidly.

The Colorado Department of Public Health and Environment provides an interactive map of safe disposal locations in Colorado.

- v. If disposing of the medication at home, patients should:
 1. Remove the medication from its original container and remove any labels or cross out identifying information.
 2. Mix the pills with an inedible substance (e.g., kitty litter, coffee grounds, sawdust, home cleanser, etc.).
 3. Place the mixture in a sealable bag, empty can or other durable container that prevents leakage.
 4. Wrap the container in newspaper or a plain brown bag to conceal its contents. Place it in the trash the day of trash collection.

Limiting Opioid Use in Dental Practice continued

- vi. The FDA allows opioids to be flushed down a toilet; however, more environmentally responsible disposal methods are encouraged.¹⁰³
 - d. Dental offices may offer opioid take-back services only if they obtain additional DEA registration status and adhere to significant compliance standards.
 - e. Additional Resources:
 - i. <http://www.Takemedsseriously.org>
 - ii. <http://www.corxconsortium.org/wp-content/uploads/Safe-Disposal-Brochure.pdf>
 - iii. http://www.deadiversion.usdoj.gov/drug_disposal/takeback/index.html
 - f. Dentists are encouraged to ask patients about their existing supplies of opioids from prior prescriptions and to advise patients to dispose safely of unused opioids.
- 10. Dentists are advised to minimize the prescription of opioids to adolescents, a group particularly susceptible to misuse and addiction.**¹⁰⁴
- a. Opioid exposure via a dental procedure in adolescence is associated with increased risk of subsequent aberrant opioid use.¹⁰⁴
 - b. For adolescents and young adults who are undergoing minor surgical procedures (e.g., third molar extraction), dentists may consider prescribing only scheduled NSAID and acetaminophen and nonpharmacologic interventions for pain management.
 - c. If the decision is made to prescribe an opioid, dentists are encouraged to prescribe the minimum quantity of opioid pills anticipated to be necessary; for the majority of patients, four to six tablets of oxycodone 5 mg (or equivalent) will be adequate. **(SEE TABLE 8, MULTIMODAL ANALGESIC PROTOCOLS FOR COMMON DENTAL PROCEDURES.)**
 - d. Dentists are encouraged to obtain informed consent from a parent or legal guardian before prescribing an opioid to a minor and explain that:
 - i. Use of opioid analgesia increases risk of addiction, particularly for adolescents with existing SUD or other behavioral health conditions and for adolescents with a family history of SUD or other behavioral health conditions.
 - ii. Exposure to even a short course of opioids is associated with increased risk of adverse effects, including nausea, vomiting, sedation, respiratory depression and overdose.
 - iii. Diversion of controlled substances by and to adolescents poses a significant risk, and opioid medications should be stored in a safe—ideally locked—location.
 - iv. Prompt disposal of unused opioids is essential for patient and community safety.
 - v. Scheduled concurrent use of an NSAID and acetaminophen provides better pain relief than opioid analgesics do. Dentists may educate parents that continuing scheduled use of nonopioid analgesics concurrent with use of an opioid for “breakthrough” pain will reduce overall opioid requirements.
 - e. Pharmacogenomic variation in opioid metabolism contributes to unpredictable response to a number of opioid medications. Codeine and tramadol are contraindicated in children younger than 12 due to variability in metabolism. It is recommended that the use of codeine and tramadol generally be avoided in those aged 12 to 17 as well, given the availability of safer, more effective medications.¹⁰⁵
 - f. Dentists are advised to consider potential opioid misuse and addiction in the risk-benefit analysis for third molar extraction and include this factor in any documentation provided to patients and parents or guardians.

Limiting Opioid Use in Dental Practice continued

11. Dentists are encouraged to review and incorporate information gained from PDMP prescriber reports, the CDA and other professional organization surveys and the opioid prescribing guidelines presented below to ensure that their prescribing patterns align with best practice recommendations. Dental practices and organizations may strongly consider collecting and sharing opioid prescribing patterns among their members to increase awareness among dentists who overprescribe opioids, educate on best practices in pain management and reduce opioid prescribing variability.

- a. Opioid prescribing patterns vary significantly among dentists. Knowledge of both an individual's current prescribing patterns and recommended prescribing and pain management guidelines is critical for reducing excessive opioid prescribing and interprescriber variability.¹⁰⁶
- b. Dentists are encouraged to respond to and examine the results of annual member surveys on opioid prescribing practices that are conducted and published by several professional organizations, including the CDA and the AAOMS.
- c. Dentists in group practices are encouraged to track members' prescribing patterns and provide comparative data to those within the practice.
- d. This information should not be used punitively but rather to help dentists understand their own treatment habits and facilitate change, if appropriate.

12. Dentists are advised to coordinate care of patients on COT with the patient's primary care clinician and/or pain specialist whenever possible.

- a. Per the AAOMS, oral and maxillofacial surgeons are encouraged to "address exacerbations of chronic or recurrent pain conditions with nonopioid analgesics, nonpharmacologic therapies and/or referral to specialists for follow-up, as clinically appropriate."⁷⁷
- b. Ideally, patients with non-dental chronic pain will receive opioid medications from one practice, preferably their primary care provider or pain specialist.
- c. In order to honor previous patient-physician agreements regarding opioid use, dentists are advised to consult with the patient's COT prescriber prior to prescribing an opioid for acute dental pain.

13. Dentists are discouraged from prescribing opioid analgesia to manage chronic dental pain. It is recommended that dentists collaborate with a patient's primary care provider or an appropriate specialist to ensure that patients with chronic orofacial pain are evaluated and receive appropriate care. Dentists are encouraged to establish relationships with pain specialists for direct referral of patients with chronic orofacial pain.

- a. In their oral health topic statement *Oral Analgesics for Acute Dental Pain*, the ADA defines chronic pain as pain lasting longer than three months, such as that associated with temporomandibular disorders (TMD), trigeminal neuralgia or migraine.¹⁰⁷⁻¹⁰⁹ Chronic pain may be associated with impairment in social function and activities of daily life, pain catastrophizing, somatization and/or other behavioral health comorbidities.^{110,111}
- b. For the rare patient with chronic dental or orofacial pain managed by a dentist, it is advised that COT be prescribed in accordance with state and national guidelines. Adherence to these guidelines promotes patient safety and minimizes the risk of developing OUD for patients receiving COT.^{112,113}
 - i. [CDC Guideline for Prescribing Opioids for Chronic Pain](#)
 - ii. [Report on Pain Management Best Practices: Updates, Gaps, Inconsistencies, and Recommendations](#) (U.S. Department of Health & Human Services)
 - iii. [Pain Management Resources and Opioid Use](#) (Colorado Department of Health Care Policy & Financing)
- c. See Alternatives to Opioids for the Treatment of Pain section for more information on the management of chronic dental pain.

Limiting Opioid Use in Dental Practice continued

14. It is recommended that dentists be vigilant in their daily practices to minimize the potential for misuse and diversion of opioid medications.

- a. A 2010 survey indicated that nearly 60% of dentists believed they were victims of prescription fraud or theft.⁴⁹ Methods of diversion suspected by dentists included altering prescriptions, faking phone-ins for prescriptions, feigning symptoms and falsely reporting lost or stolen medications.
- b. Dentists are advised to keep prescription pads in a secure location or use secure e-prescribing options.
- c. It is recommended that dentists exercise caution when a new patient or a patient who has not been seen recently specifically requests an opioid.
- d. In most cases, it is not appropriate to prescribe an opioid without a face-to-face encounter.
- e. Dentists are discouraged from prescribing an opioid prior to completing a procedure, as patients may schedule a procedure without intending to undergo it as a means of fraudulently acquiring a prescription for an opioid.
- f. Patients with OUD and patients who misuse or divert controlled medications may falsely claim their prescription was lost or stolen. Extreme vigilance is advised in reissuing a prescription reported to be lost or stolen.
 - i. Dentists are required by law to check the PDMP before issuing a replacement or second fill (“refill”) of an opioid prescription. Information from the PDMP may alert dentists to the possibility of aberrant use or diversion.
 - ii. Dentists may consider requiring patients to file a police report before issuing a replacement prescription.
- g. The CDA concurs with the ADA that dentists who are practicing in good faith and who use professional judgment regarding the prescription of opioids for the treatment of pain should not be held responsible for the willful and deceptive behavior of patients who successfully obtain opioids for non-dental purposes.

15. Dentists are encouraged to access continuing education in pain management and opioid stewardship.

- a. Per its 2018 “Policy on Opioid Prescribing” statement, the ADA supports mandatory continuing education in prescribing opioids and other controlled substances, with an emphasis on preventing drug overdoses, chemical dependency and diversion.
- b. Colorado SB 19-228 requires that health care providers complete up to four hours of opioid-related training as a condition of renewing, reactivating or reinstating a license. Consistent with this bill, beginning with the 2022 dental license renewal cycle, all Colorado dentists will be required to attest to the completion of at least one hour of opioid-related training that meets the requirements of Dental Board Rule 1.3 (J).
- c. The ADA offers free online continuing education sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA) and the American Academy of Addiction Psychiatry on a range of topics:
 - i. [The Dentist's Role in Addressing the Opioid Crisis](#)
 - ii. [Analgesic Prescribing in the Opioid Overdose Epidemic: A Milligram of Prevention is Better than a Pound of Rehabilitation](#)
 - iii. [How to Discuss Safe Use, Storage and Disposal of Medicines, including Opioids with Your Dental Patients](#)
 - iv. [Adolescent Pain Management and NSAID Considerations](#)
 - v. [CDC Guidelines for Prescribing Opioids for Chronic Pain: Considerations for Dentistry](#)
 - vi. [Legal and Ethical Issues of Opioid Prescribing for Acute Dental Pain](#)
 - vii. [Opioid Prescribing in Dental Medicine: Balancing our Compassion for Patients with Social Responsibility](#)
 - viii. [Safe Prescribing for Patients with a History of Substance Use Disorders](#)
- d. Additional training resources are available through the CDA [Opioid Training Resources](#).

Limiting Opioid Use in Dental Practice continued

Policy Recommendations

- 1. Improve PDMPs through interoperability and automated integration into electronic health records (EHRs), especially as dental integration often lags behind integration efforts for the medical community.**
 - a. Although the Colorado PDMP is an important tool for preventing inappropriate opioid prescribing, misuse and diversion, it is cumbersome to use and often incompatible with busy dental practice workflows.
 - b. Although there is no national data-sharing protocol that crosses state lines, a number of states participate in data-sharing hubs. Without data from surrounding localities, PDMPs cannot provide clinicians with the full prescribing picture. Access to nationwide data on opioid prescribing practices would enable dentists to better detect patterns of aberrant use and encourage their patients to seek treatment. Legislation is needed to establish a national PDMP and foster the broad exchange of prescribing information.
 - c. Providers are required to use two separate logins to access their EHRs and PDMPs, a drawback that can make the use of PDMPs cumbersome and disruptive. Legislation that supports the direct and automatic integration of PDMP data within EHRs, and specifically including dental practice management software, would enable the seamless reconciliation of a patient's opioid prescription history with their current medications and health care needs.
 - d. Automatic queries linked to patient registration significantly increase the use of PDMPs in clinical decision-making.¹¹⁴ Systems that incorporate such technology are overwhelmingly favored by clinicians, 98-100% of whom report improved access.¹¹⁵
- 2. State and federal agencies should expand educational outreach to clinicians and the public in safe storage and disposal of unused opioid medication and should increase opportunities for safe drug disposal.¹¹⁶**
 - a. Provide streamlined processes for clinician offices, pharmacies, hospitals and other public offices to become safe disposal sites.
 - b. Support medication safe disposal drop box locations in each county, so that safe disposal sites are easily accessible throughout Colorado.
 - c. Consider providing financial incentives for organizations that participate in safe disposal programs.
 - d. Launch targeted statewide public health campaigns to educate the public on the importance of safe disposal and the statewide locations of safe drug disposal sites.



Alternatives to Opioids for the Treatment of Pain



Alternatives to Opioids for the Treatment of Pain

The alternatives to opioids or “ALTO” approach emphasizes using multimodal nonopioid medications and nonpharmacologic treatments to mitigate pain and reduce patient and community exposure to opioids. ALTO emphasizes understanding and treating all aspects of pain, including its biologic, psychological and social components. **APPENDIX I, UNDERSTANDING PAIN: A COMPLEX BIOPSYCHOSOCIAL PHENOMENON**, provides a brief overview of how dentists may conceptualize pain.

The pharmacologic treatment of pain is best achieved by simultaneously intervening at multiple points in the physiological pathways involved in the transmission of pain signals. By selecting pharmacologic agents that act on different channels, enzymes and receptors, dentists can leverage the additive and synergistic mechanisms of analgesia provided by complementary medications to treat pain more comprehensively.

Opioid monotherapy often fails to provide adequate analgesia and exposes patients to increased risk of opioid-related adverse drug events and long-term risk of dependence and addiction. The scientific literature supports the scheduled use of ibuprofen 400 mg and acetaminophen 1000 mg as safer and more effective than any opioid monotherapy or opioid combination product for the treatment of most periprocedural dental pain. While the addition of an opioid for breakthrough pain may be appropriate in the setting of major surgical intervention, a scheduled NSAID and acetaminophen regimen is the mainstay of evidence-based pain management.⁹⁹ **FIGURE 4** lists the most effective medication regimens based on the number needed to treat (NNT) to achieve a 50% reduction in postoperative dental pain.

(FIGURE 4)

Number needed to treat (NNT) to achieve at least 50% reduction in maximal postoperative pain (moderate or severe) over 4-6 hours. A NNTB <5 is considered useful.

Drug or Drug Combination, Dose	BEST	NNTB	CI
Ibuprofen Plus Acetaminophen, 400 mg / 1,000 mg		1.5	1.4 to 1.7
Ibuprofen Plus Acetaminophen, 200 mg / 500 mg		1.6	1.5 to 1.8
Acetaminophen Plus Oxycodone, 1,000 mg / 10 mg		1.8	1.6 to 2.2
Diclofenac (Potassium), 100 mg		1.9	1.7 to 2.3
Diclofenac (Potassium), 50 mg		2.1	1.9 to 2.5
*Ibuprofen, 200 - 400 mg		2.1	1.9 to 2.4
Ibuprofen Plus Caffeine, 100 mg / 200 mg		2.1	1.9 to 3.1
Acetaminophen Plus Codeine, 800 - 1,000 mg / 60 mg		2.2	1.8 to 2.9
Ibuprofen Plus Codeine, 400 mg / 26 - 60 mg		2.2	1.8 to 2.6
Ibuprofen Plus Oxycodone, 400 mg / 10 mg		2.3	2.0 to 2.8
Ibuprofen Plus Caffeine, 100 mg / 100 mg		2.4	1.9 to 3.1
Ibuprofen, 400 mg		2.5	2.4 to 2.6
Celecoxib, 400 mg		2.6	2.3 to 3.0
Acetaminophen Plus Oxycodone, 650 mg / 10 mg		2.7	2.4 to 3.1
Ibuprofen, 600 mg		2.7	2.0 to 4.2
Naproxen, 400 - 550 mg		2.7	2.2 to 3.5
Ibuprofen, 200 mg		2.9	2.7 to 3.2
Acetaminophen, 500 - 1000 mg		3.5	2.7 to 4.8
Celecoxib, 200 mg		4.2	3.4 to 5.6
Tramadol, 100 mg		4.6	3.6 to 6.4
Tramadol, 50 mg	9.1	6.1 to 19	
Gabapentin, 250 Milliliters	11.0	6.4 to 35	
Codeine, 60 mg	12.0	8.4 to 18	
	WORST		

*Fast-acting refers to ibuprofen in a salt-based formulation (vs the typical acid-based formulation). Ibuprofen sodium is the salt-based formulation currently available in the United States.

SOURCE: British Journal of Oral and Maxillofacial Surgery¹¹⁷ and The Journal of the American Dental Association⁹⁹

Alternatives to Opioids for the Treatment of Pain continued

The superiority of NSAIDs and acetaminophen is not surprising when the pathophysiology of most dental pain is considered. In most dental surgeries, there is an acute inflammatory phase, mediated by prostaglandins, that underlies pain.¹¹⁸ NSAIDs and acetaminophen are inhibitors of prostaglandin formation and directly address the source of pain.¹¹⁹ When combined with additional agents such as

local anesthetics, most dental pain can be adequately and safely controlled with nonopioid analgesics.

Dentists who adopt ALTO approaches will manage their patients' pain more effectively and more safely, to the benefit of patients and their communities.

(TABLE 5)

Nonopioid Analgesic Agents

Type	Example
Glucocorticoids	Dexamethasone, methylprednisolone
Local anesthetics/sodium channel blockers	Articaine, bupivacaine, lidocaine
Nonsteroidal anti-inflammatory drugs	(COX-1, 2 inhibitors) celecoxib, ibuprofen, naproxen
Other	Caffeine, nitrous oxide
Prostaglandin synthesis inhibitor	Acetaminophen

Nonopioid Pharmacologic Agents for Multimodal Dental Analgesia

The following section describes a variety of ALTO medications applicable to dentistry. **TABLE 5** summarizes these medications.

ACETAMINOPHEN

EVIDENCE: Acetaminophen has been shown to significantly reduce dental pain compared to placebo without increased adverse events.^{69,120} Seventy-two percent of patients achieved at least 50% maximal pain relief postoperatively for four to six hours.⁹⁹ Combined treatment with acetaminophen (1000 mg) and ibuprofen (400 mg) has been shown to be more effective than oral opioid combinations (e.g., oxycodone or hydrocodone with acetaminophen) for the treatment of acute dental pain.⁹⁹

MECHANISM OF ACTION: While not completely understood, the drug's mechanism of action is theorized to be the activation of descending serotonergic pathways. Acetaminophen increases the pain threshold by inhibiting central prostaglandin synthesis (specifically, cyclooxygenase [COX-2]).

DOSING: Acetaminophen is a readily available, inexpensive, effective option for most dental pain conditions. In 2011, the manufacturer decreased its

recommended maximum daily dose to 3000 mg in an effort to reduce inadvertent overdoses. Acetaminophen 1000 mg was found superior to 650 mg for postsurgical dental pain, though given as a single dose.¹²¹ Health care professionals may still prescribe or recommend up to 4000 mg per day for a limited period of time (< 7 days) based on clinical judgment.

CONTRAINDICATIONS AND CAUTIONS: Life-threatening cases of acute hepatic failure that lead to liver transplant or death have been linked to the use of acetaminophen. In most cases of hepatic injury, acetaminophen doses exceeded maximum daily limits and often involved the use of more than one acetaminophen-containing product. Hepatotoxicity has been reported with doses of 4 g or more per day; therefore, a lower maximum dose of 3 g per day in adults with normal liver function is recommended, particularly if the duration of use exceeds seven days.

HEPATIC DOSING: In patients with cirrhosis and stable liver function tests, a maximum total daily dose of 2 g is recommended.¹¹⁷

DISCHARGE INSTRUCTIONS: Instruct the patient to avoid other over-the-counter products that contain acetaminophen and limit the total daily dose to less than 3000 mg if using for > 7 days.¹²²

Alternatives to Opioids for the Treatment of Pain continued

CAFFEINE

EVIDENCE: Caffeine 100 mg combined with ibuprofen 400 mg as a single dose was found to be superior to ibuprofen 400 mg alone following third molar extraction.¹²³ Similarly, adding caffeine to acetaminophen has also been found to be more effective than acetaminophen alone.¹²⁴

MECHANISM OF ACTION: While the methylxanthines are known to be phosphodiesterase enzyme inhibitors, the exact mechanism by which they exert their analgesic effect is unknown. It is thought to be due to the result of CNS stimulation. The use of caffeine as an adjunct is based on caffeine's ability to increase the level of analgesia provided by other analgesic agents, such as ibuprofen or acetaminophen.

DOSING: Usual dose to augment multimodal analgesia is 100 mg with agent prior to procedure or BID following (or a strong cup of coffee twice a day). Daily doses > 250 mg/day can produce cardiovascular adverse effects, including arrhythmias.

CONTRAINDICATIONS AND CAUTIONS: Use these agents with caution in patients with cardiac arrhythmias, as may exacerbate. Use with caution in patients with a known seizure disorder. Patients may be advised that taking afternoon or evening doses may lead to insomnia or sleep disruption.

MONITORING: Tachycardia and tachypnea, jitteriness and tremors may occur with administration.

CORTICOSTEROIDS

EVIDENCE: Glucocorticoids, and predominantly dexamethasone, have been shown to be efficacious in the treatment of dental pain and may be an effective adjunct to other anti-inflammatories. When given for postoperative dental pain, a single dose of dexamethasone

has been shown to reduce pain up to seven days postoperatively.¹²⁵ Methylprednisolone has been shown to reduce inflammation, pain and trismus in the early postoperative period following third molar extraction.¹²⁶ One review found that a perioperative corticosteroid, such as dexamethasone or methylprednisolone dose pack, may limit swelling and decrease postoperative discomfort for surgical or endodontic procedures.¹²⁷

MECHANISM OF ACTION: Glucocorticoids (e.g., dexamethasone and methylprednisolone) have many actions including analgesic, antiemetic, antipyretic and anti-inflammatory effects. Although not completely clear, analgesic effects of dexamethasone are thought to result from the inhibition of phospholipase, leading to a decrease in cyclooxygenase and lipoxygenase production. Steroids also work to reduce inflammation by decreasing the migration of neutrophils, decreasing production of inflammatory mediators and reversing capillary permeability.

AGENTS AND DOSING: Dexamethasone 4-10 mg IV/IM/PO as a single dose prior to procedure. Methylprednisolone 40 mg IV/IM or 48 mg PO as a single dose prior to procedure. May consider a short postoperative course in select patients, such as dexamethasone 2 mg by mouth every 12 hours for four doses.

CONTRAINDICATIONS AND CAUTIONS: Long-term or repetitive use of corticosteroids may increase risk of potential adverse events. Caution in patients at risk for gastric irritation. May lead to transient rise in blood glucose and require more frequent monitoring in diabetics. Repetitive or long-term use may increase risk of adrenal suppression, poor wound healing, immunosuppression, myopathy and psychiatric disturbances.

Alternatives to Opioids for the Treatment of Pain continued

Local Anesthetics

LOCAL INJECTION

EVIDENCE: Administration of local anesthetics via subcutaneous infiltration is ideal for most dental procedures and has been found to have a low incidence of adverse events.^{128,129} Several different techniques are available to dentists. Decreasing anesthetic delivery rate has demonstrated pain reduction during injection, as well as distraction techniques made at the time of the injection such as jiggling the patient's cheek.¹³⁰

MECHANISM OF ACTION: Blocks conduction of nerve impulses through inhibition of sodium channels.

OPTIONS: Articaine, bupivacaine and lidocaine are common local anesthetics used in dental practices. Articaine and lidocaine are typically used in simple dental procedures due to their short-acting nature. Bupivacaine has a longer duration of action (six to eight hours) and may be preferred for longer, more complicated procedures. Liposomal bupivacaine has been studied in some dental procedures, though results in clinical trials are mixed.¹³¹⁻¹³³ Anecdotal evidence and the expert opinion of a number of oral and maxillofacial surgeons in Colorado suggest that liposomal bupivacaine may be a valuable opioid-sparing adjunct to pain management. Effective use of liposomal bupivacaine requires use of a 25 g or larger-bore needle, adequate injection volumes (3-4 mL for third molar and 1-2 mL for maxillary molar procedures) and proper injection technique. Bupivacaine may be administered immediately before liposomal bupivacaine injection or

admixed in the same syringe; the ratio of the milligram dose of bupivacaine to liposomal bupivacaine should not exceed 1:2. Liposomal bupivacaine should not be admixed with lidocaine or other non-bupivacaine local anesthetics. Liposomal bupivacaine may be used in tissue previously infiltrated with lidocaine after 20 minutes have elapsed. Liposomal bupivacaine has not been studied in the pediatric population. For more information, see https://www.exparel.com/sites/default/files/PP-EX-US-3889_OMFS_FAQs_Dec_2018.pdf. Local anesthetics may also be administered via direct infiltration into a targeted nerve plexus. This technique has been successfully used for tooth extraction.

CAUTIONS: While adverse effects of these drugs are minimal when used sparingly or in low doses, dentists are advised to be familiar with signs and symptoms of local anesthetic systemic toxicity (LAST) and appropriate treatment with intralipid therapy.

TOPICAL

EVIDENCE: The use of a topical anesthetic agent prior to local injection is ideal for most patients.¹³⁴ A lidocaine 4% solution and benzocaine topical¹³⁵ have been found to be effective.¹³⁶

MECHANISM OF ACTION: Blocks conduction of nerve impulses through inhibition of sodium channels.

OPTIONS: Supplied for dental-related pain in various compounded mouthwashes and as a lidocaine 4% oral solution. Benzocaine 20% topical can also be considered. Some mouthwashes may need to be compounded.

CONTRAINDICATIONS AND CAUTIONS: Side effects are minimal when used in low topical doses.

NITROUS OXIDE

EVIDENCE: Featuring rapid onset and elimination (< 60 seconds), nitrous oxide exhibits both analgesic and anxiolytic properties. There is evidence to support its role as an augmentation to other therapies in the management of pain and anxiety in patients undergoing dental procedures.¹³⁷

MECHANISM OF ACTION: Nitrous oxide is a tasteless, colorless gas administered in combination with oxygen via a mask or nasal hood at a maximum concentration of 70%. The gas is absorbed via pulmonary vasculature and does not combine with hemoglobin or other body tissues.

OPTIONS: Nitrous oxide is typically used in combination with a local anesthetic or other analgesics. Benefits include

no nil per os (NPO) requirements, patients can typically drive after administration and no IV line is needed.

SPECIAL CONSIDERATIONS: Exercise caution to ensure avoidance of sedation levels requiring an anesthesia permit if used in combination with other pharmacologic modalities. Colorado Dental Board rules allow, without the need for additional anesthesia permits, the use of nitrous oxide in combination with a single dose of a single drug (at no more than the manufacturer's maximum recommended dose) that may be prescribed for unmonitored home use.

MONITORING: Pulse oximetry is the only patient monitoring suggested, though not required.

Alternatives to Opioids for the Treatment of Pain continued

NONSTEROIDAL ANTI-INFLAMMATORY AGENTS¹²⁷

EVIDENCE:⁹⁹ With or without combination with acetaminophen, ibuprofen has been shown superior to all other single agent oral comparators in postoperative dental pain. Combined with acetaminophen 1000 mg, ibuprofen 400 mg has been shown to have the most treatment benefit. As a single agent, a dose of ibuprofen 600 mg showed the highest proportion of patients who experienced at least 50% maximal pain relief for four to six hours, with 77% of patients experiencing relief.⁹⁹

MECHANISM OF ACTION: Inhibits proinflammatory prostaglandin production via the inhibition of COX-1 and COX-2 enzymes.

OPTIONS: Ibuprofen is the most commonly studied NSAID. There does not appear to be additional analgesic relief with individual doses above 400-500 mg; however, anti-inflammatory effects remain dose dependent. The maximum daily dose of ibuprofen is 3200 mg/day. Of note, a “fast-acting” formulation (ibuprofen in a salt form)¹³⁸⁻¹⁴¹ has been shown to have a quicker onset of action and likely additional pain relief over the typical formulation (ibuprofen in an acid form), though both formulations show significant analgesic benefit. Other NSAIDs are available with longer duration of action (e.g., naproxen) and COX-2 selective properties that avoid effects on platelet function (e.g., celecoxib). Other options include ketorolac, diclofenac, indomethacin and selective COX-2 inhibitors (e.g., meloxicam).

DIFFERENT SIDE EFFECT PROFILES: In general, COX-2 selective NSAIDs have a lower risk of GI side effects but a higher risk of cardiac side effects. Conversely, nonselective NSAIDs pose a lower risk of cardiac side effects but a higher risk of GI side effects. Providers may wish to use a COX-2 selective NSAID in some cases to avoid an increased risk of bleeding.

CONTRAINDICATIONS AND CAUTIONS: NSAIDs increase the risk of myocardial infarction and stroke. Contraindicated in the setting of recent coronary artery bypass graft surgery or myocardial infarction. Can also cause increased risk for GI adverse events including bleeding, ulceration and perforation of the stomach or intestines. Risk is increased in elderly (Beers Criteria) and in patients with a history of peptic ulcer disease or GI bleeding. Caution advised in patients on concomitant anticoagulants or antiplatelet agents. Avoid use in patients with chronic kidney disease, cirrhosis or heart failure. Risk of renal injury is higher in patients who are elderly, dehydrated or have comorbidities such as heart failure, diabetes and cirrhosis.

SPECIAL CONSIDERATIONS: Special caution advised in patients with renal dysfunction, heart failure and concern for bleeding.¹⁴²

MONITORING: Dentists are advised to discuss history of GI ulceration or renal dysfunction prior to initiation.

RECOMMENDED DURATION OF USE: The lowest effective dose for the shortest possible duration is recommended.

(TABLE 6)

GI Risk Factor Assessment and NSAID Therapy

GI Risk Factor Assessment	Treatment
High Risk 1. History of complicated ulcer, especially recent OR more than two risk factors: 1. Age > 65 years 2. High-dose NSAID therapy 3. Previous history of uncomplicated ulcer or 4. Concurrent use of aspirin, corticosteroids or anticoagulants	Alternative therapy or COX-2 inhibitor + PPI
Moderate Risk (one to two risk factors)	NSAID + PPI
Low Risk (no risk factors)	NSAID alone

SOURCE: American College of Gastroenterology Guidelines, 2009^{143,144}

Alternatives to Opioids for the Treatment of Pain continued

Nonopioid Pharmacologic Agents for Future Consideration

DEXTROMETHORPHAN

EVIDENCE: A dose of dextromethorphan 30 mg administered prior to oral surgery was found to reduce post-procedure analgesic consumption.¹⁴⁵ Dextromethorphan and other N-methyl-D-aspartate (NMDA) antagonist agents are more commonly used in other types of surgeries; a meta-analysis of 14 trials and 848 patients suggests that perioperative dextromethorphan use reduced postoperative opioid consumption at 24 to 48 hours and pain scores at one, four to six and 24 hours.¹⁴⁶

MECHANISM OF ACTION: NMDA receptor antagonist that binds to receptor sites in the spinal cord and CNS, thereby blocking the generation of central acute and chronic pain sensations that arise from peripheral nociceptive stimuli and reducing the amount of analgesics required for pain control.

DOSING: 30 mg orally prior to procedure. 30-90 mg PO administered prior to surgery has been studied in other types of procedures.

CONTRAINDICATIONS AND CAUTIONS: Avoid in patients taking monoamine oxidase inhibitors (MAOIs) and within 14 days of MAOI use.

MONITORING: May cause dizziness or somnolence. Additional monitoring is not required.

GABAPENTINOIDS

EVIDENCE: Gabapentin 600 mg orally before surgery has been found to be superior to placebo or an NSAID in controlling postendodontic pain.¹⁴⁷ Pregabalin 300 mg administered after third molar extraction was found superior to both placebo and ibuprofen 400 mg.¹⁴⁸ Another study compared timing of pregabalin 75 mg dose pre- vs. post-operative following third molar extraction and found post-operative dosing to be superior.¹⁴⁹ While some initial trials show promise for the gabapentinoids, it is recommended that use of gabapentinoids not supplant the well-validated use of acetaminophen, NSAIDs and local anesthetics. A role for adjunct therapy in certain populations may emerge in the future.

MECHANISM OF ACTION: Inhibits alpha 2-delta subunit of voltage-gated calcium channels, believed to decrease conduction of neuropathic pain sensation.

OPTIONS AND DOSING: Pregabalin 75-300 mg or gabapentin 600 mg given perioperatively.

RENAL DOSING: Reduced dose for renal impairment is advised.

CONTRAINDICATIONS AND CAUTIONS: It is recommended that dentists avoid use in older adults with a history of falls as it may cause syncope, impaired psychomotor function or ataxia. Caution is advised in patients taking concomitant opioids or CNS depressants, in patients with underlying respiratory diseases such as COPD and in elderly patients due to risk of increased respiratory depression.

Special Populations

Not all patients are appropriate candidates for every ALTO agent. It is recommended that all treatments be used with thoughtful consideration of patient-specific factors such as age, organ function, comorbidities and other medications.

GERIATRIC: It is recommended that great care be taken when treating elderly patients. The Beers Criteria is a well-established resource that can be used when considering treatment options for patients older than 65 years.¹⁵⁰ Some of the therapies suggested may pose a greater risk of adverse events or be inappropriate for use in the geriatric population due to declining kidney function, liver function or other age-related factors. It is advised that these risks be weighed against the increased risk of opioid-related adverse events in this population. Nonpharmacologic adjuncts may be recommended, including ice as appropriate. Topical medications have less systemic absorption and fewer side effects and should be strongly considered in this patient population.

HEART FAILURE: Not all ALTO agents are safe for use in patients with heart failure, particularly steroids and NSAIDs. In patients for whom these agents are contraindicated, consider prescribing topical applications or other alternatives.

PATIENTS IN TREATMENT FOR SUD: Discussion and practice recommendations are provided in the Treatment for Opioid Use Disorder section.

Alternatives to Opioids for the Treatment of Pain continued

PEDIATRIC: ALTO is not specifically designed for children < 15 years old or patients under 40 kg. ALTO principles can still be applied for this population, but pediatric precautions should be observed and agents dosed appropriately. Utilization of pain management principles developed by the American Academy of Pediatric Dentistry (AAPD) is recommended for pediatric patients; a summary of those recommendations is contained in **APPENDIX II**. AAPD protocols may be applied to patients up to the age of 18.

PREGNANCY: Some nonopioid agents are contraindicated in pregnancy, including but not limited to NSAIDs. However, some agents and ALTO procedures may be appropriate for use in pregnancy, and general ALTO principles can still be applied to this population.

RENAL DYSFUNCTION: Not all ALTO agents are safe to use for patients with renal dysfunction. Dosing presented below is for patients with normal renal function. It is advised that systemic NSAIDs be avoided in patients with renal dysfunction.

Nonpharmacologic Interventions

Nonpharmacologic interventions may relieve patient anxiety and pain, are often easy to implement and have few adverse events. Pediatric dentists routinely incorporate nonpharmacologic elements into their pain and anxiety management strategies, and much of the dental literature advocates for nonpharmacologic interventions in children and adolescents. Given the significant burden of anxiety over dental procedures in patients of all ages, nonpharmacologic interventions (**TABLE 7**) may also play a role in increasing adult patient comfort, reducing pain and decreasing opioid requirements.

Acupuncture	Massage
Cognitive and behavioral interventions	Music therapy
Cold compresses	Transcutaneous electrical nerve stimulation (TENS)
Distraction	Virtual reality

Below are descriptions of nonpharmacologic interventions and the evidence supporting their use:

ACUPUNCTURE

Some patients may benefit from acupuncture as an adjunct to managing acute dental pain prior to treatment as well as postoperatively.^{151–153,154(p)} Auricular acupuncture may help relieve dental anxiety as well.¹⁵⁵ Deep dry needling, traditional acupuncture and laser acupuncture have been shown to be effective in the management of temporomandibular myofascial pain.^{156–161}

COGNITIVE AND BEHAVIORAL INTERVENTIONS

Studies of cognitive behavioral interventions, mindfulness, guided imagery, relaxation, hypnosis and intraoperative suggestion have generally been shown to modestly reduce postoperative pain, analgesic use, depression, anxiety and catastrophizing attitudes with non-dental operations.^{162–164} One meta-analysis found that nonpharmacologic interventions, including cognitive and behavioral approaches, were beneficial for anxiety related to dental procedures.¹⁶⁵

Alternatives to Opioids for the Treatment of Pain continued

COLD COMPRESSES

The intermittent application of ice packs or cold compresses may provide analgesic benefit to some patients following dental procedures. Cold application in dental treatment is a simple, nontoxic adjunct to controlling postoperative pain. A study of acupressure ice massage of the web space between thumb and index finger for patients with dental pain demonstrated significant decreases in pain compared to massage without ice.¹⁶⁶

DISTRACTION

One systematic review finds strong evidence that distraction techniques reduce needle-related pain and distress in pediatric patients.¹⁶⁷ Another systematic review concluded with low certainty that a wide variety of distraction techniques are effective to reduce fear and anxiety associated with dental procedures in pediatric patients.¹⁶⁸ Distraction techniques may be generally categorized as active or passive. Passive distractions include interventions such as watching videos or listening to music. Active distractions include performing a task. A study found that asking pediatric dental patients to write letters in the air with their legs reduced pain reactions to injection of local anesthetic.¹⁶⁹ Other forms of active distraction include singing, conversation and manipulating an object or toy.¹⁷⁰

MASSAGE

Several studies have found significant reductions in pain related to bruxism and temporomandibular joint disorder as a result of concurrent use of massage therapy and occlusal splint.^{171,172}

MUSIC THERAPY

Evidence shows that music therapy reduces anxiety related to dental procedures in both pediatric and adult patients.¹⁷⁵⁻¹⁷⁷ One meta-analysis found that distracting pediatric patients with music reduces pain and anxiety associated with general medical procedures.¹⁷³ Similar evidence supports the use of music therapy, both passive and active, to reduce pain and anxiety in pediatric patients undergoing dental procedures.¹⁷⁴ Music therapy may also reduce the total dosage of pharmacologic agents needed for pain control during dental procedures in pediatric patients.¹⁷⁴

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)

While not a replacement for local anesthetic, TENS may be a useful adjunct for some dental procedures. Several studies evaluating the use of TENS for periprocedural dental pain in pediatric patients found no significant difference in pain control compared to local anesthetic; however, most patients preferred TENS to local anesthetic.¹⁷⁸⁻¹⁸² In adult patients, the use of TENS was found to reduce pain from dental block injections more than use of topical anesthetic.¹⁸³⁻¹⁸⁵

VIRTUAL REALITY

A systematic review and meta-analysis found virtual reality effective in reducing dental pain but not anxiety in pediatric patients.¹⁸⁶ A single-blinded randomized trial found that virtual reality was more effective in reducing pre-injection dental anxiety than counter-stimulation in pediatric patients undergoing extraction or pulpectomy.¹⁸⁷ Limited preliminary research suggests that virtual reality may provide analgesic benefit for adult dental patients.^{186,188,189}

Alternatives to Opioids for the Treatment of Pain continued

Practice Recommendations

1. Dentists are encouraged to apply the following ALTO principles when managing pain:

- a. Use nonopioid approaches as first-line therapies.
- b. Use several agents for multimodal pain control rather than relying on monotherapies.
- c. Utilize opioids rarely and predominantly as rescue medications after other modalities have failed.
- d. Do not prescribe opioids as scheduled medications when treating acute pain.
- e. Discuss realistic, functional pain management goals with patients.
- f. Use empathic language when discussing pain.

2. Dentists are advised to manage patient expectations relative to pain and pain management by:

- a. Developing a pain management strategy with the patient as part of the pretreatment consultation.
- b. Working with patients, guardians or caregivers to establish realistic goals and expectations of pain management and the expected course of recovery.
- c. Educating patients that postoperative pain is often less than preoperative pain if infection or pulpal inflammation was present. A pain medication that was not effective prior to treatment may be sufficient postoperatively.¹⁹⁰

3. Dental practices are encouraged to implement ALTO programs and provide opioid-sparing or opioid-free pain treatment pathways when clinically appropriate. TABLE 8 provides examples of pain management protocols and recommended opioid prescribing ranges for a number of common dental procedures.

- a. The procedures included in TABLE 8 are based on expert opinion and studies of patient reports of opioid requirements following common dental procedures. The list of procedures included is not exhaustive; dentists are encouraged to extrapolate guidance from this table as appropriate to their unique practice settings.
- b. In all cases clinical judgment may supersede the recommendations offered in these guidelines. Dentists are advised to tailor analgesic regimens to meet the needs of individual patients and procedures. It is recommended that medication selection and dosages be adjusted based on patient-specific factors, including organ function, comorbidities, home medication regimens and previous medication intolerances.
- c. When utilizing any pharmacologic therapy, dentists must ensure that they comply with any applicable Colorado Dental Board regulations or permit requirements regarding analgesia, sedation and anesthesia.

Alternatives to Opioids for the Treatment of Pain continued

(TABLE 8)

Multimodal Analgesic Protocols for Common Dental Procedures

	Common Interventions	Procedural Recommendations	Oral Analgesic Recommendations	Opioid Recommendations
ANTICIPATED PAIN MILD	Frenectomy Routine endodontics Scaling and root planing Simple extraction Simple gingivectomy Subgingival restorative procedures	Short-acting anesthetic: lidocaine or articaine	Ibuprofen 400 mg plus acetaminophen 500-1000 mg q6 hours	Opioids not recommended
ANTICIPATED PAIN MODERATE	Apicoectomy Implant placement Lateral ridge augmentation Periodontal surgery Simple 3rd molar extraction Soft tissue grafting Surgical extraction	Consider long-acting anesthetic: bupivacaine or liposomal bupivacaine +/- dexamethasone 8-10 mg PO	Ibuprofen 400 mg plus acetaminophen 500-1000 mg q6 hours +/- dexamethasone 2 mg PO q12 hours x 4 doses +/- caffeine 100 mg BID	Consider no opioids or prescription of 4-6 pills oxycodone 5 mg PO q6hrs PRN pain
ANTICIPATED PAIN SEVERE	Full-arch extraction with alveoloplasty Impacted or complicated 3rd molar extraction Lateral window sinus augmentation	Use long-acting anesthetic: bupivacaine or liposomal bupivacaine + dexamethasone 8-10 mg PO	Ibuprofen 400 mg plus acetaminophen 500-1000 mg q6 hours *scheduled for first 72 hours +/- dexamethasone 2 mg PO q12 hours x 4 doses +/- caffeine 100 mg BID	Consider no opioids or prescription of 4-10 pills oxycodone 5 mg PO q6hrs PRN pain

If contraindication or allergy to NSAIDs or acetaminophen, strongly consider the following, even for minor procedures:

- Using long-acting local anesthetic (bupivacaine or liposomal bupivacaine) and periprocedural dexamethasone
- Maximizing agent that is not contraindicated (600 mg ibuprofen or acetaminophen 1000 mg q6 hours)
- Prescribing postprocedural dexamethasone (2 mg PO every 12 hours x 4 doses)

Additional considerations:

- *Dentists are advised to counsel patients to take nonopioids on a scheduled basis, adding an opioid only if pain is not adequately controlled.
- Opioid monoproducts are favored over combination formulations. Use of opioid monoproducts for breakthrough pain allows acetaminophen and/or NSAID to be taken as scheduled first-line agents without risk of suprathreshold dosing or accidental poisoning.
- Ibuprofen sodium may provide faster onset of analgesia than the more commonly available acid formulation.
- If a nonselective NSAID is contraindicated, consider use of celecoxib 200-400 mg.
- If infection is contributing to inflammatory pain, consider addition of topical chlorhexidine and oral antibiotics.
- It is advised that patients with TMD and/or chronic orofacial pain not be prescribed opioids and be referred to specialists.
- Consider managing trauma/pulpitis with analgesia similar to mild/moderate or moderate +/- antibiotics until definitive therapy can be performed or symptoms resolve.

Alternatives to Opioids for the Treatment of Pain continued

4. Unless contraindicated, it is recommended that a combination of an NSAID and acetaminophen be the first-line treatment for all postprocedural dental pain.

Table 8 provides guidance on oral analgesics after specific dental interventions.

- a. Postprocedural pain—which is predominantly inflammatory—can be reduced by targeting inflammation with NSAID therapy. The ADA House of Delegates states, “Dentists should consider nonsteroidal anti-inflammatory analgesics as the first-line therapy for acute pain management.”¹⁰⁷
- b. Ibuprofen and acetaminophen given in combination are more effective than either agent alone.^{128,191–196}
 - i. A systematic overview in JADA with over 58,000 patients following third molar extractions found that the combination of 400 mg ibuprofen with 1000 mg acetaminophen was more effective than any opioid-containing regimen and was also associated with a lower risk of adverse events. Opioids produced side effects in 27.5% of patients as compared to only 7.5% of patients taking NSAIDs.⁹⁹
- c. Opioid products with a single ingredient (e.g., oxycodone) are favored over combination formulations (e.g., oxycodone/acetaminophen), as patients are encouraged to take nonopioid analgesics (e.g., acetaminophen, NSAID) consistently prior to resorting to an opioid. Use of monoproducts allows acetaminophen or NSAID to be taken preferentially and used as a first-line agent with a lower risk of

supratherapeutic dosing or accidental poisoning.

- d. Unless contraindicated, it is recommended that scheduled nonopioid analgesics be continued concurrently with opioid analgesics.

5. Patients with chronic pain or complex pain syndromes are best managed by an interdisciplinary team.

Dentists are encouraged to build a network of pain specialists, physical therapists, TMD specialists and otolaryngologists to refer patients with complex pain needs.

6. Anxiety is common in dental patients and a major contributor to pain. Dentists are encouraged to assess and address patient anxiety prior to procedures and consider utilizing nonpharmacologic modalities to address pain and anxiety.

- a. One in seven adult patients undergoing dental treatment report being highly anxious.¹⁹⁷
- b. It is well established that in all clinical settings anxiety can significantly contribute to pain.¹⁹⁸ The relationship between fear and pain is highly relevant to dental practitioners, as patients with dental anxiety can have both exaggerated pain expectancies and pain perceptions.^{199–201}
- c. Dentists may refer their patients to the ADA online resource *Dental Anxiety: 3 Ways to Stop Fearing the Dentist*.
- d. Many nonpharmacologic techniques can be used by dentists to assist anxious individuals, including those shown in **TABLE 9**.

(TABLE 9)

Nonpharmacologic Techniques to Address Dental Anxiety

General Principles	In-the-chair Techniques	Referral to cognitive and behavioral specialty care
<ul style="list-style-type: none"> Good communication and establishing rapport^{202–205} Providing both procedural and sensory information²⁰⁶ Providing control Initiating rest breaks during procedures Establishing a “stop” signal²⁰⁷ 	<ul style="list-style-type: none"> Distraction techniques, such as alternative visual or auditory stimuli, music therapy¹⁷³, virtual reality^{188,208} Positive reinforcement²⁰⁹ Diaphragmatic or relaxation breathing^{210,211} Progressive muscle relaxation²¹² Guided imagery 	<ul style="list-style-type: none"> Cognitive restructuring²¹³ Systematic desensitization^{214–216} Hypnosis^{217,218}

Alternatives to Opioids for the Treatment of Pain continued

- e. For patients who would benefit from pharmacologic therapy in addition to nonpharmacologic intervention, consider preprocedural administration of oral clonidine or melatonin or periprocedural inhaled nitrous oxide. It is recommended that benzodiazepines be reserved for the most anxious patients undergoing major dental procedures.
 - i. Clonidine 0.1-0.2 mg orally once 90 minutes prior to procedure.²¹⁹ Clonidine 0.15 mg orally has been shown to be equally efficacious to midazolam 7.5 mg in surgical extraction of wisdom teeth,²²⁰ another study also found clonidine equally efficacious to midazolam in reducing anxiety in patients undergoing operations on the face with local anesthetic, but clonidine was superior to midazolam in pain reduction.²²¹
 - ii. Melatonin 3-6 mg orally once 90 minutes prior to procedure. Although the dental literature studying use of melatonin is limited,²²² fairly robust general medical and surgical literature supports the use as a preoperative medication to reduce anxiety.²²³
 - iii. Midazolam oral and IV have both been used prior to procedure to reduce anxiety in patients undergoing dental procedures. However, concerns regarding side effects such as retrograde amnesia, impaired coordination and drowsiness exist.
 - iv. Nitrous oxide—**SEE NONOPIOID PHARMACOLOGIC AGENTS FOR MULTIMODAL DENTAL ANALGESIA** earlier in this section for more information. A study comparing midazolam, diazepam and nitrous oxide found nitrous oxide to be as effective as a benzodiazepine in reducing anxiety.²²⁴ Similar results have been found in the pediatric dental literature.²²⁵
 - f. In utilizing pharmacologic therapy, dentists must ensure that they comply with any applicable Colorado Dental Board regulations or permit requirements regarding sedation and anesthesia.
- 7. Consider the following pharmacologic interventions if a patient cannot receive treatment within eight hours after the onset of acute dental pain:**
- a. Administration of a long-acting anesthetic (i.e., bupivacaine or liposomal bupivacaine)
 - b. Concurrent scheduled ibuprofen (or other NSAID) and acetaminophen
 - c. Prescription of an antibiotic, if clinically indicated
 - d. Topical anesthetic rinses when indicated (e.g., for stomatitis, mucositis or mouth ulcers)
 - e. Chlorhexidine antimicrobial mouth rinse (e.g., for localized gum inflammation and infection and to soothe gum tissue)
 - f. Patients may be advised that some pain is to be expected until definitive treatment is performed and that accessing care as soon as possible both addresses pain and reduces the likelihood of worsening of the condition causing pain.
 - i. Dentists may use the CDA directory of clinics that provide [low-cost dental care](#) in Colorado to help patients without insurance or the capacity to pay for care access treatment.
 - g. Dentists are discouraged from prescribing opioids to patients awaiting definitive care.
- 8. Dentists are encouraged to document in the patient record all instructions provided for patient analgesia and analgesic prescriptions. When deviating from these prescribing recommendations or those required by state laws or institutions, dentists are advised to document in the patient record the justification for doing so.**
- 9. Patients with OUD who are undergoing treatment with methadone, buprenorphine or naltrexone may present challenges for postoperative analgesia. Dentists are encouraged to make efforts to coordinate care with a patient's addiction specialist. Patients in recovery from SUD may be at increased risk for relapse in the setting of dental pain and require careful management. SEE TREATMENT OF OPIOID USE DISORDER SECTION FOR FURTHER RECOMMENDATIONS.**

Alternatives to Opioids for the Treatment of Pain continued

(TABLE 10)

Managing Acute and Perioperative Dental Pain in Patients Receiving Medication for Addiction Treatment (MAT)

1. The use of methadone, buprenorphine or naltrexone for the treatment of OUD may complicate periprocedural dental pain management.
 - a. As a full opioid antagonist, naltrexone blocks the analgesic effects of most opioids. For elective dental procedures, it is recommended that oral naltrexone be held for at least 72 hours prior to surgery. Patients receiving monthly depot injections of naltrexone should skip their monthly injection a month before an elective procedure, bridging treatment with oral naltrexone until 72 hours prior to their procedure.
2. A patient's usual dose of buprenorphine or methadone is generally not sufficient for pain control. OUD pharmacotherapy works toward meeting a patient's baseline opioid requirement and will not provide relief from acute pain.
 - a. Splitting home doses of buprenorphine to three times per day leverages the early analgesic effects of these medications; however, the analgesic effect of splitting doses is minimal and will not address moderate or severe pain.^{226,227}
 - b. Although buprenorphine is a partial opioid agonist, it does not block the effects of full opioid agonists.²²⁸⁻²³¹
 - c. Naloxone present in combination products (e.g., Suboxone) is not bioavailable and does not block analgesia. It is added solely as a deterrent to injection use.
3. If fully optimized nonopioid multimodal analgesia fails to control pain, it is appropriate to offer opioids to patients receiving MAT. Prescription opioids are safer for the patient than illicit, self-obtained alternatives, and no patient should be denied analgesia.
 - a. Higher doses than typical of a short-acting opioid will generally be needed due to drug tolerance and increased pain sensitivity.⁶⁷
 - b. Consider consulting the patient's addiction medicine provider to determine appropriate opioid dosing. Documenting and notifying the MAT prescriber of any opioids administered or prescribed is recommended; an unexplained positive urine toxicology may appear as a patient treatment contract violation.
 - c. As with all patients receiving opioids, it is recommended that patients be advised of the risk of opioid-related adverse effects, including sedation, respiratory depression and overdose.
 - i. Patients receiving methadone are at elevated risk of respiratory depression, and it is advised they be carefully managed while under anesthesia and cautioned if discharged with a prescription for an opioid.
 - d. Dentists are encouraged to confirm that patients receiving MAT have naloxone at home and that such patients and their families are educated in recognizing and responding to overdose (See Harm Reduction section for further detail).

Alternatives to Opioids for the Treatment of Pain continued

10. As of this writing, no definitive, high-quality studies support the safety and efficacy of dispensary or pharmaceutical cannabinoids for analgesia. Unless better supporting evidence becomes available, dentists are discouraged from endorsing the use of cannabinoids for pain management (SEE APPENDIX III, CANNABINOIDS, PAIN AND ANESTHESIA, FOR A BRIEF REVIEW OF THIS TOPIC AND RECOMMENDATIONS FOR COUNSELING PATIENTS).

- a. While the sale of cannabinoids is legal in Colorado, it remains illegal by federal law. The degree of medicolegal risk for dentists who recommend use of cannabinoids is unknown.
- b. The CDA strongly cautions Colorado dentists against recommending cannabinoids to their patients for use as analgesics due to the uncertain regulatory environment and limited literature on this intervention in dentistry at this time.
- c. Dentists and their patients should be aware that prescriptions for dispensary cannabinoids for pain management will likely not be covered by public or private insurers.
- d. With significant and growing rates of dispensary cannabis use in Colorado, dentists increasingly provide anesthesia to patients who regularly use cannabis. It is recommended that dentists be familiar with anesthetic complications frequently encountered when providing anesthesia to such patients.

Policy Recommendations

1. **Private and public insurers should provide reimbursement protocols that align with nonopioid pain management initiatives and offer greater flexibility in the design of reimbursement models.**²³⁵
 - a. Pharmacy benefit managers and payers, including dental plans, should offer a comprehensive array of nonopioid options in their formularies and be more transparent in communicating the availability of those alternatives to clinicians and patients.
 - b. Pharmacy benefit managers and state and federal regulators should ensure that nonopioid analgesics are included on low-cost tiers.



Harm Reduction



Harm Reduction

Harm reduction is a set of practical strategies and ideas aimed at mitigating the negative consequences associated with illicit drug use. The harm reduction approach seeks to protect patients from the harms associated with SUD until they are ready to seek treatment and recovery. Harm reduction aims to prevent infectious diseases, including HIV/AIDS, hepatitis B and C, sepsis and endocarditis; reduce the risk of overdose and other drug-related fatalities; and decrease the other negative consequences of drug use on individuals, families and communities.

Per The ADA Practical Guide to Substance Use Disorders and Safe Prescribing:

Although society as a whole generally evaluates successful addiction therapy terms of patients “being in recovery” or “not in recovery,” it is important to understand the more global concept that any reduction in negative behaviors or outcomes (such as needle sharing, duration of impairment, absenteeism from work, health care associated costs, etc.) should be considered, in part, as successful treatment.²³²

Dental patients who use illicit substances have markedly poorer oral health than average.²³³ The oral health consequences of use of illicit substances are numerous—OUD alone is associated with xerostomia, taste dysfunction, eating difficulties, mucosal infections, dental caries, periodontal disease, bruxism, candidiasis, necrotizing gingivitis and mucosal dysplasia.²³⁴ While the dental and oral health harms associated with methamphetamine use are well known, a study comparing the oral and dental health of people who inject methamphetamine to those who inject heroin found no significant difference in the serious impact on oral health of people who inject these drugs.²³³ It is worth noting that many patients who inject drugs use multiple different illicit substances (knowingly and unknowingly), as well as alcohol, cannabis and/or tobacco. Given the prevalence of polysubstance use among people who inject drugs, it is often difficult to establish which substance is responsible for which oral and dental findings.

Dental diseases profoundly impact the daily function and self-esteem of people with SUD and, particularly, people who inject drugs (PWID). The cosmetic and functional consequences of dental disease can have profound social and emotional consequences for PWID.^{235,236} The general health consequences of periodontal disease are many, putting PWID with periodontal disease at additional risk for diabetes, cardiovascular disease, stroke and respiratory illness.^{237–241} Research suggests that primary drivers of poor oral and dental health in PWID are inadequate oral hygiene, increased rates of accidents and injury, increased consumption of sugary drinks and snacks, and hypofunction of the salivary glands, though further research is needed to determine the pathophysiology of substance-related disease.^{43,242}

Dentists often care for patients with SUD. By adopting harm reduction principles, dentists can have an impact that far exceeds improving patients’ dental health. By treating patients with compassion and understanding, dentists can help eliminate the stigma that often prevents patients from seeking appropriate care. By encouraging PWID to not share needles and to access syringe exchange programs, dentists can help prevent soft tissue infections, HIV and viral hepatitis. By prescribing naloxone to patients who are misusing opioids or injecting heroin or fentanyl, dentists can provide an essential medication that decreases patient mortality and helps curb opioid overdoses. Lastly, through knowledge of the effects of drug use on dental health, dentists can intervene more effectively to improve dental outcomes.

Harm Reduction continued

Stigma and Bias as Obstacles to Health Care

SUDs are medical diseases, defined by genetic predisposition and long-term changes in brain structure and function. While federal law dictates that behavioral health disorders and medical illnesses be treated on an equal footing, in reality patients with SUD—and PWID particularly—face substantial cultural and institutional barriers to accessing care. While many of these structural obstacles are beyond the capacity of dentists to address, dentists and their clinic staff can improve their care of this vulnerable patient population by identifying and eliminating stigmatizing attitudes and behaviors in their own approach to the care of patients with SUD.

The stigma surrounding SUD prompts many patients to avoid contact with medical and dental clinicians; many may not present until an advanced state of disease makes seeking care unavoidable. One study of people seeking care at a harm reduction organization found that despite 68%

reporting oral health concerns, only 29% sought dental care; about half of the study group reported that they only go to the dentist if they are in severe pain. The most common reasons for not going to the dentist were fear and a perceived lack of sympathy from the dentist.²⁴³

While people with SUD may care deeply about their health, they often lack the practical, organizational and behavioral resources to access regular care.²³⁵ Dentists who treat these patients with respect and empathy are better able to establish a trusting, therapeutic alliance and may be able to effectively refer patients with SUD to addiction treatment and/or to harm reduction agencies. In addition, dental patients with SUD are more likely to return for care to a dental practice where all staff treat them with compassion and without judgment. Dentists who adopt such best practices as described in **TABLE 11** may discover a greater sense of competence, efficacy and satisfaction when practicing dentistry with people with active SUD.

(TABLE 11)

Best Practices for the Care of Patients with Substance Use Disorder (SUD)

- When patients are suspected of having SUD, dentists are encouraged to inquire about substance use in a nonjudgmental way and emphasize concern for their health.
- Dentists should assume people who use drugs care about their health. It is not uncommon for dentists to assume that people who use drugs don't care about their health; such misperceptions are noticed by patients. Fearing negativity and condescension, many people who use drugs avoid seeking dental care and attempt to treat their dental pain and disease with illicit opioids and/or antibiotics.^{234,235}
- Dentists are advised to treat patients' pain. Some providers reflexively undertreat or minimize pain when they suspect drug-seeking behavior in order to "teach the patient a lesson" or out of fear of "feeding their addiction."
- Dentists are encouraged to provide patients with targeted educational information about risk reduction rather than judgmental speeches or shaming lectures about drug use.
- It is important to respect patients at all times. Patients often overhear health care providers talking about them negatively outside of the room or behind a curtain. Assuming patients can't hear them, clinicians can be heard labeling them as "druggies" or "drug seekers."
- Dentists are encouraged to educate dental hygienists, dental assistants and dental administrative staff on harm reduction and the compassionate treatment of all patients.

Harm Reduction continued

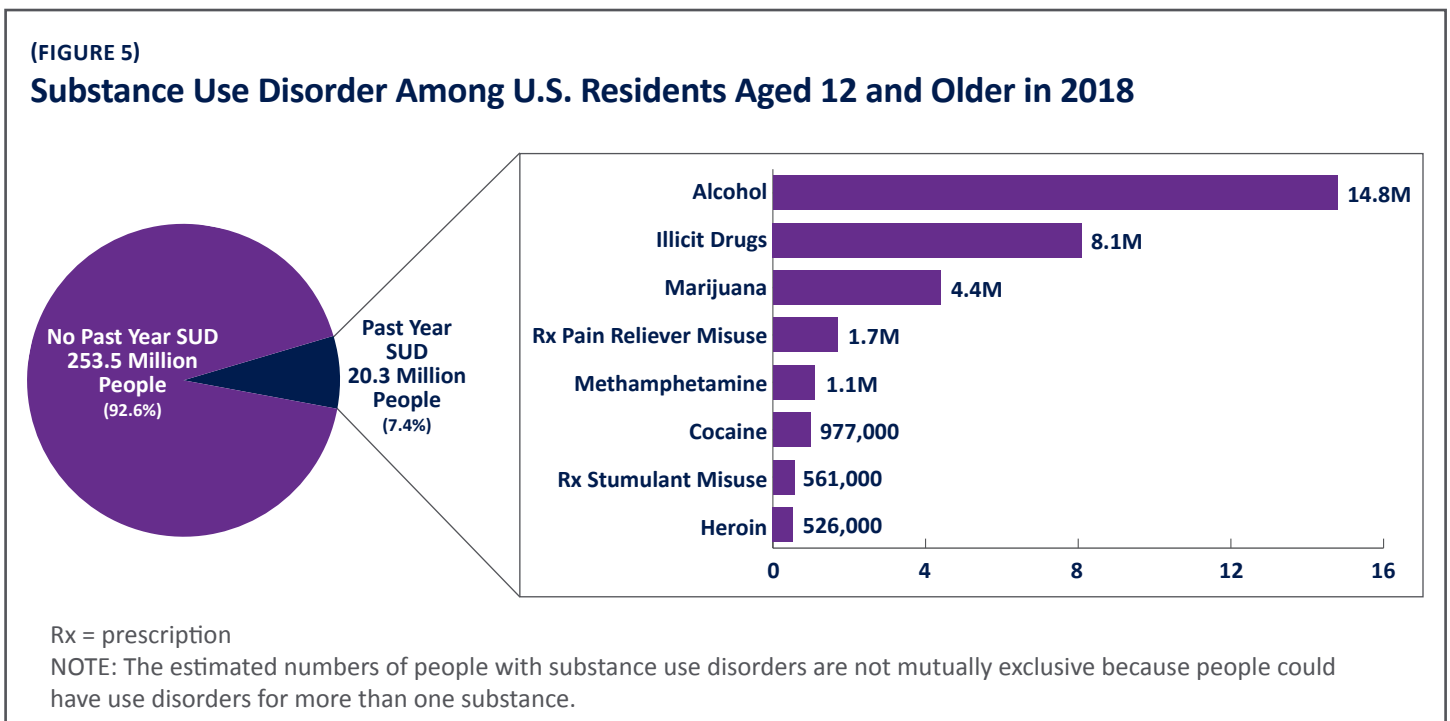
Practice Recommendations

1. **Dentists are encouraged to manage patients with SUD without judgment. Addiction is a medical condition and not a moral failure, and dentists are encouraged to meet patients “where they are,” infusing empathy and respect into the patient/dentist relationship.**
 - a. Patients who feel stigmatized, devalued or disrespected are less likely to access regular dental care.
 - b. Abstinence is an ideal; it is recommended that dental care and patient education provide specific, useful information on preventing and treating dental harms associated with SUD and directly address health concerns rather than lecturing on moral or societal standards.
 - c. Dentists are encouraged to counsel patients and allow them to seek treatment—or not—at their own pace (**TABLE 11**). Pressuring or forcing patients into treatment for SUD is ineffective, violates patient autonomy and creates an adversarial rather than therapeutic relationship.
 - d. While treating underlying SUD is the most reliable way to improve patients’ dental health, dentists are advised to provide acute and preventive care to patients with active SUD. Although patients with untreated SUD may fail to adhere to dental care

and preventive recommendations, terminating relationships with such patients may increase harm to the patient and is not advised.

- e. Addiction care is rarely taught in dental or dental hygiene school or dental assistant training programs.^{43,244} Dentists and dental team members are encouraged to seek out educational opportunities to better understand addiction and the stigma associated with OUD and other SUDs.
 - i. [An Introduction to Substance Use Disorders for Dental Professionals](#)
 - ii. [The Dental Professional’s Role in the Opioid Crisis](#)

2. **It is recommended that dentists be knowledgeable about the diagnosis, treatment and prevention of oral and dental diseases associated with SUD.**
 - a. In 2018, it was estimated that approximately 20.3 million U.S. residents aged 12 or older (7.4%) had active SUD and 2.0 million (0.7%) had untreated OUD (**FIGURE 5**).²⁴⁵
 - b. Surveys of dental claims and visits indicate that in some practice settings, as many as 20.6% of patients may have SUD.²⁴⁶ A study that surveyed patients in the waiting room of a university dental clinic found that 38% of patients self-reported nonmedical use of an opioid in the 30 days prior to their visit.²⁴⁷



SOURCE: SAMHSA²⁴⁵

Harm Reduction continued

- c. While a survey of the many adverse dental effects of illicit drug use is beyond the scope of these guidelines, dentists are encouraged to access educational resources as appropriate to their practices.
 - i. The *ADA Practical Guide to Substance Use Disorders and Safe Prescribing* is a comprehensive resource for dentists.
- d. Addiction treatment centers that provide oral health care have higher rates of favorable dental and general health outcomes.²⁴⁸
 - i. Multiple studies have shown that PWID self-medicate with illicit substances to treat dental pain.^{234,236,249} In one study, 52% of people who use intravenous heroin admitted to using illicit drugs for pain control compared to 21% of people who use other illicit drugs.
 - ii. Patients with SUD have higher rates of chronic dental pain related to periodontitis, dental caries, tooth fracture and/or necrotizing gingivitis^{234,250–253} and are more likely to sustain traumatic orofacial injuries such as tooth fractures and tooth loss.^{235,254,255}
 - iii. Opioid withdrawal may cause dental pain.²⁵⁶
- e. It has been suggested that harm reduction specifically aimed at preventing adverse oral health consequences to PWID could be achieved by distribution of low-intensity preventive measures such as distribution of dental hygiene kits and xylitol gum^{257–259} by harm reduction centers and/or outreach workers.²³³ The application of fluoride varnishes may also have the potential to reduce the incidence of dental caries in this population.^{260–263}
- f. Use of opioids (including methadone for the treatment of OUD) has been linked to higher sugar cravings and intake, making patients more susceptible to dental complications.^{264–266} The activation of μ and κ -opioid receptors enhances reward pathways stimulated by food ingestion.²⁶⁷
- g. Opioids cause impaired peripheral signaling at parasympathetic muscarinic receptors and primary salivary centers, which causes a decrease in salivary secretion.^{250,268} Salivary hypofunction from long-term opioid use may produce xerostomia, burning mouth, taste impairment, eating difficulties, mucosal infections and periodontal disease.²⁵⁰ Opioid use can also cause bruxism, candidiasis and mucosal dysplasia.²⁵⁰
 - i. The most common dental diseases in people who use heroin are periodontitis and dental caries, but there have been studies linking heroin use to necrotizing gingivitis.^{234,250–253}
 - ii. Dental caries from heroin use may have its own specific identifying characteristics described as dark, atypically wide cervical lesions most commonly limited to buccal and labial surfaces.^{234,269,270}
- h. Patients with untreated SUD and patients in all stages of treatment and recovery benefit from regular dental care.

Dental Recommendations for Patients Treated with Methadone

- Use of methadone for the treatment of OUD is associated with salivary hypofunction, xerostomia, burning mouth, taste impairment, eating difficulties, mucosal infections, periodontal diseases and increased craving for sweet food.^{271,272} For these reasons, methadone treatment is associated with increased rates of dental disease.²⁷³
- Dentists should be aware that while methadone is available in a sugar-free preparation, sugar-based formulations are the most commonly used due to the bitter taste of methadone.²⁶⁶
- While dentists do not prescribe methadone for treatment of OUD, dentists may recommend use of sugar-free methadone preparations for their patients with evidence of decay and erosion.
- It is suggested that any dental patient receiving methadone for treatment of OUD be advised of the dental harms associated with daily ingestion of sugar-based methadone formulations.
- Dentists can reduce harm associated with use of sugar-based methadone preparations for addiction treatment by advising patients to clean and rinse their teeth following daily methadone dosing.

Harm Reduction continued

3. Dentists are encouraged to prescribe naloxone to any patient at risk for opioid overdose and inform patients and families about the availability of naloxone without a prescription in most Colorado pharmacies. Dental patients at risk for opioid overdose should have access to this life-saving medication.

- a. In 2018 the U.S. Office of the Surgeon General issued an advisory supporting broader access to naloxone, joining the CDC, World Health Organization (WHO) and American Medical Association (AMA) in advocating for the wider availability of naloxone.
 - i. The advisory states, “For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and

friends of people who have OUD, and community members who come into contact with people at risk for opioid overdose, knowing how to use naloxone and keeping it within reach can save a life.”²⁷⁴

- b. Dental practices can facilitate patients' access to naloxone by writing a prescription, advising patients and family of the over-the-counter availability of naloxone at most pharmacies via standing order and/or through referral to a community organization that provides naloxone and overdose education. **TABLE 12** lists risk factors for opioid overdose; it is recommended that patients with any of these risk factors have access to naloxone and receive overdose education.

(TABLE 12)

Criteria for Dispensing Naloxone to High-Risk Patients

Patients at elevated risk for opioid overdose include those who:

- Have suspected OUD or nonmedical opioid use
- Use IV drugs
- Are prescribed more than 50 mg MME per day
- Are receiving an opioid prescription for pain AND
 - A prescription for methadone or buprenorphine
 - Have a history of acute or chronic pulmonary disease
 - Have a history of renal dysfunction, hepatic disease or cardiac comorbidities
 - Have known or suspected excessive alcohol use or dependency
 - Concurrently use benzodiazepines or other sedatives
 - Have known or suspected poorly controlled depression
- Are taking opioids but have unreliable access to emergency medical services
- Were recently released from incarceration
- Have resumed opioid use after a period of abstinence

- c. It is recommended that family members and friends be counseled on recognizing the signs of overdose and using naloxone, and advised of the availability of naloxone at most Colorado pharmacies.
 - i. A list of pharmacies that participate in Colorado's standing-order naloxone protocols can be found at www.stoptheclockcolorado.org.
 - ii. Instructional videos and resources for naloxone are available at www.ERNaloxone.org.

4. Dentists are encouraged to be familiar with Colorado laws pertaining to naloxone. Colorado law eliminates liability risk for prescribing naloxone, encourages Good Samaritan reporting of overdose, and makes naloxone legal and readily available at Colorado pharmacies.

- a. Colorado State-Specific Policy Summaries Third-Party Naloxone Bill (Colorado SB 13-014). Passed in 2013, the bill removes the following:
 - i. Civil liability for prescribers
 - ii. Criminal liability for prescribers
 - iii. Civil liability for layperson administration
 - iv. Criminal liability for layperson administration

Harm Reduction continued

- b. Colorado Good Samaritan Law (Colorado Revised Statutes §18-1-711 and HB 16-1390)
 - i. Samaritan acting in good faith
 - ii. No arrest or prosecution for possession
 - iii. No arrest or prosecution for paraphernalia and protection from other crimes
- c. Standing Orders for Naloxone (Colorado SB 15-053)
 - i. Any health care professional with prescriptive authority can write a standing order for naloxone that can be dispensed by other designated individuals (such as pharmacists and harm reduction organizations)

5. Dentists are advised to refer patients who inject drugs to syringe access programs and/or harm reduction centers where they can obtain sterile injection materials and support services such as counseling, HIV and hepatitis testing, referral to treatment and recovery support and additional resources.

- a. The WHO suggests a “compelling case that needle and syringe programs substantially and cost effectively reduce the spread of HIV among IV drug users and do so without evidence of exacerbating injecting drug use at either the individual or societal level.”⁷³
- b. In 2000, the AMA adopted a position strongly supporting the efficacy of these programs when combined with addiction counseling.⁷⁴
- c. Syringe access programs have demonstrated cost-effectiveness in reducing HIV transmission and prevalence.⁷²
- d. By referring patients to organizations and resources that support safer injection practices, dentists may help prevent infectious complications of IV drug use. The additional resources these centers often provide (e.g., sterile water, cooking units and cleaning solutions) can also help reduce such dangers. Preventing the acquisition and transmission of infectious diseases improves patients’ dental and general health, reduces health care costs and decreases risk for dental care teams.
- e. A complete list of local Colorado syringe access programs can be found at <https://www.colorado.gov/pacific/cdphe/reducing-infections-injection-drug-use>. A national list can be found at the North American Syringe Exchange Network (<https://www.nasen.org/map/>).

Policy Recommendation

- 1. Harm reduction agencies and community programs that provide resources for patients with SUD (and particularly patients who inject drugs) should be made readily available to all Coloradans in need and up-to-date referral information be made available to clinicians.**
 - a. The passage of C.R.S. §25-1-520 in 2010 legalized the establishment of syringe access programs with local jurisdiction approval.
 - b. Community programs aimed at providing needle exchange and disposal services, sterile equipment, free counseling and HIV/hepatitis screening are cost-effective strategies for preventing the transmission of bloodborne pathogens.
 - c. These programs, many of which also provide basic medical and social services to this high-risk population, should be well funded and expanded beyond their current levels.



Treatment of Opioid Use Disorder



Treatment of Opioid Use Disorder

There are patients with SUD for whom contact with a dentist is the sole engagement with the health care system. While few dentists enter their profession to treat SUD and few dental schools offer formal training in addiction medicine, the treatment of SUD is a reliable means of improving patients' dental and general health. It is recommended that similar standardized screening, education, counseling and referral to treatment that dentists advise for their patients with alcohol use disorder and tobacco use disorder be extended to patients with illicit substance use disorders.^{275–278} Ideally, patients with untreated OUD will be identified in dental care settings and referred to an addiction specialist or clinic able to prescribe MAT. While dental schools are increasingly incorporating training in the best care of patients with SUD as an essential element of dentistry and well within the scope of dental practice, some dentists may benefit from continuing education in the field of addiction care.⁴³

Like patients with other chronic illnesses, patients diagnosed with OUD need ongoing comprehensive, evidence-based care. Abstinence-oriented treatments are ineffective for the treatment of OUD, with relapse rates of greater than 80%.¹⁴⁸ The gold standard for treatment of OUD employs one of the three FDA-approved medications for addiction treatment: methadone, buprenorphine or naltrexone. Overwhelming evidence demonstrates that patients receiving MAT have lower morbidity and mortality, higher treatment retention rates and lower health care costs.¹⁴⁹ Of the estimated 2.1 million people in the United States with OUD, fewer than 20% receive evidence-based treatment with MAT.¹⁴⁷ The consequences of this treatment gap are substantial, including dramatically increased risks of overdose injury and death, transmission of HIV and viral hepatitis, invasive bacterial infections and a range of risky and criminal behaviors.

Patients treated for OUD can lead fulfilling, productive lives while maintained on medication. It is important to recognize that opioid dependence and opioid addiction are different entities; patients may be physically dependent on buprenorphine or methadone, but when maintained on these medications the risks and behaviors seen in addiction are avoided. OUD cuts across all social demographics and is frequently seen in people seeking medical and dental care. Dentists, as frequently accessed health care providers, are in an ideal position not only to identify OUD but also to intervene and direct patients toward evidence-based treatment and recovery.

Practice Recommendations

1. Dentists are encouraged to screen all patients for SUD.

- a. The Screening, Brief Intervention and Referral to Treatment (SBIRT) model provides a valuable framework for dentists to recognize and address risky substance use and SUD in their patients.
- b. SBIRT is an early intervention screening strategy suitable for use in a wide range of health care settings, including dentistry. SBIRT is comprised of universal screening of patients for risky patterns of substance use and/or SUD, brief intervention (targeted counseling) for patients who misuse substances but do not have full SUD and referral to treatment of patients with untreated SUD.²⁷⁹
- c. SBIRT has been shown²⁷⁹ to reduce alcohol consumption, ED visits, nonfatal injuries, hospitalizations, arrests and motor vehicle accidents, and to increase rates of patient follow-up for treatment.⁴³ Although research on the effectiveness of SBIRT for drug use is mixed, SAMHSA recommends SBIRT for both alcohol and illicit drug use.^{43,280}

Treatment of Opioid Use Disorder continued

- d. Multiple organizations, including SAMHSA and SBIRT Colorado, provide valuable resources for health care practitioners interested in implementing SBIRT programs.
 - i. In addition, a SBIRT mobile application has been developed to aid in the chairside identification of high-risk patients and provide a template for interventions and treatment referrals.
 - e. A number of validated screening tools may be used as part of the SBIRT protocol. The following validated screening instruments are short, easily administered and available for free use in dental care settings:
 - i. Tobacco, Alcohol, Prescription Medication and Other Substance Use Tool (TAPS)
 - ii. NIDA quick screen
 - iii. Alcohol, Smoking, Substance Involvement, Screening Test (ASSIST)
 - iv. Drug Abuse Screening Test (DAST)
 - v. Alcohol Use Disorders Identification Test (AUDIT)
 - vi. Opioid Risk Tool
 - vii. NIDA-Modified Assist
 - viii. Screener and Opioid Assessment for Patients with Pain – Revised (SOAPP-R)
 - ix. Pain Medication Questionnaire (PMQ)
 - f. A 2010 study found a single question—“How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?”—to be highly sensitive in detecting illicit drug use in patients in primary care settings.²⁸¹
 - g. Dental clinicians are encouraged to access the many available resources for training in motivational interviewing and brief counseling. Motivational interviewing is a brief, patient-centered therapeutic approach that supports patients' readiness to change by exploring their ambivalence about their risky or harmful behaviors and their interest in modifying them. The technique has been demonstrated to increase patients' motivation to change and reduce unwanted behaviors.^{282–287}
 - i. The principles of motivational interviewing can be applied to any patient behavior in need of modification. Some training programs for dental hygienists incorporate training in motivational interviewing.^{288,289}
 - ii. SBIRT Colorado offers a free one-hour online training, Addressing Alcohol and Drug Use in Healthcare, for Colorado clinicians.
 - iii. SBIRT Colorado offers live training in SBIRT periodically throughout the year across Colorado.
- 2. It is recommended that dentists refer patients whose screening indicates possible OUD or another SUD to an addiction specialist or primary care physician for evaluation and care.**
- a. Interprofessional collaboration by dentists with other health care clinicians improves patient care, as dental health and general health are inextricably related. Close communication and collaboration between dentists and other health care clinicians is essential to addressing not just SUD in dental and medical practice, but a wide range of other conditions as well.
 - b. Dentists are encouraged to develop referral networks of addiction medicine specialists, pain medicine specialists and behavioral health clinicians to ensure that dental patients with SUD are consistently and successfully referred for evaluation. It is recommended that dentists be familiar with MAT providers in their area in order to refer patients with OUD to evidence-based care with methadone, buprenorphine or naltrexone.
 - i. OpiRescue, a free mobile application and website (opirescue.com), provides an up-to-date MAT treatment locator. It ranks providers based on the distance the patient lives from the provider and gives each provider's treatment options (i.e., methadone, buprenorphine or naltrexone).
 - ii. A list and map of MAT facilities can be accessed on the Colorado Hospital Association website or at SAMHSA (findtreatment.samhsa.gov).
 - iii. For patients with other SUDs, Rocky Mountain Crisis Partners can be contacted at 844-493-8255 or rmcrisispartners.org.
 - c. OUD is defined by the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, (DSM-5) and replaces “opioid addiction” and “opioid dependence” as a diagnostic entity.

Treatment of Opioid Use Disorder continued

(TABLE 13)

Summarized DSM-5 Diagnostic Categories and Criteria for OUD

CATEGORY	CRITERIA
Impaired Control	<ul style="list-style-type: none"> • Opioids used in larger amounts or for longer than intended • Unsuccessful efforts or desire to cut back or control opioid use • Excessive amount of time spent obtaining, using or recovering from opioids • Craving to use opioids
Social Impairment	<ul style="list-style-type: none"> • Failure to fulfill major role obligations at work, school, or home as a result of recurrent opioid use • Persistent or recurrent social or interpersonal problems that are exacerbated by opioids or continued use of opioids despite these problems • Reduced or given up important social, occupational, or recreational activities because of opioid use
Risky Use	<ul style="list-style-type: none"> • Opioid use in physically hazardous situations • Continued opioid use despite knowledge of persistent physical or psychological problem that is likely caused by opioid use
Pharmacological Properties	<ul style="list-style-type: none"> • Tolerance as demonstrated by increased amounts of opioids needed to achieve desired effect; diminished effect with continued use of the same amount • Withdrawal as demonstrated by symptoms of opioid withdrawal syndrome; opioids taken to relieve or avoid withdrawal

SOURCE: Psychiatric Times, DSM-5²⁹⁰

3. Dentists should be aware that MAT with buprenorphine, methadone or naltrexone is the evidence-based treatment for OUD. “Detox” and other abstinence-oriented therapies are generally ineffective for the treatment of OUD, and dentists are discouraged from endorsing or referring patients to such non-evidence-based treatments.

- a. MAT using buprenorphine, methadone or naltrexone is the cornerstone of the treatment of OUD. A Cochrane review found the addition of counseling to medication conferred no added benefit; MAT plays a central—not adjunctive—role in the treatment of OUD.²⁹¹
- b. Detox and abstinence-based therapies for the treatment of OUD have unacceptably high failure rates, with markedly elevated risks of relapse and overdose death.^{292–295}
- c. Most patients with OUD are not adequately treated. As of 2019, the Colorado Department of Human Services Office of Behavioral Health estimates a treatment gap of approximately 70%, with only 30% of patients with OUD in Colorado receiving treatment.
- d. Like many medical conditions, OUD is a chronic, relapsing disease in which biochemical derangements, behavior and medications contribute to disease management and recovery. As with any chronic disease, it is recommended that relapse not preclude continued treatment.
- e. MAT is not “substituting one addiction for another.” While patients may continue to have a physiologic dependence on buprenorphine or methadone, they do not exhibit the behavioral hallmarks of addiction. MAT substitutes dependence for addiction and in so doing decreases morbidity and mortality while improving quality of life.
- f. MAT for OUD can be maintained for years or be a lifelong drug, and it is advised that buprenorphine or methadone for addiction treatment not be prematurely tapered.

Treatment of Opioid Use Disorder continued

(TABLE 14)

Characteristics of Medication for Addiction Treatment (MAT)

CHARACTERISTIC	METHADONE	BUPRENORPHINE	NALTREXONE
Brand Names	Dolophine, Methadose	Subutex, Suboxone, Zubsolv	Depade, ReVia, Vivitrol
Class	Agonist (fully activates opioid receptors)	Partial agonist (activates opioid receptors but produces a diminished response even with full occupancy)	Antagonist (blocks the opioid receptors and interferes with the rewarding and analgesic effects of opioids)
Use and effects	Taken once per day orally to reduce opioid cravings and withdrawal symptoms	Taken orally or sublingually (usually once a day) to relieve opioid cravings and withdrawal symptoms	Taken orally or by injection to diminish the reinforcing effects of opioids (potentially extinguishing the association between conditioned stimuli and opioid use)
Advantages	High strength and efficacy as long as oral dosing (which slows brain uptake and reduces euphoria) is adhered to; excellent option for patients who have no response to other medications	Eligible to be prescribed by certified physicians, which eliminates the need to visit specialized treatment clinics and thus widens availability	Not addictive or sedating and does not result in physical dependence; a recently approved depot injection formulation, Vivitrol, eliminates need for daily dosing
Disadvantages	Mostly available through approved outpatient treatment programs, which patients must visit daily	Subutex has measurable abuse liability; Suboxone diminishes this risk by including naloxone, an antagonist that induces withdrawal if the drug is injected	Poor patient compliance (but Vivitrol should improve compliance); initiation requires attaining prolonged (e.g. 7-day) abstinence, during which withdrawal, relapse, and early dropout may occur

SOURCE: NEJM²⁹⁶

Treatment of Opioid Use Disorder continued

4. It is advised that patients receiving methadone or buprenorphine for treatment of OUD be continued on their addiction treatment medication and offered analgesia for acute dental and/or perioperative pain.²³²

- a. It is recommended that dental patients who are receiving methadone or buprenorphine while being treated for a dental condition be maintained on their MAT regimens.
 - i. Continuing opioid agonist medications for OUD in the setting of acute dental pain and/or before, during and after a dental procedure improves pain control, reduces the use of additional opioid analgesia and reduces the risk of relapse.^{297–299}
 - ii. Discontinuation of MAT with opioid agonists in the perioperative period is strongly discouraged, as it may complicate clinical assessment, increase risk of relapse and increase discomfort during reinduction.^{229,230}
- b. It is recommended that patients receiving MAT for the treatment of OUD be offered analgesia for dental pain with maximal use of nonopioid multimodal analgesia. If pain control is inadequate with nonopioid management, patients may be offered opioid analgesia at the lowest dose and shortest duration possible (see Table 8). Failing to manage the patient’s pain adequately can increase the risk of relapse, particularly if the patient uses illicit opioids to manage acute dental pain.
- c. Per *The ADA Practical Guide to Substance Use Disorders and Safe Prescribing*:

Other than anecdotal reports, there is no evidence that patients receiving methadone or buprenorphine maintenance therapy for opioid addiction and who are also prescribed opioids for acute pain are at a greater risk of relapse of addiction than patients not receiving opioids for acute pain management if monitored appropriately. Limited information does suggest that inadequate treatment of acute pain, onset of physiologic withdrawal or anticipatory anxiety in patients [receiving MAT] **may be a greater stressor for relapse.**²³²
- d. Dentists may collaborate with a patient’s MAT prescriber to develop a patient-centered pain management plan, particularly if a need for opioid analgesia is anticipated. It is suggested that the patient also be involved in developing a pain management strategy.
- e. Dentists are encouraged to reassure patients receiving MAT that questions about their methadone or buprenorphine treatment are intended to optimize their dental pain management, not minimize or deny analgesia.
 - i. Due to the stigma surrounding OUD and MAT, many patients with OUD will have had past experiences with health care professionals that make them fearful and distrustful; they may fear inadequate treatment of their pain.²³²
 - ii. Anticipation or perception of inadequate analgesia may encourage patients to exaggerate their current analgesic needs.²³²
 - iii. Reassuring the patient that the primary goal is adequate analgesia may be helpful in disarming self-protecting behaviors.²³²
- f. See **TABLE 10** in the **ALTERNATIVES TO OPIOIDS** for the Treatment of Pain section for guidance in pain management for patients receiving naltrexone for treatment of addiction. Consultation with the patient’s naltrexone prescriber may be appropriate.
- g. Consider consultation with a pain specialist for patients who are anticipated to have difficult-to-manage postoperative pain.

Treatment of Opioid Use Disorder continued

5. Patients in recovery from SUD may be at increased risk of relapse due to dental or postoperative pain and/or opioid exposure. It is suggested that dentists candidly discuss the risk of relapse, reassure the patient that their pain will be treated and develop a pain management plan with the patient that maximizes use of nonopioid multimodal analgesia.

- a. It is recommended that pain management protocols recognize the risk of relapse in patients in recovery from SUD. Addiction is a chronic, relapsing disease, and dentists are advised to minimize risk of relapse as much as possible in patients who present with dental pain and patients undergoing dental procedures.
- b. A candid, non-stigmatizing discussion of the risk of relapse is recommended prior to any painful dental procedure. It is advised that patients be urged to boost their recovery tools and supports in preparation for a painful dental procedure.
- c. Dentists are encouraged to provide clear reassurance that any postoperative pain will be adequately treated. Many patients with SUD have had encounters with dental or medical clinicians who failed to address their pain. Fear of pain may prompt patients to delay treatment, and severe postoperative pain could be a trigger for relapse.
- d. Patients in recovery from SUD may be educated that a scheduled regimen of an NSAID and acetaminophen has been demonstrated to be the most effective pharmacologic treatment for pain. Use of long-acting local anesthetics and nonpharmacologic interventions should be strongly considered, unless contraindicated.
- e. No patient should be denied analgesia; if opioids are required for patient comfort, they may be prescribed, with the direction to use them for breakthrough pain only and for the shortest duration possible. It is advised that the patient's tolerance for opioids be normalized for patients who are no longer receiving treatment with methadone or buprenorphine.
- f. Dentists are encouraged to consult with a patient's behavioral health, chronic pain and/or addiction care specialist in crafting a pain management plan.

Policy Recommendations

- 1. Private and public dental insurers should provide adequate compensation for the additional time and expertise required for the provision of SUD screening in dental practice and for the additional resources needed to ensure that patients with untreated SUD are appropriately referred to providers of evidence-based care.¹¹⁶**
 - a. Identification and referral to treatment of patients with SUD is vital to improving both dental and overall health.
 - b. Patients are often reluctant to disclose information about their substance use, particularly on written or quickly administered verbal questionnaires. Obtaining an accurate substance use history, reviewing PDMP and medical record data and conferring with other clinicians involved in a patient's care often requires additional clinical skill, resources and time.
 - c. Dental patients with untreated SUD often require referrals to primary care clinicians, addiction medicine, pain management and/or behavioral health specialists. Adequate reimbursement for coordinated care supports the consistent, comprehensive management of dental patients with complex behavioral health needs.
 - d. Inclusion of dentists and dental practices in Health First Colorado's list of clinicians able to train in, implement and bill for SBIRT protocols would facilitate broader adoption of this evidence-based approach in dental practice.

The Future and Ending the Opioid Epidemic in Colorado

As clinicians, we stand with our patients and their families who are impacted by the current epidemic of opioid use disorder (OUD) and opioid overdose death. We have witnessed the devastation this epidemic has wrought across Colorado and are committed to ending the suffering of our patients and communities.

This set of CO's CURE guidelines was developed by and for dentists and offers a vision for how we on the front lines of this epidemic can change how we deliver care to better serve our patients. If all clinicians take to heart the need to reduce opioid prescribing, we can decrease the number of Coloradans who develop OUD in our care. If we embrace and continue to innovate in using alternatives to opioids for pain control, we will be able to manage pain more effectively and more safely than ever before. If we integrate harm reduction into our practices and strive to better understand patients who struggle with injection drug use and OUD, we can help to end the stigma that surrounds this disease and decrease overdose deaths. If we consistently refer patients with OUD to medication for addiction treatment programs, we can help close the treatment gap and ensure that all who yearn for recovery are provided the tools and the resources they need. The time to make these changes is now. In doing so, we can uphold our sacred oath to serve our patients and communities in their times of need and resolve to address this epidemic together.

CO's CURE aims to harness the power of health care professionals across Colorado working together with common purpose. CO's CURE resources are available to any Colorado health care provider. As you endeavor to change your practice and adopt these guidelines, you can rest assured that medical and dental practices across our state are doing the same. CO's CURE represents a philosophy of care that is inclusive and collaborative, and recognizes that the only way we can end the epidemic in Colorado and across the nation is by acting together.

On behalf of our sponsoring organizations—Colorado Hospital Association, Colorado Medical Society and Colorado Consortium for Prescription Drug Abuse Prevention—as well as the Colorado Dental Association and the 12 other medical specialties that have stepped forward to participate, we offer our gratitude and appreciation for the care and consideration you give these guidelines. The health of our state and its people depends on clinicians and leaders like you who are willing to be agents of change. Together we can make a profound difference in the lives of Coloradans as we implement new, better standards of care. Together we can bring this deadly epidemic to an end.

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Appendices

- I. Understanding Pain: A Complex Biopsychosocial Phenomenon
- II. Summary of 2018 American Academy of Pediatric Dentistry Recommendations
- III. Cannabinoids, Pain and Anesthesia

Appendix I

Understanding Pain: A Complex Biopsychosocial Phenomenon

The United States is experiencing not only an epidemic of OUD, but also an epidemic of pain. Despite the fact that the United States consumes a disproportionately large fraction of the world's opioids, one-fifth of Americans suffer from pain. Pain, common sense and neuroscience agree—it is not simply a process defined by receptors, neurological afferents and the interactions with the spinal cord and brainstem. Instead, it is an experience that incorporates all these biological elements and integrates them with psychological and social conditions to produce the experience of pain. To an extent not seen with other conditions, the biology of pain, the psychology of the patient and the social circumstances of a patient are intertwined and indivisible. Whether it is acute or chronic, easily treated or intractable, pain is a complex interplay of peripheral and CNS processes. The experience of pain is literally “all in the head,” and it is heavily influenced by the context of a painful experience, past experiences of pain, genetics, mental health comorbidity, culture and patients' life experiences. One helpful model of conceptualizing pain is the biopsychosocial model, which incorporates elements of biology, psychology and social context into an understanding of the pain experience.

The Biology of Pain

Most dentists are aware of the distinctions between nociceptive pain, which can be somatic or visceral, neuropathic pain, inflammatory pain and types of pain less easily categorized, such as cancer pain, headache syndromes and fibromyalgic pain. Pain differs, too, in its duration, intensity, location and etiology. Sensorimotor pathways relay information about the nature of the pain stimulus. The cognitive and affective pathways incorporate sensorimotor information and evaluate it, integrating it with information based on prior experience and emotions. Because the biology of pain differs, it is recommended that treatments be targeted wherever possible to the type of pain. Dentists are encouraged to use opioid-sparing multimodal analgesia as outlined in these guidelines, consulting pain specialists whenever pain is not well managed. Regrettably, the indiscriminate prescription of opioids may have contributed to an epidemic of chronic pain. Opioid-induced hyperalgesia, in which sensitization of pronociceptive mechanisms occurs (resulting in a decrease in the pain threshold), may contribute to persistent pain for many patients.³⁰⁰⁻³⁰²

Advances in the neurobiology of pain shed light on the physiological explanations for individual differences in pain thresholds and analgesic responses. While every patient is different, fresh insights into the genetic and molecular basis of pain perception from model organisms and human twin studies underscore that there are significant genetic contributors and polymorphisms in pain tolerance and analgesic responsiveness.³⁰³⁻³⁰⁵ Gender

differences in pain processing are another important area of ongoing research, consistently demonstrating differences between males and females in pain threshold, susceptibility to chronic pain and analgesia sensitivity.³⁰⁶ Electroencephalogram (EEG) studies, too, have identified measurable EEG signatures that predict differences in pain tolerance among individuals.³⁰⁷

The Psychology of Pain

Neuroimaging studies demonstrate the significant extent to which cognitive and affective factors impact the experience of pain. The anticipation of pain, attention or distraction, mood, catastrophizing and perceived control over pain can modulate peripheral, spinal and central activity before, during and after a painful experience. The context of a painful stimulus and a person's prior life experiences greatly affect pain experiences.

For example: A woman who grew up loving dogs is at home with her new puppy. If she is suddenly nipped in the middle of the night with intensity “x,” she will experience pain. However, her prior positive experiences with dogs, being safe at home and knowing the nip probably came from the puppy modulates her negativity of the experience. The same woman, who has always been wary of the ocean, is now at the beach. After finally mustering the courage to wade in, she hears a lifeguard shout, “Shark!” If she feels a nip at her ankles with the same intensity “x,” she will now have a drastically different pain experience.

Appendix I continued

Anticipation of pain, expectations surrounding painful experiences and expectations of relief impact the experience of pain on neuroimaging and by patient report. Studies of normal subjects demonstrate the power of both the placebo effect and the nocebo effect; the same noxious stimulus can produce markedly different neuroimaging and patient experiences. Accordingly, a host of psychological interventions have demonstrated evidence for relieving the negative effects of the pain experience. These include the use of supportive therapy, cognitive behavioral therapy, acceptance and commitment therapy, virtual reality therapy and mindfulness-oriented interventions, which leverage insights into the cognitive and affective components of pain signaling.

Mental health and SUD are often major contributors to the experience of pain.³⁰⁸ The association between mental and behavioral health disorders and chronic pain is well established. The vicious cycle of pain begetting depression and anxiety, which then impair patients' effective management of their pain, is familiar to most clinicians. Functional neuroimaging demonstrates shared neural mechanisms for pain, depression and anxiety.^{309–311}

Finally, when pain is viewed as a cognitive, affective and sensory phenomenon, it is unsurprising that clinician empathy has been identified as promoting pain relief.³¹² The psychology of the patient-clinician interaction impacts the experience of pain and analgesia. Clinician desensitization to patient pain complaints may play a significant role not just in undermining quality of care, but also in decreasing clinicians' professional satisfaction.³¹³ When clinicians recognize that treating pain can be emotionally draining, that self-awareness can help restore empathy. Clinicians who find themselves frustrated in treating a patient with intractable pain are advised to consult with specialists in pain medicine and mental health.

Social Determinants of Pain

While few dentists are equipped to address the deeply rooted social factors that contribute to their patients' pain, it is important to understand that poverty, racism, social stress and isolation have been shown to affect patients' experiences of pain.³¹⁴ Pain, while universally experienced, it is not universally understood. Patients, families and communities all value and understand pain

differently. Types of pain can be influenced by their social repercussions—genital pain, for example, is perhaps more isolating than back pain, as the former cannot be easily talked about with others. This isolation itself can intensify the pain experience. It is interesting to note that brain activation by social rejection or exclusion is very similar to that seen in physical pain. In an age of ever-widening income inequality and persistent racial disparities in health status, dentists should know that the complex stresses of poverty and racism have studied, measurable impacts on pain perception.

The Biopsychosocial Model of Pain: Implications for Clinicians

The biopsychosocial model of pain underscores the importance of valuing and addressing each of these components when treating patients in pain. While a review of the state of pain neuroscience is beyond the scope of these guidelines, clinicians should be aware that functional neuroimaging suggests that there is far more interconnection between the sensory-discriminative and the cognitive-affective circuits than previously appreciated. The model in which "real" pain is biological and the psychological or affective components of pain are secondary (and, therefore, implicitly or explicitly perceived as less valid) is inaccurate and misleading. Researchers theorize that the neural networks involved in pain processing may integrate the sensory, cognitive and affective aspects of pain into a "common currency" that gives rise to one unified pain experience.¹⁹¹ To an extent not seen with other conditions, the biology of pain is the socio-psychology of pain. Dentists are encouraged to educate patients that the experience of pain is distinct for every individual and that the psychological and social determinants of pain are just as "real" to pain as tissue injury. Dentists and patients alike need to understand that all pain is in our heads, and all pain deserves care.

Dentists serve their patients best when they recognize the complexity of pain and involve pain specialists and behavioral health clinicians, as appropriate, for patients with complex pain presentations.

Appendix II

Summary of 2018 American Academy of Pediatric Dentistry Recommendations

Summary of 2018 American Academy of Pediatric Dentistry Recommendations

https://www.aapd.org/media/Policies_Guidelines/BP_Pain.pdf¹³⁰

Infants, children and adolescents can and do experience pain due to dental/orofacial injury, infection and dental procedures. Inadequate pain management may have significant physical and psychological consequences for the patient. Adherence to the following recommendations can help practitioners prevent or substantially relieve pediatric dental pain and minimize risk of associated morbidities.

1. Pain assessment should be considered for all patients.
2. Careful technique should be used to minimize tissue damage when providing dental treatment.
3. Profound anesthesia should be achieved prior to invasive treatment.
4. Use of preemptive analgesia should be considered when postoperative pain is anticipated.
5. Nonpharmacologic techniques (e.g., distraction) should carefully be considered as potentially valuable interventions for pain management.
6. Acetaminophen/NSAIDs should be used as first-line pharmacologic therapy for pain management.
7. Use of opioids should be rare for pain management for pediatric dental patients.
8. To help minimize the risk of opioid abuse, pediatric patients and their parents should be screened regarding previous/current opioid use before prescribing opioid analgesics.
9. To avoid diversion of controlled substances, practitioners should utilize prescription monitoring databases and encourage patients to properly discard any unused medications.
10. Providers should be knowledgeable of risks associated with prescribed analgesic medications and anticipate and manage adverse effects (e.g., asthma and NSAIDs, sedation and opioids).
11. Seeking expert consultation for patients with chronic pain or other complicated pain conditions should be considered.
12. Providers should be familiar with analgesic properties of agents used during sedation or general anesthesia.
13. Prescribing opioid analgesics should be avoided if the patient is using benzodiazepines.
14. Synergistic effect from multiple medications (multimodal analgesia) may be considered.

Appendix III

Cannabinoids, Pain and Anesthesia

The opioid epidemic has motivated dentists, physicians, researchers and patients to seek alternatives to opioids for the management of pain. Legalization and wider societal acceptance of cannabinoids, a broad term that describes the drugs derived from the plants of the genus *Cannabis*, has prompted some to ask whether cannabinoids might offer a safer, less-addictive alternative to opioid analgesia.

Dentists in Colorado are likely aware of the high rates of cannabis use in the state. An estimated 39% of patients who receive chronic opioid therapy for pain report also using cannabis.^{315,316} Ironically, the legalization of cannabis in Colorado has contributed to a widespread popular misperception that cannabinoids are effective analgesics; in fact, evidence increasingly suggests that regular cannabinoid use increases postoperative pain and analgesic consumption.^{317–319} There is a clear, urgent need to investigate the impact of cannabinoid use on anesthesia and pain, and to educate the public on the ways in which cannabinoid use may complicate perioperative dental care. While cannabinoids carry little risk of overdose death, there is ample evidence of their many adverse effects, and no evidence that they have opioid-sparing potential or analgesic efficacy.³¹⁷ Recent meta-analyses and systematic reviews of cannabinoid research find little or no benefit of cannabinoids for chronic, neuropathic or cancer pain, and significant evidence of an unacceptably high incidence of adverse effects.^{305, 306} It is the case that these meta-analyses are hampered by the poor quality of existing research, with most studies underpowered, unblinded or uncontrolled; further high-quality research is warranted given the substantial interrelatedness of the human opioid and cannabinoid systems.^{315, 316} Dentists and anesthesiologists in Colorado are increasingly finding that patients who use cannabis regularly experience more complications with anesthesia and analgesia. Dentists are encouraged to advise patients that current evidence does not support the use of cannabis as a safe, effective analgesic and to further caution them as suggested below. It is recommended that dental patients with chronic pain who inquire about cannabis for analgesia be referred to a pain management specialist.

Appendix III continued

Cannabinoids, Pain and Anesthesia: Counseling Dental Patients

- Although many patients believe that cannabinoids are effective analgesics for chronic or acute pain,^{320,321} no definitive, high-quality studies support the safety and efficacy of dispensary or pharmaceutical cannabinoids for analgesia. Unless better evidence becomes available, dentists are discouraged from endorsing the use of cannabinoids for pain management.
- Dentists are encouraged to educate their patients that chronic cannabis use may increase the risk of complications with dental anesthesia and may complicate postoperative pain management.^{317,322}
- Anesthetic complications in the perioperative period may differ depending on whether the patient uses cannabis in an episodic or chronic manner.³¹⁷
 - Patients who use cannabis chronically who are undergoing dental procedures may have atypical anesthetic and analgesic needs including but not limited to:
 - Difficult-to-control pain following surgery
 - A higher incidence of bradycardia (though patients may also exhibit tachycardia), postural/orthostatic hypotension, sinus arrest, hyperreactive airway, intraoperative hypothermia “shivering,” stroke and coronary vasospasm or myocardial infarction³¹⁸
 - Cannabis withdrawal syndrome
 - Acute use is more likely to produce tachycardia, hypertension, arrhythmias, coronary vasospasm or airway hyperreactivity.
 - Cannabinoids may inhibit platelet aggregation, which could theoretically lead to increased operative site bleeding.
 - In addition, cannabinoids are extensively metabolized by hepatic cytochromes, resulting in drug interactions due to inhibition or induction of these and other enzymes or transporters.^{323,324} Thus, patients may experience unpredictable interaction of cannabinoids with other pharmaceutical agents.
- It is recommended that patients be counseled that the use of any drug that lacks rigorous FDA drug development and safety profiles carries inherent risks.
 - The testing and regulation of dispensary cannabis is poor to nonexistent.
 - Dispensary cannabinoid products available now are far more potent than those sold even a few years ago. Rates of cannabis use disorder (CUD) associated with use of potent dispensary cannabinoids may be as high as 30%.³²⁵
 - Products purchased at dispensaries may be mislabeled, of undetermined content and/or contaminated with harmful substances.
 - It is important to remind patients that cannabis dispensary workers are not trained to give health care advice.

continued

Appendix III continued

Cannabinoids, Pain and Anesthesia: Counseling Dental Patients *continued*

- Adverse effects associated with cannabinoid use include:
 - The development of CUD, which may occur in as many as one in six people who use cannabis regularly and which is associated with an increased likelihood of developing other SUDs³²⁶
 - Deficits in attention, memory and learning,^{327,328} anxiety, paranoia, psychosis and an increased risk of developing schizophrenia, depression and suicidality³²⁹⁻³⁴¹
 - Increased risk for stroke and heart disease among people who smoke or vape cannabinoids^{342,343}
 - Potential harm to lung tissues, scarring of small blood vessels and exposure to many of the same toxins, irritants and carcinogens found in tobacco smoke (among people who smoke or vape cannabis in any form)^{344,345}
 - Second-hand cannabis smoke is harmful to the health of exposed contacts, particularly children and adolescents.³⁴⁶
 - Potential increased risk of testicular cancer and HPV-related head and neck squamous cell carcinoma among people who use cannabis regularly^{347,348}
- It is recommended that any patient with chronic pain be encouraged to seek care from a pain medicine specialist.
- Pregnant or breastfeeding patients are strongly advised to avoid cannabis use due to known and unknown risks to the developing brain, potential birth defects, possible autism or spectrum disorders and future drug-seeking behavior and other behavioral abnormalities.³⁴⁹
- Despite the cautions above, medical clinicians may counsel their patients that many physicians, dentists, researchers, the AMA and the organizations represented in CO's CURE advocate for better scientific research into the safety and efficacy of cannabinoids for pain management.

References

- ¹ Centers for Disease Control and Prevention. Ten Leading Causes of Death and Injury. Published April 10, 2019. Accessed Sept. 12, 2019. <https://www.cdc.gov/injury/wisqars/LeadingCauses>
- ² Scholl L. Drug and Opioid-Involved Overdose Deaths—United States, 2013—2017. *MMWR Morb Mortal Wkly Rep.* 2019;67. doi:10.15585/mmwr.mm6751521e1
- ³ Centers for Disease Control and Prevention. Understanding the Epidemic. Published July 24, 2019. Accessed July 24, 2019. <https://www.cdc.gov/drugoverdose/epidemic/index.html>
- ⁴ Centers for Disease Control and Prevention. 2018 Annual Surveillance Report of Drug-Related Risks and Outcomes—United States. Surveillance Special Report. Published Aug. 31, 2018. Accessed Sept. 12, 2019. <https://www.cdc.gov/drugoverdose/pdf/pubs/2018-cdc-drug-surveillance-report.pdf>
- ⁵ Joranson DE, Ryan KM, Gilson AM, Dahl JL. Trends in Medical Use and Abuse of Opioid Analgesics. *JAMA.* 2000;283(13):1710-1714. doi:10.1001/jama.283.13.1710
- ⁶ Centers for Disease Control and Prevention. Prescription Opioid Data. Published July 11, 2019. Accessed Sept. 12, 2019. <https://www.cdc.gov/drugoverdose/data/prescribing.html>
- ⁷ Substance Abuse and Mental Health Services Administration. The TEDS Report: Length of Time from First Use to Adult Treatment Admission. Published Sept. 29, 2011. Accessed Sept. 12, 2019. <https://www.datafiles.samhsa.gov/study-publication/length-time-first-use-adult-treatment-admission-nid15982>
- ⁸ Hedegaard H. Drug Overdose Deaths in the United States, 1999—2016. 2017;(294):8.
- ⁹ Substance Abuse and Mental Health Services Administration. Treatment Episode Data Set (TEDS): 2017 Admissions to and Discharges from Publicly-Funded Substance Use Treatment. Published May 15, 2019. Accessed Sept. 12, 2019. <https://www.samhsa.gov/data/report/treatment-episode-data-set-teds-2017-admissions-and-discharges-publicly-funded-substance-use>
- ¹⁰ Altarum. Economic Toll of Opioid Crisis in U.S. Exceeded \$1 Trillion Since 2001. Altarum. Published Sept. 27, 2018. Accessed Sept. 12, 2019. <https://altarum.org/news/economic-toll-opioid-crisis-us-exceeded-1-trillion-2001>
- ¹¹ Colorado Department of Public Health and Environment. Drug overdose deaths in Colorado, 2000-2018. Published 2019. Accessed Aug. 18, 2019. <https://www.colorado.gov/pacific/cdphe>
- ¹² Colorado Department of Public Health and Environment, Violence and Injury Prevention-Mental Health Promotion Branch, Opioid Overdose Prevention Unit. Colorado Opioid Profile. Published 2018. Accessed Aug. 18, 2019. <https://www.colorado.gov/pacific/cdphe/prescription-drug-data-profiles>
- ¹³ Colorado Consortium for Prescription Drug Abuse Prevention, OMNI Institute. Consortium Dashboard. Published March 4, 2019. Accessed Sept. 12, 2019. <https://public.tableau.com/profile/omni#!/vizhome/RXConsortiumdashboard/Readmefirst>
- ¹⁴ Ingalls J. Drug Overdoses Continued to Increase in 2017. Colorado Health Institute. Published Aug. 29, 2018. Accessed June 16, 2020. <https://www.coloradohealthinstitute.org/research/drug-overdoses-continued-increase-2017>
- ¹⁵ Wilkerson R, Kim H, Windsor T, Mareiniss D. The Opioid Epidemic in the United States. *Emerg Med Clin North Am.* 2016;34(2):e1-e23. doi:10.1016/j.emc.2015.11.002
- ¹⁶ Portenoy RK, Foley KM. Chronic use of opioid analgesics in non-malignant pain: Report of 38 cases. *Pain.* 1986;25(2):171-186. doi:10.1016/0304-3959(86)90091-6
- ¹⁷ Catan T, Perez E. A Pain-Drug Champion Has Second Thoughts. *The Wall Street Journal.* <http://www.wsj.com/articles/SB10001424127887324478304578173342657044604>. Published 2012. Accessed Sept. 12, 2019.
- ¹⁸ Von Korff M, Kolodny A, Deyo RA, Chou R. Long-Term Opioid Therapy Reconsidered. *Ann Intern Med.* 2011;155(5):325. doi:10.7326/0003-4819-155-5-201109060-00011
- ¹⁹ Grady D, Berkowitz SA, Katz MH. Opioids for chronic pain. *Arch Intern Med.* 2011;171(16):1426-1427. doi:10.1001/archinternmed.2011.213
- ²⁰ Dhalla IA, Persaud N, Juurlink DN. Facing up to the prescription opioid crisis. *BMJ.* 2011;343:d5142. doi:10.1136/bmj.d5142
- ²¹ American Academy of Pain Medicine. Use of Opioids for the Treatment of Chronic Pain. Published March 7, 2013. Accessed Sept. 12, 2019. <https://painmed.org/about/position-statements/use-of-opioids-for-the-treatment-of-chronic-pain>
- ²² Lanser P, Gesell S. Pain management: the fifth vital sign. *Healthc Benchmarks.* 2001;8(6):68-70, 62.
- ²³ Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.* National Academies Press (US); 2011. Accessed Feb. 12, 2020. <http://www.ncbi.nlm.nih.gov/books/NBK91497/>
- ²⁴ Bhakta HC, Marco CA. Pain Management: Association with Patient Satisfaction among Emergency Department Patients. *J Emerg Med.* 2014;46(4):456-464. doi:10.1016/j.jemermed.2013.04.018
- ²⁵ Lembke A. Why Doctors Prescribe Opioids to Known Opioid Abusers. *N Engl J Med.* 2012;367(17):1580-1581. doi:10.1056/NEJMp1208498
- ²⁶ Governale L. Outpatient prescription opioid utilization in the US, years 2000–2009. *Drug Util Data Anal Team Lead Div Epidemiol Off Surveill Epidemiol Present US Food Drug Adm.* 2010;22.
- ²⁷ The Colorado Opioid Safety Collaborative. 2017 Colorado Opioid Safety Pilot Results Report. Published online May 2018. Accessed Sept. 12, 2019. <https://cha.com/wp-content/uploads/2018/06/CHA-Opioid-Pilot-Results-Report-May-2018.pdf>
- ²⁸ American Dental Association. Policy on Opioid Prescribing (2018). Published 2018. <https://www.ada.org/en/advocacy/current-policies/substance-use-disorders>

References continued

- ²⁹ Volkow ND, McLellan TA, Cotto JH, Karithanom M, Weiss SRB. Characteristics of Opioid Prescriptions in 2009. *JAMA*. 2011;305(13):1299-1301. doi:10.1001/jama.2011.401
- ³⁰ Guy GP, Zhang K. Opioid Prescribing by Specialty and Volume in the U.S. *Am J Prev Med*. 2018;55(5):e153-e155. doi:10.1016/j.amepre.2018.06.008
- ³¹ Shah A, Hayes CJ, Martin BC. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use—United States, 2006–2015. *MMWR Morb Mortal Wkly Rep*. 2017;66(10):265-269. doi:10.15585/mmwr.mm6610a1
- ³² Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review. *JAMA Surg*. 2017;152(11):1066-1071. doi:10.1001/jamasurg.2017.0831
- ³³ Holdgate A, Pollock T. Nonsteroidal anti-inflammatory drugs (NSAIDs) versus opioids for acute renal colic. *Cochrane Database Syst Rev*. 2004;(1). doi:10.1002/14651858.CD004137.pub3
- ³⁴ Gupta N, Vujcic M, Blatz A. Opioid prescribing practices from 2010 through 2015 among dentists in the United States: What do claims data tell us? *J Am Dent Assoc*. 2018;149(4):237-245.e6. doi:10.1016/j.adaj.2018.01.005
- ³⁵ Weiland BM, Wach AG, Kanar BP, et al. Use of Opioid Pain Relievers Following Extraction of Third Molars. 2015;36(2):7.
- ³⁶ Baker JA, Avorn J, Levin R, Bateman BT. Opioid Prescribing After Surgical Extraction of Teeth in Medicaid Patients, 2000-2010. *JAMA*. 2016;315(15):1653-1654. doi:10.1001/jama.2015.19058
- ³⁷ Suda KJ, Durkin MJ, Calip GS, et al. Comparison of Opioid Prescribing by Dentists in the United States and England. *JAMA Netw Open*. 2019;2(5):e194303. doi:10.1001/jamanetworkopen.2019.4303
- ³⁸ CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016. *MMWR Recomm Rep*. 2016;65. doi:10.15585/mmwr.rr6501e1er
- ³⁹ Wong YJ, Keenan J, Hudson K, et al. Opioid, NSAID, and OTC Analgesic Medications for Dental Procedures: PEARL Network Findings. *Compend Contin Educ Dent Jamesburg NJ* 1995. 2016;37(10):710-718.
- ⁴⁰ 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. doi:10.1001/jamanetworkopen.2018.6007
- ⁴¹ Baker DW. History of The Joint Commission's Pain Standards: Lessons for Today's Prescription Opioid Epidemic. *JAMA*. 2017;317(11):1117-1118. doi:10.1001/jama.2017.0935
- ⁴² Rummans TA, Burton MC, Dawson NL. How Good Intentions Contributed to Bad Outcomes: The Opioid Crisis. *Mayo Clin Proc*. 2018;93(3):344-350. doi:10.1016/j.mayocp.2017.12.020
- ⁴³ Bennett, Ph.D J, Contreras, M.P.H. O. Dental Schools Addiction Education Regional Summit Proceedings. Published Aug. 29, 2017. Accessed June 17, 2020. https://www.adea.org/uploadedfiles/adea/content_conversion_final/policy_advocacy/dental-schools-addiction-education-regional-summit-proceeding.pdf
- ⁴⁴ Yorkgitis BK, Brat GA. Postoperative opioid prescribing: Getting it RIGHTT. *Am J Surg*. 2018;215(4):707-711. doi:10.1016/j.amjsurg.2018.02.001
- ⁴⁵ Feinberg AE, Chesney TR, Srikandarajah S, Acuna SA, McLeod RS, Group on behalf of the BP in S. Opioid Use After Discharge in Postoperative Patients: A Systematic Review. *Ann Surg*. 2018;267(6):1056–1062. doi:10.1097/SLA.0000000000002591
- ⁴⁶ Hill MV, McMahon ML, Stucke RS, Barth RJ. Wide Variation and Excessive Dosage of Opioid Prescriptions for Common General Surgical Procedures. *Ann Surg*. 2017;265(4):709-714. doi:10.1097/SLA.0000000000001993
- ⁴⁷ Chen EY, Marcantonio A, Tornetta P. Correlation Between 24-Hour PredischARGE Opioid Use and Amount of Opioids Prescribed at Hospital Discharge. *JAMA Surg*. 2018;153(2). doi:10.1001/jamasurg.2017.4859
- ⁴⁸ Maughan BC, Hersh EV, Shofer FS, et al. Unused opioid analgesics and drug disposal following outpatient dental surgery: A randomized controlled trial. *Drug Alcohol Depend*. 2016;168:328-334. doi:10.1016/j.drugalcdep.2016.08.016
- ⁴⁹ Denisco RC, Kenna GA, O'Neil MG, et al. Prevention of prescription opioid abuse: The role of the dentist. *J Am Dent Assoc*. 2011;142(7):800-810. doi:10.14219/jada.archive.2011.0268
- ⁵⁰ Mutlu I, Abubaker AO, Laskin DM. Narcotic Prescribing Habits and Other Methods of Pain Control by Oral and Maxillofacial Surgeons After Impacted Third Molar Removal. *J Oral Maxillofac Surg*. 2013;71(9):1500-1503. doi:10.1016/j.joms.2013.04.031
- ⁵¹ Suda KJ, Zhou J, Rowan SA, et al. Overprescribing of Opioids to Adults by Dentists in the U.S., 2011–2015. *Am J Prev Med*. 2020;58(4):473-486. doi:10.1016/j.amepre.2019.11.006
- ⁵² Levy B, Paulozzi L, Mack KA, Jones CM. Trends in Opioid Analgesic—Prescribing Rates by Specialty, U.S., 2007–2012. *Am J Prev Med*. 2015;49(3):409-413. doi:10.1016/j.amepre.2015.02.020
- ⁵³ Fox TR, Li J, Stevens S, Tippie T. A performance improvement prescribing guideline reduces opioid prescriptions for emergency department dental pain patients. *Ann Emerg Med*. 2013;62(3):237-240. doi:10.1016/j.annemergmed.2012.11.020
- ⁵⁴ American Dental Association. ADA Statement on New Study in The Journal of the American Medical Association. Published May 25, 2019. <https://www.ada.org/en/press-room/news-releases/2019-archives/may/ada-statement-on-new-study-in-the-journal-of-the-american-medical-association>
- ⁵⁵ Tompach PC, Wagner CL, Sunstrum AB, Nadeau RA, Tu HK. Investigation of an Opioid Prescribing Protocol After Third Molar Extraction Procedures. *J Oral Maxillofac Surg*. 2019;77(4):705-714. doi:10.1016/j.joms.2018.12.007
- ⁵⁶ Guan Q, Campbell T, Martins D, et al. Assessing the impact of an opioid prescribing guideline for dentists in Ontario, Canada. *J Am Dent Assoc*. 2020;151(1):43-50. doi:10.1016/j.adaj.2019.08.021

References continued

- 57 Abrahamsson T, Berge J, Öjehagen A, Håkansson A. Benzodiazepine, z-drug and pregabalin prescriptions and mortality among patients in opioid maintenance treatment—A nation-wide register-based open cohort study. *Drug Alcohol Depend.* 2017;174:58-64. doi:10.1016/j.drugalcdep.2017.01.013
- 58 Williams JT, Ingram SL, Henderson G, et al. Regulation of μ -Opioid Receptors: Desensitization, Phosphorylation, Internalization, and Tolerance. *Pharmacol Rev.* 2013;65(1):223-254. doi:10.1124/pr.112.005942
- 59 Colvin LA, Bull F, Hales TG. Perioperative opioid analgesia—when is enough too much? A review of opioid-induced tolerance and hyperalgesia. *The Lancet.* 2019;393(10180):1558-1568. doi:10.1016/S0140-6736(19)30430-1
- 60 Møller LF, Matic S, van den Bergh BJ, Moloney K, Hayton P, Gatherer A. Acute drug-related mortality of people recently released from prisons. *Public Health.* 2010;124(11):637-639. doi:10.1016/j.puhe.2010.08.012
- 61 Buster MCA, Brussel GHA van, Brink W van den. An increase in overdose mortality during the first 2 weeks after entering or re-entering methadone treatment in Amsterdam. *Addiction.* 2002;97(8):993-1001. doi:10.1046/j.1360-0443.2002.00179.x
- 62 Martin PR, Hubbard JR. Substance-related disorders. In: Ebert MH, Loosen PT, Nurcombe B: *Current Diagnosis & Treatment in Psychiatry.* McGraw Hill; 2000:233-259.
- 63 Brown JT, Bishop JR, Sangkuhl K, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for Cytochrome P450 (CYP)2D6 Genotype and Atomoxetine Therapy. *Clin Pharmacol Ther.* 2019;106(1):94-102. doi:10.1002/cpt.1409
- 64 Swen JJ, Nijenhuis M, Boer A de, et al. Pharmacogenetics: From Bench to Byte—An Update of Guidelines. *Clin Pharmacol Ther.* 2011;89(5):662-673. doi:10.1038/clpt.2011.34
- 65 Obeng AO, Hamadeh I, Smith M. Review of Opioid Pharmacogenetics and Considerations for Pain Management. *Pharmacother J Hum Pharmacol Drug Ther.* 2017;37(9):1105-1121. doi:10.1002/phar.1986
- 66 Fletcher D, Martinez V. Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis. *BJA Br J Anaesth.* 2014;112(6):991-1004. doi:10.1093/bja/aeu137
- 67 Ramaswamy S, Wilson JA, Colvin L. Non-opioid-based adjuvant analgesia in perioperative care. *Contin Educ Anaesth Crit Care Pain.* 2013;13(5):152-157. doi:10.1093/bjaceaccp/mkt012
- 68 Chang AK, Bijur PE, Esses D, Barnaby DP, Baer J. Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency Department: A Randomized Clinical Trial. *JAMA.* 2017;318(17):1661-1667. doi:10.1001/jama.2017.16190
- 69 Moore RA, Derry S, McQuay HJ, Wiffen PJ. Single dose oral analgesics for acute postoperative pain in adults. *Cochrane Database Syst Rev.* 2011;(9). doi:10.1002/14651858.CD008659.pub2
- 70 Moore RA, Derry S, Aldington D, Wiffen PJ. Adverse events associated with single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database Syst Rev.* 2015;(10):CD011407. doi:10.1002/14651858.CD011407.pub2
- 71 Jones P, Dalziel SR, Lamdin R, Miles-Chan JL, Frampton C. Oral non-steroidal anti-inflammatory drugs versus other oral analgesic agents for acute soft tissue injury. *Cochrane Database Syst Rev.* 2015;(7). doi:10.1002/14651858.CD007789.pub2
- 72 Colorado DORA, Stakely T. Colorado Prescription Monitoring program open forum presentation. <http://www.ichpcolorado.com/docs/RCCO-Opioid-Forum-Presentation.pdf>
- 73 Colorado Dental Association. Colorado's Prescription Drug Monitoring Program 2019. Published 2019. <https://cdaonline.org/colorados-prescription-drug-monitoring-program/>
- 74 Creehan K. Enforcement Coming: Register and Use the Prescription Drug Monitoring Program (PDMP). Colorado Dental Association. Published Sept. 11, 2019. Accessed June 17, 2020. <https://cdaonline.org/news/latest-news/enforcement-coming-register-and-use-the-prescription-drug-monitoring-program-pdmp/>
- 75 Cantrill SV, Brown MD, Carlisle RJ, et al. Clinical policy: critical issues in the prescribing of opioids for adult patients in the emergency department. *Ann Emerg Med.* 2012;60(4):499-525. doi:10.1016/j.annemergmed.2012.06.013
- 76 Substance Use Disorders. American Dental Association. Published October 2018. Accessed June 17, 2020. <https://www.ada.org/en/advocacy/current-policies/substance-use-disorders>
- 77 American Association of Oral and Maxillofacial Surgeons. Opioid Prescribing: Acute and Postoperative Pain Management. Published 2020. https://www.aaoms.org/docs/govt_affairs/advocacy_white_papers/opioid_prescribing.pdf
- 78 Rasubala L, Pernapati L, Velasquez X, Burk J, Ren Y-F. Impact of a Mandatory Prescription Drug Monitoring Program on Prescription of Opioid Analgesics by Dentists. *PLoS ONE.* 2015;10(8). doi:10.1371/journal.pone.0135957
- 79 Baehren DF, Marco CA, Droz DE, Sinha S, Callan EM, Akpunonu P. A Statewide Prescription Monitoring Program Affects Emergency Department Prescribing Behaviors. *Ann Emerg Med.* 2010;56(1):19-23.e3. doi:10.1016/j.annemergmed.2009.12.011
- 80 McCauley JL, Hyer JM, Ramakrishnan VR, et al. Dental opioid prescribing and multiple opioid prescriptions among dental patients: Administrative data from the South Carolina prescription drug monitoring program. *J Am Dent Assoc.* 2016;147(7):537-544. doi:10.1016/j.adaj.2016.02.017
- 81 Webster LR, Webster RM. Predicting Aberrant Behaviors in Opioid-Treated Patients: Preliminary Validation of the Opioid Risk Tool. *Pain Med.* 2005;6(6):432-442. doi:10.1111/j.1526-4637.2005.00072.x
- 82 Parish CL, Pereyra MR, Pollack HA, et al. Screening for substance misuse in the dental care setting: findings from a nationally representative survey of dentists. *Addiction.* 2015;110(9):1516-1523. doi:10.1111/add.13004

References continued

- ⁸³ Wasan AD, Butler SF, Budman SH, Benoit C, Fernandez K, Jamison RN. Psychiatric History and Psychologic Adjustment as Risk Factors for Aberrant Drug-related Behavior Among Patients With Chronic Pain. *Clin J Pain*. 2007;23(4):307–315. doi:10.1097/AJP.0b013e3180330dc5
- ⁸⁴ Kulich RJ, Backstrom J, Brownstein J, Finkelman M, Dhadwal S, DiBenedetto D. A Model for Opioid Risk Stratification: Assessing the Psychosocial Components of Orofacial Pain. *Oral Maxillofac Surg Clin*. 2016;28(3):261-273. doi:10.1016/j.coms.2016.03.006
- ⁸⁵ Schatman M. Identifying Abusers Prior to Initiating Chronic Opioid Therapy. *Practical Pain Management*. Published 2008. <https://www.practicalpainmanagement.com/treatments/pharmacological/opioids/identifying-abusers-prior-initiating-chronic-opioid-therapy>
- ⁸⁶ Danovitch I, Vanle B, Van Groningen N, Ishak W, Nuckols T. Opioid Overdose in the Hospital Setting: A Systematic Review. *J Addict Med*. 2020;14(1):39–47. doi:10.1097/ADM.0000000000000536
- ⁸⁷ Boscarino JA, Rukstalis M, Hoffman SN, et al. Risk factors for drug dependence among out-patients on opioid therapy in a large US health-care system. *Addiction*. 2010;105(10):1776-1782. doi:10.1111/j.1360-0443.2010.03052.x
- ⁸⁸ 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. doi:10.1542/peds.2015-1364
- ⁸⁹ What Americans believe about opioid prescription painkiller use. Presented at the: National Safety Council—Opioid Painkiller Media Briefing; 2015. Accessed Dec. 16, 2019. <https://www.nsc.org/Portals/0/Documents/NewsDocuments/031115-Public-Opinion-Poll.pdf>
- ⁹⁰ Deyo RA, Hallvik SE, Hildebran C, et al. Association Between Initial Opioid Prescribing Patterns and Subsequent Long-Term Use Among Opioid-Naïve Patients: A Statewide Retrospective Cohort Study. *J Gen Intern Med*. 2017;32(1):21-27. doi:10.1007/s11606-016-3810-3
- ⁹¹ Franklin GM, Stover BD, Turner JA, Fulton-Kehoe D, Wickizer TM. Early Opioid Prescription and Subsequent Disability Among Workers With Back Injuries: The Disability Risk Identification Study Cohort. *Spine*. 2008;33(2):199–204. doi:10.1097/BRS.0b013e318160455c
- ⁹² Webster BS, Verma SK, Gatchel RJ. Relationship Between Early Opioid Prescribing for Acute Occupational Low Back Pain and Disability Duration, Medical Costs, Subsequent Surgery and Late Opioid Use. *Spine*. 2007;32(19):2127–2132. doi:10.1097/BRS.0b013e318145a731
- ⁹³ Oderda GM, Said Q, Evans RS, et al. Opioid-Related Adverse Drug Events in Surgical Hospitalizations: Impact on Costs and Length of Stay. *Ann Pharmacother*. 2007;41(3):400-407. doi:10.1345/aph.1H386
- ⁹⁴ Weingarten TN, Herasevich V, McGlinch MC, et al. Predictors of Delayed Postoperative Respiratory Depression Assessed From Naloxone Administration. *Anesth Analg*. 2015;121(2):422-429. doi:10.1213/ANE.0000000000000792
- ⁹⁵ Inciardi JA, Surratt HL, Cicero TJ, Beard RA. Prescription opioid abuse and diversion in an urban community: the results of an ultrarapid assessment. *Pain Med Malden Mass*. 2009;10(3):537-548. doi:10.1111/j.1526-4637.2009.00603.x
- ⁹⁶ Chou R, Peterson K, Helfand M. Comparative efficacy and safety of skeletal muscle relaxants for spasticity and musculoskeletal conditions: a systematic review. *J Pain Symptom Manage*. 2004;28(2):140-175. doi:10.1016/j.jpainsymman.2004.05.002
- ⁹⁷ Gong L, Stamer UM, Tzvetkov MV, Altman RB, Klein TE. PharmGKB summary: tramadol pathway. *Pharmacogenet Genomics*. 2014;24(7):374-380. doi:10.1097/FPC.0000000000000057
- ⁹⁸ Thiels CA, Habermann EB, Hooten WM, Jeffery MM. Chronic use of tramadol after acute pain episode: cohort study. *BMJ*. 2019;365. doi:10.1136/bmj.l1849
- ⁹⁹ Moore PA, Ziegler KM, Lipman RD, Aminoshariae A, Carrasco-Labra A, Mariotti A. Benefits and harms associated with analgesic medications used in the management of acute dental pain: An overview of systematic reviews. *J Am Dent Assoc*. 2018;149(4):256-265.e3. doi:10.1016/j.adaj.2018.02.012
- ¹⁰⁰ Dasgupta N, Funk MJ, Proescholdbell S, Hirsch A, Ribisl KM, Marshall S. Cohort Study of the Impact of High-Dose Opioid Analgesics on Overdose Mortality. *Pain Med*. 2016;17(1):85-98. doi:10.1111/pme.12907
- ¹⁰¹ Pawasauskas J, Stevens B, Youssef R, Kelley M. Predictors of naloxone use for respiratory depression and oversedation in hospitalized adults. *Am J Health Syst Pharm*. 2014;71(9):746-750. doi:10.2146/ajhp130568
- ¹⁰² Substance Abuse and Mental Health Services Administration. Reports and Detailed Tables From the 2018 National Survey on Drug Use and Health (NSDUH). Published August 2019. <https://www.samhsa.gov/data/report/2018-nsduh-detailed-tables>.
- ¹⁰³ U.S. Food and Drug Administration. Disposal of Unused Medicines: What You Should Know. Published Feb. 1, 2019. Accessed Sept. 12, 2019. <http://www.fda.gov/drugs/safe-disposal-medicines/disposal-unused-medicines-what-you-should-know>.
- ¹⁰⁴ 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. doi:10.1001/jamainternmed.2018.5419
- ¹⁰⁵ Washington State Agency Medical Directors' Group, Dr. Robert Bree Collaborative. Dental Guideline on Prescribing Opioids for Acute Pain Management. Published September 2017. http://www.breecollaborative.org/wp-content/uploads/2017-10-26-FINAL-Dental-Opioid-Recommendations_Web.pdf
- ¹⁰⁶ Nataraj N, Zhang K, Guy GP, Losby JL. Identifying opioid prescribing patterns for high-volume prescribers via cluster analysis. *Drug Alcohol Depend*. 2019;197:250-254. doi:10.1016/j.drugalcdep.2019.01.012
- ¹⁰⁷ American Dental Association. Oral Analgesics for Acute Dental Pain. Published Sept. 17, 2019. <https://www.ada.org/en/member-center/oral-health-topics/oral-analgesics-for-acute-dental-pain>

References continued

- ¹⁰⁸ Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. *Pain*. 2015;156(6):1003-1007. doi:10.1097/j.pain.000000000000160
- ¹⁰⁹ Benoliel R, Sharav Y. Chronic Orofacial Pain. *Curr Pain Headache Rep*. 2010;14(1):33-40. doi:10.1007/s11916-009-0085-y
- ¹¹⁰ Zakrzewska JM. Multi-dimensionality of chronic pain of the oral cavity and face. *J Headache Pain*. 2013;14(1):37. doi:10.1186/1129-2377-14-37
- ¹¹¹ Davis CE, Stockstill JW, Stanley WD, Wu Q. Pain-related worry in patients with chronic orofacial pain. *J Am Dent Assoc*. 2014;145(7):722-730. doi:10.14219/jada.2014.37
- ¹¹² Peppin JF, Passik SD, Couto JE, et al. Recommendations for urine drug monitoring as a component of opioid therapy in the treatment of chronic pain. *Pain Med Malden Mass*. 2012;13(7):886-896. doi:10.1111/j.1526-4637.2012.01414.x
- ¹¹³ Jamison RN, Mao J. Opioid Analgesics. *Mayo Clin Proc*. 2015;90(7):957-968. doi:10.1016/j.mayocp.2015.04.010
- ¹¹⁴ The MITRE Corporation. Enhancing Access to Prescription Drug Monitoring Programs Using Health Information Technology: Integrating Health IT and PDMPs to Improve Patient Care. Published 2013. Accessed Sept. 12, 2019. https://www.healthit.gov/sites/default/files/connecting_for_impact-final-508.pdf
- ¹¹⁵ The MITRE Corporation. Enhancing Access to Prescription Drug Monitoring Programs Using Health Information Technology: Connecting Prescribers and Dispensers to PDMPs through Health IT: Six Pilot Studies and Their Impact. Published 2012. Accessed Sept. 12, 2019. https://www.healthit.gov/sites/default/files/pdmp_pilot_studies_summary_0.pdf
- ¹¹⁶ The United States Department of Health & Human Services. Pain Management Best Practices. Published May 9, 2019. Accessed Feb. 12, 2020. <https://www.hhs.gov/sites/default/files/pmtf-final-report-2019-05-23.pdf>
- ¹¹⁷ Evans SW, McCahon RA. Management of postoperative pain in maxillofacial surgery. *Br J Oral Maxillofac Surg*. 2019;57(1):4-11. doi:10.1016/j.bjoms.2018.11.010
- ¹¹⁸ Reynolds WR, Schwarz ES. Dentists' Current and Optimal Opioid Prescribing Practices: A Proactive Review. *Mo Med*. 2019;116(5):347-350.
- ¹¹⁹ Lee Y-S, Kim H, Brahim JS, Rowan J, Lee G, Dionne RA. Acetaminophen selectively suppresses peripheral prostaglandin E2 release and increases COX-2 gene expression in a clinical model of acute inflammation. *PAIN*. 2007;129(3):279-286. doi:10.1016/j.pain.2006.10.020
- ¹²⁰ Moore RA, Wiffen PJ, Derry S, Maguire T, Roy YM, Tyrrell L. Non-prescription (OTC) oral analgesics for acute pain - an overview of Cochrane reviews. *Cochrane Database Syst Rev*. 2015;(11). doi:10.1002/14651858.CD010794.pub2
- ¹²¹ Qi DS, May LG, Zimmerman B, et al. A randomized, double-blind, placebo-controlled study of acetaminophen 1000 mg versus acetaminophen 650 mg for the treatment of postsurgical dental pain. *Clin Ther*. 2012;34(12):2247-2258.e3. doi:10.1016/j.clinthera.2012.11.003
- ¹²² AAOMS issues opioid prescribing recommendations | AAOMS. AAOMS. Published Aug. 28, 2017. Accessed June 17, 2020. <https://www.aaoms.org/media/press-releases/aaoms-issues-opioid-prescribing-recommendations>
- ¹²³ Weiser T, Richter E, Hegewisch A, Muse DD, Lange R. Efficacy and safety of a fixed-dose combination of ibuprofen and caffeine in the management of moderate to severe dental pain after third molar extraction. *Eur J Pain Lond Engl*. 2018;22(1):28-38. doi:10.1002/ejp.1068
- ¹²⁴ Abou-Atme YS, Melis M, Zawawi KH. Efficacy and safety of acetaminophen and caffeine for the management of acute dental pain: A systematic review. *Saudi Dent J*. 2019;31(4):417-423. doi:10.1016/j.sdentj.2019.04.008
- ¹²⁵ Klongnoi B, Kaewpradub P, Boonsiriseth K, Wongsirichat N. Effect of single dose preoperative intramuscular dexamethasone injection on lower impacted third molar surgery. *Int J Oral Maxillofac Surg*. 2012;41(3):376-379. doi:10.1016/j.ijom.2011.12.014
- ¹²⁶ Nagori SA, Jose A, Roy ID, Chattopadhyay PK, Roychoudhury A. Does methylprednisolone improve postoperative outcomes after mandibular third molar surgery? A systematic review and meta-analysis. *Int J Oral Maxillofac Surg*. 2019;48(6):787-800. doi:10.1016/j.ijom.2018.09.005
- ¹²⁷ Aminoshariae A, Kulild JC, Donaldson M, Hersh EV. Evidence-based recommendations for analgesic efficacy to treat pain of endodontic origin: A systematic review of randomized controlled trials. *J Am Dent Assoc*. 2016;147(10):826-839. doi:10.1016/j.adaj.2016.05.010
- ¹²⁸ Hersh EV, Kane WT, O'Neil MG, et al. Prescribing recommendations for the treatment of acute pain in dentistry. *Compend Contin Educ Dent Jamesburg NJ* 1995. 2011;32(3):22, 24-30; quiz 31-32.
- ¹²⁹ St George G, Morgan A, Meechan J, et al. Injectable local anaesthetic agents for dental anaesthesia. *Cochrane Database Syst Rev*. 2018;7:CD006487. doi:10.1002/14651858.CD006487.pub2
- ¹³⁰ American Academy of Pediatric Dentists. Pain Management in Infants, Children, Adolescents and Individuals with Special Health Care Needs. Published 2018. https://www.aapd.org/globalassets/media/policies_guidelines/bp_pain.pdf
- ¹³¹ Iero PT, Mulherin DR, Jensen O, Berry T, Danesi H, Razook SJ. A Prospective, Randomized, Open-Label Study Comparing an Opioid-Sparing Postsurgical Pain Management Protocol With and Without Liposomal Bupivacaine for Full-Arch Implant Surgery. *Int J Oral Maxillofac Implants*. 2018;33(5):1155-1164. doi:10.11607/jomi.5938
- ¹³² Lieblisch SE, Danesi H. Liposomal Bupivacaine Use in Third Molar Impaction Surgery: INNOVATE Study. *Anesth Prog*. 2017;64(3):127-135. doi:10.2344/anpr-64-02-03
- ¹³³ Bultema K, Fowler S, Drum M, Reader A, Nusstein J, Beck M. Pain Reduction in Untreated Symptomatic Irreversible Pulpitis Using Liposomal Bupivacaine (Exparel): A Prospective, Randomized, Double-blind Trial. *J Endod*. 2016;42(12):1707-1712. doi:10.1016/j.joen.2016.08.018

References continued

- ¹³⁴ Meechan JG. Effective topical anesthetic agents and techniques. *Dent Clin North Am.* 2002;46(4):759-766. doi:10.1016/s0011-8532(02)00035-6
- ¹³⁵ Lee H-S. Recent advances in topical anesthesia. *J Dent Anesth Pain Med.* 2016;16(4):237-244. doi:10.17245/jdapm.2016.16.4.237
- ¹³⁶ Ando T, Shimoo Y, Nakasato M, Yoshida H. Development and Clinical Evaluation of New Topical Anesthetic Formulations for Dental Care. *Biol Pharm Bull.* 2016;39(3):423-427. doi:10.1248/bpb.b15-00380
- ¹³⁷ Gupta PD, Mahajan P, Monga P, Thaman D, Khinda VIS, Gupta A. Evaluation of the efficacy of nitrous oxide inhalation sedation on anxiety and pain levels of patients undergoing endodontic treatment in a vital tooth: A prospective randomized controlled trial. *J Conserv Dent JCD.* 2019;22(4):356-361. doi:10.4103/JCD.JCD_332_18
- ¹³⁸ Black P, Max MB, Desjardins P, Norwood T, Ardia A, Pallotta T. A randomized, double-blind, placebo-controlled comparison of the analgesic efficacy, onset of action, and tolerability of ibuprofen arginate and ibuprofen in postoperative dental pain. *Clin Ther.* 2002;24(7):1072-1089. doi:10.1016/s0149-2918(02)80020-0
- ¹³⁹ Miles L, Hall J, Jenner B, Addis R, Hutchings S. Predicting rapid analgesic onset of ibuprofen salts compared with ibuprofen acid: Tlag, Tlow, Tmed, and a novel parameter, TCmaxRef. *Curr Med Res Opin.* 2018;34(8):1483-1490. doi:10.1080/03007995.2018.1466697
- ¹⁴⁰ Seibel K, Schaffler K, Reeh P, Reitmeir P. Comparison of two different preparations of ibuprofen with regard to the time course of their analgesic effect. A randomized, placebo-controlled, double-blind cross-over study using laser somatosensory evoked potentials obtained from UW-irritated skin in healthy volunteers. *Arzneimittelforschung.* 2004;54(8):444-451. doi:10.1055/s-0031-1296997
- ¹⁴¹ Legg TJ, Laurent AL, Leyva R, Kellstein D. Ibuprofen sodium is absorbed faster than standard Ibuprofen tablets: results of two open-label, randomized, crossover pharmacokinetic studies. *Drugs RD.* 2014;14(4):283-290. doi:10.1007/s40268-014-0070-8
- ¹⁴² García Rodríguez LA, Cattaruzzi C, Troncon MG, Agostinis L. Risk of hospitalization for upper gastrointestinal tract bleeding associated with ketorolac, other nonsteroidal anti-inflammatory drugs, calcium antagonists, and other antihypertensive drugs. *Arch Intern Med.* 1998;158(1):33-39. doi:10.1001/archinte.158.1.33
- ¹⁴³ Lanza FL, Chan FKL, Quigley EMM, Practice Parameters Committee of the American College of Gastroenterology. Guidelines for prevention of NSAID-related ulcer complications. *Am J Gastroenterol.* 2009;104(3):728-738. doi:10.1038/ajg.2009.115
- ¹⁴⁴ Acute Pain Management Meeting the Challenges. A VA Clinician's Guide. Published July 2017. Accessed June 18, 2020. https://www.pbm.va.gov/PBM/AcademicDetailingService/Documents/Academic_Detailing_Educational_Material_Catalog/Pain_Provider_AcutePainProviderEducationalGuide_IB10998.pdf
- ¹⁴⁵ Aoki T, Yamaguchi H, Naito H, Shiiki K, Ota Y, Kaneko A. Dextromethorphan premedication reduced postoperative analgesic consumption in patients after oral surgery. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006;102(5):591-595. doi:10.1016/j.tripleo.2005.10.060
- ¹⁴⁶ King MR, Ladha KS, Gelineau AM, Anderson TA. Perioperative Dextromethorphan as an Adjunct for Postoperative Pain: A Meta-analysis of Randomized Controlled Trials. *Anesthesiology.* 2016;124(3):696-705. doi:10.1097/ALN.0000000000000950
- ¹⁴⁷ İşik B, Yaman S, Aktuna S, Turan A. Analgesic efficacy of prophylactic gabapentin and lornoxicam in preventing postendodontic pain. *Pain Med Malden Mass.* 2014;15(12):2150-2155. doi:10.1111/pme.12536
- ¹⁴⁸ Hill CM, Balkenohl M, Thomas DW, Walker R, Mathé H, Murray G. Pregabalin in patients with postoperative dental pain. *Eur J Pain Lond Engl.* 2001;5(2):119-124. doi:10.1053/eujp.2001.0235
- ¹⁴⁹ Cheung CW, Choi WS, Leung YY, et al. A double-blind randomized crossover study to evaluate the timing of pregabalin for third molar surgery under local anesthesia. *J Oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg.* 2012;70(1):25-30. doi:10.1016/j.joms.2011.03.056
- ¹⁵⁰ American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc.* 2015;63(11):2227-2246. doi:10.1111/jgs.13702
- ¹⁵¹ Grillo CM, Wada RS, da Luz Rosário de Sousa M. Acupuncture in the management of acute dental pain. *J Acupunct Meridian Stud.* 2014;7(2):65-70. doi:10.1016/j.jams.2013.03.005
- ¹⁵² NIH Consensus Conference. Acupuncture. *JAMA.* 1998;280(17):1518-1524.
- ¹⁵³ Ernst E, Pittler MH. The effectiveness of acupuncture in treating acute dental pain: a systematic review. *Br Dent J.* 1998;184(9):443-447. doi:10.1038/sj.bdj.4809654
- ¹⁵⁴ Tavares MG, Machado AP, Motta BG, Borsatto MC, Rosa AL, Xavier SP. Electro-acupuncture efficacy on pain control after mandibular third molar surgery. *Braz Dent J.* 2007;18(2):158-162. doi:10.1590/s0103-64402007000200014
- ¹⁵⁵ Karst M, Winterhalter M, Münte S, et al. Auricular acupuncture for dental anxiety: a randomized controlled trial. *Anesth Analg.* 2007;104(2):295-300. doi:10.1213/01.ane.0000242531.12722.fd
- ¹⁵⁶ Itoh K, Asai S, Ohyabu H, Imai K, Kitakoji H. Effects of trigger point acupuncture treatment on temporomandibular disorders: a preliminary randomized clinical trial. *J Acupunct Meridian Stud.* 2012;5(2):57-62. doi:10.1016/j.jams.2012.01.013
- ¹⁵⁷ Noiman M, Garty A, Maimon Y, Miller U, Lev-Ari S. Acupuncture for treating temporomandibular disorder: retrospective study on safety and efficacy. *J Acupunct Meridian Stud.* 2010;3(4):260-266. doi:10.1016/S2005-2901(10)60046-5
- ¹⁵⁸ Huang Y-F, Lin J-C, Yang H-W, Lee Y-H, Yu C-H. Clinical effectiveness of laser acupuncture in the treatment of temporomandibular joint disorder. *J Formos Med Assoc Taiwan Yi Zhi.* 2014;113(8):535-539. doi:10.1016/j.jfma.2012.07.039
- ¹⁵⁹ Shen YF, Younger J, Goddard G, Mackey S. Randomized clinical trial of acupuncture for myofascial pain of the jaw muscles. *J Orofac Pain.* 2009;23(4):353-359.

References continued

- ¹⁶⁰ Vicente-Barrero M, Yu-Lu S-L, Zhang B, et al. The efficacy of acupuncture and decompression splints in the treatment of temporomandibular joint pain-dysfunction syndrome. *Med Oral Patol Oral Cirugia Bucal*. 2012;17(6):e1028-1033. doi:10.4317/medoral.17567
- ¹⁶¹ Gonzalez-Perez L-M, Infante-Cossio P, Granados-Nuñez M, Urresti-Lopez F-J. Treatment of temporomandibular myofascial pain with deep dry needling. *Med Oral Patol Oral Cirugia Bucal*. 2012;17(5):e781-785. doi:10.4317/medoral.17822
- ¹⁶² Garland EL, Baker AK, Larsen P, et al. Randomized Controlled Trial of Brief Mindfulness Training and Hypnotic Suggestion for Acute Pain Relief in the Hospital Setting. *J Gen Intern Med*. 2017;32(10):1106-1113. doi:10.1007/s11606-017-4116-9
- ¹⁶³ Nicholls JL, Azam MA, Burns LC, et al. Psychological treatments for the management of postsurgical pain: a systematic review of randomized controlled trials. *Patient Relat Outcome Meas*. 2018;9:49-64. doi:10.2147/PROM.S121251
- ¹⁶⁴ Vranceanu A-M, Hageman M, Strooker J, ter Meulen D, Vrahas M, Ring D. A preliminary RCT of a mind body skills based intervention addressing mood and coping strategies in patients with acute orthopaedic trauma. *Injury*. 2015;46(4):552-557. doi:10.1016/j.injury.2014.11.001
- ¹⁶⁵ Burghardt S, Koranyi S, Magnucki G, Strauss B, Rosendahl J. Non-pharmacological interventions for reducing mental distress in patients undergoing dental procedures: Systematic review and meta-analysis. *J Dent*. 2018;69:22-31. doi:10.1016/j.jdent.2017.11.005
- ¹⁶⁶ Melzack R, Guité S, Gonshor A. Relief of dental pain by ice massage of the hand. *Can Med Assoc J*. 1980;122(2):189-191.
- ¹⁶⁷ Uman LS, Birnie KA, Noel M, et al. Psychological interventions for needle-related procedural pain and distress in children and adolescents. *Cochrane Database Syst Rev*. 2013;(10):CD005179. doi:10.1002/14651858.CD005179.pub3
- ¹⁶⁸ Prado IM, Carcavalli L, Abreu LG, Serra-Negra JM, Paiva SM, Martins CC. Use of distraction techniques for the management of anxiety and fear in paediatric dental practice: A systematic review of randomized controlled trials. *Int J Paediatr Dent*. 2019;29(5):650-668. doi:10.1111/ipd.12499
- ¹⁶⁹ Kamath PS. A novel distraction technique for pain management during local anesthesia administration in pediatric patients. *J Clin Pediatr Dent*. 2013;38(1):45-47. doi:10.17796/jcpd.38.1.265807t236570hx7
- ¹⁷⁰ Abdelmoniem SA, Mahmoud SA. Comparative evaluation of passive, active, and passive-active distraction techniques on pain perception during local anesthesia administration in children. *J Adv Res*. 2016;7(3):551-556. doi:10.1016/j.jare.2015.10.001
- ¹⁷¹ Gomes CAF de P, El-Hage Y, Amaral AP, et al. Effects of Massage Therapy and Occlusal Splint Usage on Quality of Life and Pain in Individuals with Sleep Bruxism: A Randomized Controlled Trial. *J Jpn Phys Ther Assoc Rigaku Ryoho*. 2015;18(1):1-6. doi:10.1298/jjpta.18.1
- ¹⁷² Gomes CAF de P, El Hage Y, Amaral AP, Politti F, Biasotto-Gonzalez DA. Effects of massage therapy and occlusal splint therapy on electromyographic activity and the intensity of signs and symptoms in individuals with temporomandibular disorder and sleep bruxism: a randomized clinical trial. *Chiropr Man Ther*. 2014;22(1):43. doi:10.1186/s12998-014-0043-6
- ¹⁷³ Klassen JA, Liang Y, Tjosvold L, Klassen TP, Hartling L. Music for Pain and Anxiety in Children Undergoing Medical Procedures: A Systematic Review of Randomized Controlled Trials. *Ambul Pediatr*. 2008;8(2):117-128. doi:10.1016/j.ambp.2007.12.005
- ¹⁷⁴ Bekhuis T. Music therapy may reduce pain and anxiety in children undergoing medical and dental procedures. *J Evid-Based Dent Pract*. 2009;9(4):213-214. doi:10.1016/j.jebdp.2009.03.002
- ¹⁷⁵ Lai H-L, Hwang M-J, Chen C-J, Chang K-F, Peng T-C, Chang F-M. Randomised controlled trial of music on state anxiety and physiological indices in patients undergoing root canal treatment. *J Clin Nurs*. 2008;17(19):2654-2660. doi:10.1111/j.1365-2702.2008.02350.x
- ¹⁷⁶ Packyanathan JS, Lakshmanan R, Jayashri P. Effect of music therapy on anxiety levels on patient undergoing dental extractions. *J Fam Med Prim Care*. 2019;8(12):3854-3860. doi:10.4103/jfmpc.jfmpc_789_19
- ¹⁷⁷ Moola S, Pearson A, Hagger C. Effectiveness of music interventions on dental anxiety in paediatric and adult patients: a systematic review. *JBI Libr Syst Rev*. 2011;9(18):588-630. doi:10.11124/01938924-201109180-00001
- ¹⁷⁸ Baghdadi ZD. Evaluation of electronic dental anesthesia in children. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1999;88(4):418-423. doi:10.1016/s1079-2104(99)70055-7
- ¹⁷⁹ teDuits E, Goepferd S, Donly K, Pinkham J, Jakobsen J. The effectiveness of electronic dental anesthesia in children. *Pediatr Dent*. 1993;15(3):191-196.
- ¹⁸⁰ Oztaş N, Olmez A, Yel B. Clinical evaluation of transcutaneous electronic nerve stimulation for pain control during tooth preparation. *Quintessence Int Berl Ger* 1985. 1997;28(9):603-608.
- ¹⁸¹ Harvey M, Elliott M. Transcutaneous electrical nerve stimulation (TENS) for pain management during cavity preparations in pediatric patients. *ASDC J Dent Child*. 1995;62(1):49-51.
- ¹⁸² Dhindsa A, Pandit IK, Srivastava N, Gugnani N. Comparative evaluation of the effectiveness of electronic dental anesthesia with 2% lignocaine in various minor pediatric dental procedures: A clinical study. *Contemp Clin Dent*. 2011;2(1):27-30. doi:10.4103/0976-237X.79305
- ¹⁸³ Quarnstrom F, Libed EN. Electronic anesthesia versus topical anesthesia for the control of injection pain. *Quintessence Int Berl Ger* 1985. 1994;25(10):713-716.
- ¹⁸⁴ Meechan JG, Gowans AJ, Welbury RR. The use of patient-controlled transcutaneous electronic nerve stimulation (TENS) to decrease the discomfort of regional anaesthesia in dentistry: a randomised controlled clinical trial. *J Dent*. 1998;26(5-6):417-420. doi:10.1016/s0300-5712(97)00062-6

References continued

- ¹⁸⁵ Kasat V, Gupta A, Ladda R, Kathariya M, Saluja H, Farooqui A-A. Transcutaneous electric nerve stimulation (TENS) in dentistry- A review. *J Clin Exp Dent*. 2014;6(5):e562-568. doi:10.4317/jced.51586
- ¹⁸⁶ López-Valverde N, Muriel Fernández J, López-Valverde A, et al. Use of Virtual Reality for the Management of Anxiety and Pain in Dental Treatments: Systematic Review and Meta-Analysis. *J Clin Med*. 2020;9(4). doi:10.3390/jcm9041025
- ¹⁸⁷ Nunna M, Dasaraju RK, Kamatham R, Mallineni SK, Nuvvula S. Comparative evaluation of virtual reality distraction and counter-stimulation on dental anxiety and pain perception in children. *J Dent Anesth Pain Med*. 2019;19(5):277-288. doi:10.17245/jdapm.2019.19.5.277
- ¹⁸⁸ Hoffman HG, Garcia-Palacios A, Patterson DR, Jensen M, Furness T, Ammons WF. The Effectiveness of Virtual Reality for Dental Pain Control: A Case Study. *Cyberpsychol Behav*. 2001;4(4):527-535. doi:10.1089/109493101750527088
- ¹⁸⁹ Wiederhold MD, Gao K, Wiederhold BK. Clinical Use of Virtual Reality Distraction System to Reduce Anxiety and Pain in Dental Procedures. *Cyberpsychology Behav Soc Netw*. 2014;17(6):359-365. doi:10.1089/cyber.2014.0203
- ¹⁹⁰ Indian Health Service Division of Oral Health (DOH), & Indian Health Service National Committee on Heroin, Opioid and Pain Efforts (HOPE). Recommendations for Management of Acute Dental Pain. Published online July 2018:20.
- ¹⁹¹ Breivik EK, Barkvoll P, Skovlund E. Combining diclofenac with acetaminophen or acetaminophen-codeine after oral surgery: A randomized, double-blind single-dose study. *Clin Pharmacol Ther*. 1999;66(6):625-635. doi:10.1053/cp.1999.v66.103629001
- ¹⁹² Ong CKS, Seymour RA, Lirk P, Merry AF. Combining Paracetamol (Acetaminophen) with Nonsteroidal Antiinflammatory Drugs: A Qualitative Systematic Review of Analgesic Efficacy for Acute Postoperative Pain. *Anesth Analg*. 2010;110(4):1170-1179. doi:10.1213/ANE.0b013e3181cf9281
- ¹⁹³ Mehlich DR, Aspley S, Daniels SE, Bandy DP. Comparison of the analgesic efficacy of concurrent ibuprofen and paracetamol with ibuprofen or paracetamol alone in the management of moderate to severe acute postoperative dental pain in adolescents and adults: A randomized, double-blind, placebo-controlled, parallel-group, single-dose, two-center, modified factorial study. *Clin Ther*. 2010;32(5):882-895. doi:10.1016/j.clinthera.2010.04.022
- ¹⁹⁴ Mehlich DR, Aspley S, Daniels SE, Southerden KA, Christensen KS. A single-tablet fixed-dose combination of racemic ibuprofen/paracetamol in the management of moderate to severe postoperative dental pain in adult and adolescent patients: A multicenter, two-stage, randomized, double-blind, parallel-group, placebo-controlled, factorial study. *Clin Ther*. 2010;32(6):1033-1049. doi:10.1016/j.clinthera.2010.06.002
- ¹⁹⁵ Haglund B, Bültzingslöwen IV. Combining paracetamol with a selective cyclooxygenase-2 inhibitor for acute pain relief after third molar surgery: a randomized, double-blind, placebo-controlled study. *Eur J Oral Sci*. 2006;114(4):293-301. doi:10.1111/j.1600-0722.2006.00365.x
- ¹⁹⁶ Menhinick KA, Gutmann JL, Regan JD, Taylor SE, Buschang PH. The efficacy of pain control following nonsurgical root canal treatment using ibuprofen or a combination of ibuprofen and acetaminophen in a randomized, double-blind, placebo-controlled study. *Int Endod J*. 2004;37(8):531-541. doi:10.1111/j.1365-2591.2004.00836.x
- ¹⁹⁷ Armfield JM, Heaton LJ. Management of fear and anxiety in the dental clinic: a review. *Aust Dent J*. 2013;58(4):390-407. doi:10.1111/adj.12118
- ¹⁹⁸ Woo AK. Depression and Anxiety in Pain. *Rev Pain*. 2010;4(1):8-12. doi:10.1177/204946371000400103
- ¹⁹⁹ van Wijk AJ, Hoogstraten J. Anxiety and pain during dental injections. *J Dent*. 2009;37(9):700-704. doi:10.1016/j.jdent.2009.05.023
- ²⁰⁰ van Wijk AJ, Makkes PC. Highly anxious dental patients report more pain during dental injections. *Br Dent J*. 2008;205(3):E7-E7. doi:10.1038/sj.bdj.2008.583
- ²⁰¹ Maggiri J, Locker D. Psychological factors and perceptions of pain associated with dental treatment. *Community Dent Oral Epidemiol*. 2002;30(2):151-159. doi:10.1034/j.1600-0528.2002.300209.x
- ²⁰² Corah NL, O'Shea RM, Bissell GD, Thines TJ, Mendola P. The dentist-patient relationship: perceived dentist behaviors that reduce patient anxiety and increase satisfaction. *J Am Dent Assoc*. 1988;116(1):73-76. doi:10.14219/jada.archive.1988.0162
- ²⁰³ Corah NL. Dental anxiety. Assessment, reduction and increasing patient satisfaction. *Dent Clin North Am*. 1988;32(4):779-790.
- ²⁰⁴ Liddell A, Ackerman C, Locker D. What dental phobics say about their dental experiences. *J Can Dent Assoc*. 1990;56(9):863-866.
- ²⁰⁵ Hamasaki T, Soh I, Takehara T, Hagihara A. Applicability of both dentist and patient perceptions of dentists' explanations to the evaluation of dentist-patient communication. *Community Dent Health*. 2011;28(4):274-279.
- ²⁰⁶ Kent G, Croucher R. *Achieving Oral Health: The Social Context of Dental Care*. 2nd ed. Oxford: Butterworth Heinemann; 1998.
- ²⁰⁷ Singh H, Meshram G, Warhadpande M, Kapoor P. Effect of 'Perceived control' in management of anxious patients undergoing endodontic therapy by use of an electronic communication system. *J Conserv Dent JCD*. 2012;15(1):51-55. doi:10.4103/0972-0707.92607
- ²⁰⁸ Furman E, Jasinevicius TR, Bissada NF, Victoroff KZ, Skillicorn R, Buchner M. Virtual Reality Distraction for Pain Control During Periodontal Scaling and Root Planing Procedures. *J Am Dent Assoc*. 2009;140(12):1508-1516. doi:10.14219/jada.archive.2009.0102
- ²⁰⁹ Deci EL, Koestner R, Ryan RM. A meta-analytic review of experiments examining the effects of extrinsic rewards on intrinsic motivation. *Psychol Bull*. 1999;125(6):627-668; discussion 692-700. doi:10.1037/0033-2909.125.6.627
- ²¹⁰ Schaffer SD, Yucha CB. Relaxation & Pain Management: The relaxation response can play a role in managing chronic and acute pain. *Lead Voice Nurs* 1900 *AJN*. 2004;104(8):75-82.

References continued

- 211 Park E, Oh H, Kim T. The effects of relaxation breathing on procedural pain and anxiety during burn care. *Burns*. 2013;39(6):1101-1106. doi:10.1016/j.burns.2013.01.006
- 212 Berggren U, Hakeberg M, Carlsson SG. Relaxation vs. Cognitively Oriented Therapies for Dental Fear. *J Dent Res*. 2000;79(9):1645-1651. doi:10.1177/00220345000790090201
- 213 Willumsen T, Vassend O, Hoffart A. A comparison of cognitive therapy, applied relaxation, and nitrous oxide sedation in the treatment of dental fear. *Acta Odontol Scand*. 2001;59(5):290-296. doi:10.1080/000163501750541156
- 214 Hakeberg M, Berggren U, Carlsson SG. A 10-year follow-up of patients treated for dental fear. *Eur J Oral Sci*. 1990;98(1):53-59. doi:10.1111/j.1600-0722.1990.tb00939.x
- 215 Coldwell SE, Getz T, Milgrom P, Prall CW, Spadafora A, Ramsay DS. CARL: A LabVIEW 3 computer program for conducting exposure therapy for the treatment of dental injection fear. *Behav Res Ther*. 1998;36(4):429-441. doi:10.1016/S0005-7967(97)10038-9
- 216 Coldwell SE, Wilhelm FH, Milgrom P, et al. Combining alprazolam with systematic desensitization therapy for dental injection phobia. *J Anxiety Disord*. 2007;21(7):871-887. doi:10.1016/j.janxdis.2007.01.001
- 217 Gow M. Hypnosis in dentistry. In: Weiner AA, ed. *The Fearful Dental Patient: A Guide to Understanding and Managing*. Wiley; 2011:139-171.
- 218 Holden A. The art of suggestion: the use of hypnosis in dentistry. *Br Dent J*. 2012;212(11):549-551. doi:10.1038/sj.bdj.2012.467
- 219 Fanini D, Poglio M, Marci MC, Iovinelli G, Antenucci F. [Oral premedication with clonidine as an alternative in dental practice. The effects on the pain threshold, blood pressure and salivary flow]. *Minerva Stomatol*. 1998;47(9):453-464.
- 220 Studer FR, Grätz KW, Mutzbauer TS. Comparison of clonidine and midazolam as anxiolytic premedication before wisdom tooth surgery: a randomized, double-blind, crossover pilot study. *Oral Maxillofac Surg*. 2012;16(4):341-347. doi:10.1007/s10006-012-0319-8
- 221 Beer GM, Spicher I, Seifert B, Emanuel B, Kompatscher P, Meyer VE. Oral premedication for operations on the face under local anesthesia: a placebo-controlled double-blind trial. *Plast Reconstr Surg*. 2001;108(3):637-643. doi:10.1097/00006534-200109010-00006
- 222 Brignardello-Petersen R. Melatonin probably reduces anxiety in patients undergoing third-molar surgical extractions but maybe not as much as midazolam. *J Am Dent Assoc*. 2019;150(10):e159. doi:10.1016/j.adaj.2019.05.013
- 223 Perez-Heredia M, Clavero-González J, Marchena-Rodríguez L. Use of melatonin in oral health and as dental premedication. *J Biol Res Thessalon Greece*. 2015;22:13. doi:10.1186/s40709-015-0036-1
- 224 de Moares MB, Barbier WS, Raldi FV, Nascimento RD, Dos Santos LM, Loureiro Sato FR. Comparison of Three Anxiety Management Protocols for Extraction of Third Molars With the Use of Midazolam, Diazepam, and Nitrous Oxide: A Randomized Clinical Trial. *J Oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg*. 2019;77(11):2258.e1-2258.e8. doi:10.1016/j.joms.2019.06.001
- 225 Wilson KE, Girdler NM, Welbury RR. Randomized, controlled, cross-over clinical trial comparing intravenous midazolam sedation with nitrous oxide sedation in children undergoing dental extractions. *Br J Anaesth*. 2003;91(6):850-856. doi:10.1093/bja/aeg278
- 226 Alford DP, Compton P, Samet JH. Acute Pain Management for Patients Receiving Maintenance Methadone or Buprenorphine Therapy. *Ann Intern Med*. 2006;144(2):127-134.
- 227 Substance Abuse and Mental Health Services Administration. Special Circumstances for Providing Buprenorphine. Published 2016. <https://www.samhsa.gov/medication-assisted-treatment/legislation-regulations-guidelines/special-circumstances-providing-buprenorphine>.
- 228 Mercadante S, Villari P, Ferrera P, et al. Safety and Effectiveness of Intravenous Morphine for Episodic Breakthrough Pain in Patients Receiving Transdermal Buprenorphine. *J Pain Symptom Manage*. 2006;32(2):175-179. doi:10.1016/j.jpainsymman.2006.01.013
- 229 Jones HE, O'Grady K, Dahne J, et al. Management of Acute Postpartum Pain in Patients Maintained on Methadone or Buprenorphine During Pregnancy. *Am J Drug Alcohol Abuse*. 2009;35(3):151-156. doi:10.1080/00952990902825413
- 230 van Niel JCG, Schneider J, Tzschentke TM. Efficacy of Full μ -Opioid Receptor Agonists is not Impaired by Concomitant Buprenorphine or Mixed Opioid Agonists/Antagonists - Preclinical and Clinical Evidence. *Drug Res*. 2016;66(11):562-570. doi:10.1055/s-0042-109393
- 231 Vilkins AL, Bagley SM, Hahn KA, et al. Comparison of Post-Cesarean Section Opioid Analgesic Requirements in Women With Opioid Use Disorder Treated With Methadone or Buprenorphine. *J Addict Med*. 2017;11(5):397-401. doi:10.1097/ADM.0000000000000339
- 232 American Dental Association. *The ADA Practical Guide to Substance Use Disorders and Safe Prescribing*. (O'Neil M, ed.); 2015. <https://onlinelibrary.wiley.com/doi/book/10.1002/9781119062738>
- 233 Brown C, Krishnan S, Hursh K, et al. Dental disease prevalence among methamphetamine and heroin users in an urban setting: A pilot study. *J Am Dent Assoc*. 2012;143(9):992-1001. doi:10.14219/jada.archive.2012.0326
- 234 SHEKARCHIZADEH H, KHAMIRI MR, MOHEBBI SZ, EKHTIARI H, VIRTANEN JI. Oral Health of Drug Abusers: A Review of Health Effects and Care. *Iran J Public Health*. 2013;42(9):929-940.
- 235 Robinson PG, Acquah S, Gibson B. Drug users: oral health-related attitudes and behaviours. *Br Dent J*. 2005;198(4):219-224. doi:10.1038/sj.bdj.4812090
- 236 Madinier I, Harrosch J, Dugourd M, Giraud-Morin C, Fosse T. [The buccal-dental health of drug addicts treated in the University hospital centre in Nice]. *Presse Medicale Paris Fr*. 1983. 2003;32(20):919-923.

References continued

- 237 Grossi SG, Genco RJ. Periodontal Disease and Diabetes Mellitus: A Two-Way Relationship. *Ann Periodontol*. 1998;3(1):51-61. doi:10.1902/annals.1998.3.1.51
- 238 Dhadse P, Gattani D, Mishra R. The link between periodontal disease and cardiovascular disease: How far we have come in last two decades ? *J Indian Soc Periodontol*. 2010;14(3):148-154. doi:10.4103/0972-124X.75908
- 239 Janket S-J, Baird AE, Chuang S-K, Jones JA. Meta-analysis of periodontal disease and risk of coronary heart disease and stroke. *Oral Surg Oral Med Oral Pathol Oral Radiol Endodontology*. 2003;95(5):559-569. doi:10.1067/moe.2003.107
- 240 Sfyroeras GS, Roussas N, Saleptsis VG, Argyriou C, Giannoukas AD. Association between periodontal disease and stroke. *J Vasc Surg*. 2012;55(4):1178-1184. doi:10.1016/j.jvs.2011.10.008
- 241 Noorudeen A, Shereef M. Relationship between periodontal disease and respiratory diseases. *IJCDS*. 2012;3(2):28-31.
- 242 Colon PG. Dental disease in the narcotic addict. *Oral Surg Oral Med Oral Pathol*. 1972;33(6):905-910. doi:10.1016/0030-4220(72)90181-8
- 243 Charnock S, Owen S, Brookes V, Williams M. A community based programme to improve access to dental services for drug users. *Br Dent J*. 2004;196(7):385-388. doi:10.1038/sj.bdj.4811193
- 244 Odusola F, Smith JL, Bisaga A, et al. Innovations in pre-doctoral dental education: Influencing attitudes and opinions about patients with substance use disorder. *J Dent Educ*. n/a(n/a). doi:10.1002/jdd.12048
- 245 Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). Published 2019. Accessed Jan. 14, 2020. <https://www.samhsa.gov/data/>. August 2019
- 246 Ilgen M, Edwards P, Kleinberg F, Bohnert ASB, Barry K, Blow FC. The prevalence of substance use among patients at a dental school clinic in Michigan. *J Am Dent Assoc*. 2012;143(8):890-896. doi:10.14219/jada.archive.2012.0293
- 247 Ashrafioun L, Edwards PC, Bohnert ASB, Ilgen MA. Nonmedical use of pain medications in dental patients. *Am J Drug Alcohol Abuse*. 2014;40(4):312-316. doi:10.3109/00952990.2014.930152
- 248 Jing Fan MD M, PhD Y-IH, MA DH. Tooth Retention, Tooth Loss and Use of Dental Care Among Long-Term Narcotics Abusers. *Subst Abuse*. 2006;27(1-2):25-32. doi:10.1300/J465v27n01_04
- 249 Madinier I. Illicit drugs for toothache. *Br Dent J*. 2002;192(3):120. doi:10.1038/sj.bdj.4801311a
- 250 Titsas A, Ferguson MM. Impact of Opioid Use on Dentistry. *Aust Dent J*. 2002;47(2):94-98. doi:10.1111/j.1834-7819.2002.tb00311.x
- 251 Picozzi A, Dworkin SF, Leeds JG, Nash J. Dental and Associated Attitudinal Aspects of Heroin Addiction: A Pilot Study. *J Dent Res*. 1972;51(3):869-869. doi:10.1177/00220345720510032901
- 252 Angelillo IF, Grasso GM, Saggiocco G, Villari P, D'Errico MM. Dental health in a group of drug addicts in Italy. *Community Dent Oral Epidemiol*. 1991;19(1):36-37. doi:10.1111/j.1600-0528.1991.tb00102.x
- 253 Davis RK, Baer PN. Necrotizing ulcerative gingivitis in drug addict patients being withdrawn from drugs: Report of two cases. *Oral Surg Oral Med Oral Pathol*. 1971;31(2):200-204. doi:10.1016/0030-4220(71)90074-0
- 254 Reece AS. Dentition of addiction in Queensland: poor dental status and major contributing drugs. *Aust Dent J*. 2007;52(2):144-149. doi:10.1111/j.1834-7819.2007.tb00480.x
- 255 Scheutz F. Five-year evaluation of a dental care delivery system for drug addicts in Denmark. *Community Dent Oral Epidemiol*. 1984;12(1):29-34. doi:10.1111/j.1600-0528.1984.tb01405.x
- 256 Bullock K. Dental care of patients with substance abuse. *Dent Clin North Am*. 1999;43(3):513-526.
- 257 Ly KA, Milgrom P, Rothen M. Xylitol, sweeteners, and dental caries. *Pediatr Dent*. 2006;28(2):154-163; discussion 192-198.
- 258 Nayak PA, Nayak UA, Khandelwal V. The effect of xylitol on dental caries and oral flora. *Clin Cosmet Investig Dent*. 2014;6:89-94. doi:10.2147/CCIDE.S55761
- 259 Janakiram C, Deepan Kumar CV, Joseph J. Xylitol in preventing dental caries: A systematic review and meta-analyses. *J Nat Sci Biol Med*. 2017;8(1):16-21. doi:10.4103/0976-9668.198344
- 260 Marinho VC, Worthington HV, Walsh T, Clarkson JE. Fluoride varnishes for preventing dental caries in children and adolescents. *Cochrane Database Syst Rev*. 2013;(7). doi:10.1002/14651858.CD002279.pub2
- 261 Weintraub JA, Ramos-Gomez F, Jue B, et al. Fluoride Varnish Efficacy in Preventing Early Childhood Caries. *J Dent Res*. 2006;85(2):172-176. doi:10.1177/154405910608500211
- 262 Weyant RJ, Tracy SL, Anselmo T (Tracy), et al. Topical fluoride for caries prevention. *J Am Dent Assoc*. 2013;144(11):1279-1291. doi:10.14219/jada.archive.2013.0057
- 263 How to use fluoride varnish in patients with 'meth mouth.' *Dental Products Report*. Accessed April 24, 2020. <http://www.dentalproductsreport.com/dental/article/how-use-fluoride-varnish-patients-meth-mouth>
- 264 Brondani M, Park PE. Methadone and Oral Health—A Brief Review. 2011;85(2):7.
- 265 Zador D, Wall PML, Webster I. High sugar intake in a group of women on methadone maintenance in South Western Sydney, Australia. *Addiction*. 1996;91(7):1053-1061. doi:10.1046/j.1360-0443.1996.917105311.x
- 266 Nathwani NS, Gallagher JE. Methadone: Dental Risks and Preventive Action. *Dent Update*. 2008;35(8):542-548. doi:10.12968/denu.2008.35.8.542
- 267 Carr KD, Papadouka V. The role of multiple opioid receptors in the potentiation of reward by food restriction. *Brain Res*. 1994;639(2):253-260. doi:10.1016/0006-8993(94)91738-8

References continued

- 268 Götrick B, Åkerman S, Ericson D, Torstenson R, Tobin G. Oral Pilocarpine for Treatment of Opioid-induced Oral Dryness in Healthy Adults. *J Dent Res*. 2004;83(5):393-397. doi:10.1177/154405910408300508
- 269 Lowenthal AH. Atypical caries of the narcotics addict. *Dent Surv*. 1967;43(12):44-47.
- 270 Nives P, Marina K, Irina F, Željko V. Caries Prevalence in Heroin Addicts. *Acta Clin Croat*. 2013;52.(4.):436-443.
- 271 Bigwood CS, Coelho AJ. Methadone and caries. *Br Dent J*. 1990;168(6):231-231. doi:10.1038/sj.bdj.4807160
- 272 Birnbaum W. Dental health access—are drug users encouraged to use our services? *Br Dent J*. 2001;191(8):446-446. doi:10.1038/sj.bdj.4801204
- 273 Tripathee S, Akbar T, Richards D, Themessl-Huber M, Freeman R. The relationship between sugar-containing methadone and dental caries: A systematic review. *Health Educ J*. 2013;72(4):469-485. doi:10.1177/0017896912450247
- 274 Office of the Surgeon General. Surgeon General's Advisory on Naloxone and Opioid Overdose. Published April 5, 2018. Accessed Sept. 12, 2019. <https://www.hhs.gov/surgeongeneral/priorities/opioids-and-addiction/naloxone-advisory/index.html>.
- 275 Gordon JS, Severson HH. Tobacco cessation through dental office settings. *J Dent Educ*. 2001;65(4):354-363.
- 276 Koerber A, Crawford J, O'Connell K. The effects of teaching dental students brief motivational interviewing for smoking-cessation counseling: a pilot study. *J Dent Educ*. 2003;67(4):439-447.
- 277 Gelskey SC. Impact of a dental/dental hygiene tobacco-use cessation curriculum on practice. *J Dent Educ*. 2002;66(9):1074-1078.
- 278 Warnakulasuriya S. Effectiveness of tobacco counseling in the dental office. *J Dent Educ*. 2002;66(9):1079-1087.
- 279 Madras BK, Compton WM, Avula D, Stegbauer T, Stein JB, Clark HW. Screening, brief interventions, referral to treatment (SBIRT) for illicit drug and alcohol use at multiple healthcare sites: Comparison at intake and 6 months later. *Drug Alcohol Depend*. 2009;99(1):280-295. doi:10.1016/j.drugalcdep.2008.08.003
- 280 Screening, Brief Intervention and Referral to Treatment (SBIRT) in Behavioral Health. SAMHSA. Published April 1, 2011. Accessed June 18, 2020. https://www.samhsa.gov/sites/default/files/sbirtwhitepaper_0.pdf
- 281 Smith PC, Schmidt SM, Allensworth-Davies D, Saitz R. A single-question screening test for drug use in primary care. *Arch Intern Med*. 2010;170(13):1155-1160. doi:10.1001/archinternmed.2010.140
- 282 Jensen CD, Cushing CC, Aylward BS, Craig JT, Sorell DM, Steele RG. Effectiveness of motivational interviewing interventions for adolescent substance use behavior change: a meta-analytic review. *J Consult Clin Psychol*. 2011;79(4):433-440. doi:10.1037/a0023992
- 283 Mitchell SG, Gryczynski J, O'Grady KE, Schwartz RP. SBIRT for adolescent drug and alcohol use: current status and future directions. *J Subst Abuse Treat*. 2013;44(5):463-472. doi:10.1016/j.jsat.2012.11.005
- 284 Stockings E, Hall WD, Lynskey M, et al. Prevention, early intervention, harm reduction, and treatment of substance use in young people. *Lancet Psychiatry*. 2016;3(3):280-296. doi:10.1016/S2215-0366(16)00002-X
- 285 DiClemente CC, Corno CM, Graydon MM, Wiprovnick AE, Knobloch DJ. Motivational interviewing, enhancement, and brief interventions over the last decade: A review of reviews of efficacy and effectiveness. *Psychol Addict Behav J Soc Psychol Addict Behav*. 2017;31(8):862-887. doi:10.1037/adb0000318
- 286 Miller WR, Rollnick S. *Motivational Interviewing: Helping People Change*. Guilford Press; 2012.
- 287 Miller WR, Forcehimes AA, Zweben A. *Treating Addiction, Second Edition: A Guide for Professionals*. Guilford Publications; 2019.
- 288 Curry-Chiu ME, Catley D, Voelker MA, Bray KK. Dental Hygienists' Experiences with Motivational Interviewing: A Qualitative Study. *J Dent Educ*. 2015;79(8):897-906.
- 289 Bray KK, Catley D, Voelker MA, Liston R, Williams KB. Motivational interviewing in dental hygiene education: curriculum modification and evaluation. *J Dent Educ*. 2013;77(12):1662-1669.
- 290 Brezing C. Opioid Use Disorder: Update on Diagnosis and Treatment. *Psychiatric Times*. Published April 30, 2015. Accessed Feb. 16, 2020. <https://www.psychiatrytimes.com/opioid-use-disorder-update-diagnosis-and-treatment>
- 291 Amato L, Minozzi S, Davoli M, Vecchi S. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. *Cochrane Database Syst Rev*. 2011;(10). doi:10.1002/14651858.CD004147.pub4
- 292 Chutuape MA, Jasinski DR, Fingerhood MI, Stitzer ML. One-, Three-, and Six-Month Outcomes After Brief Inpatient Opioid Detoxification. *Am J Drug Alcohol Abuse*. 2001;27(1):19-44. doi:10.1081/ADA-100103117
- 293 Woody GE, Poole SA, Subramaniam G, et al. Extended vs Short-term Buprenorphine-Naloxone for Treatment of Opioid-Addicted Youth: A Randomized Trial. *JAMA*. 2008;300(17):2003-2011. doi:10.1001/jama.2008.574
- 294 Sigmon SC, Dunn KE, Saulsgiver K, et al. A Randomized, Double-blind Evaluation of Buprenorphine Taper Duration in Primary Prescription Opioid Abusers. *JAMA Psychiatry*. 2013;70(12):1347-1354. doi:10.1001/jamapsychiatry.2013.2216
- 295 Weiss RD, Potter JS, Provost SE, et al. A multi-site, two-phase, Prescription Opioid Addiction Treatment Study (POATS): Rationale, design, and methodology. *Contemp Clin Trials*. 2010;31(2):189-199. doi:10.1016/j.cct.2010.01.003
- 296 Volkow ND, Frieden TR, Hyde PS, Cha SS. Medication-Assisted Therapies—Tackling the Opioid-Overdose Epidemic. *N Engl J Med*. 2014;370(22):2063-2066. doi:10.1056/NEJMp1402780
- 297 Macintyre PE, Russell RA, Usher K a. N, Gaughwin M, Huxtable CA. Pain relief and opioid requirements in the first 24 hours after surgery in patients taking buprenorphine and methadone opioid substitution therapy. *Anaesth Intensive Care*. 2013;41(2):222-230. doi:10.1177/0310057X1304100212

References continued

- ²⁹⁸ Oifa S, Sydoruk T, White I, et al. Effects of intravenous patient-controlled analgesia with buprenorphine and morphine alone and in combination during the first 12 postoperative hours: A randomized, double-blind, four-arm trial in adults undergoing abdominal surgery. *Clin Ther.* 2009;31(3):527-541. doi:10.1016/j.clinthera.2009.03.018
- ²⁹⁹ Sen S, Arulkumar S, Cornett EM, et al. New Pain Management Options for the Surgical Patient on Methadone and Buprenorphine. *Curr Pain Headache Rep.* 2016;20(3):16. doi:10.1007/s11916-016-0549-9
- ³⁰⁰ Rivat C, Ballantyne J. The dark side of opioids in pain management: basic science explains clinical observation. *Pain Rep.* 2016;1(2). doi:10.1097/PR9.0000000000000570
- ³⁰¹ Nassif GJ, Miller TE. Evolving the management of acute perioperative pain towards opioid free protocols: a narrative review. *Curr Med Res Opin.* 2019;35(12):2129-2136. doi:10.1080/03007995.2019.1646001
- ³⁰² Weinstein EJ, Levene JL, Cohen MS, et al. Local anaesthetics and regional anaesthesia versus conventional analgesia for preventing persistent postoperative pain in adults and children. *Cochrane Database Syst Rev.* 2018;(6). doi:10.1002/14651858.CD007105.pub4
- ³⁰³ Andrae MH, Andrae DA. Regional anaesthesia to prevent chronic pain after surgery: a Cochrane systematic review and meta-analysis. *BJA Br J Anaesth.* 2013;111(5):711-720. doi:10.1093/bja/aet213
- ³⁰⁴ Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. *JAMA Surg.* 2017;152(3):292-298. doi:10.1001/jamasurg.2016.4952
- ³⁰⁵ Pędziwiatr M, Wierdak M, Nowakowski M, et al. Cost minimization analysis of laparoscopic surgery for colorectal cancer within the enhanced recovery after surgery (ERAS) protocol: a single-centre, case-matched study. *Videosurgery Miniinvasive Tech.* 2016;11(1):14-21. doi:10.5114/wiitm.2016.58617
- ³⁰⁶ Ljungqvist O. ERAS--enhanced recovery after surgery: moving evidence-based perioperative care to practice. *JPEN J Parenter Enteral Nutr.* 2014;38(5):559-566. doi:10.1177/0148607114523451
- ³⁰⁷ Wick EC, Grant MC, Wu CL. Postoperative Multimodal Analgesia Pain Management With Nonopioid Analgesics and Techniques: A Review. *JAMA Surg.* 2017;152(7):691-697. doi:10.1001/jamasurg.2017.0898
- ³⁰⁸ Hu L, Iannetti GD. Neural indicators of perceptual variability of pain across species. *Proc Natl Acad Sci.* 2019;116(5):1782-1791. doi:10.1073/pnas.1812499116
- ³⁰⁹ Hooten WM. Chronic Pain and Mental Health Disorders: Shared Neural Mechanisms, Epidemiology, and Treatment. *Mayo Clin Proc.* 2016;91(7):955-970. doi:10.1016/j.mayocp.2016.04.029
- ³¹⁰ Shin LM, Liberzon I. The Neurocircuitry of Fear, Stress, and Anxiety Disorders. *Neuropsychopharmacology.* 2010;35(1):169-191. doi:10.1038/npp.2009.83
- ³¹¹ Doan L, Manders T, Wang J. Neuroplasticity Underlying the Comorbidity of Pain and Depression. *Neural Plasticity.* doi:https://doi.org/10.1155/2015/504691
- ³¹² Cánovas L, Carrascosa A-J, García M, et al. Impact of Empathy in the Patient-Doctor Relationship on Chronic Pain Relief and Quality of Life: A Prospective Study in Spanish Pain Clinics. *Pain Med.* 2018;19(7):1304-1314. doi:10.1093/pm/pnx160
- ³¹³ Gleichgerrcht E, Decety J. The relationship between different facets of empathy, pain perception and compassion fatigue among physicians. *Front Behav Neurosci.* 2014;8. doi:10.3389/fnbeh.2014.00243
- ³¹⁴ Xia N, Li H. Loneliness, Social Isolation, and Cardiovascular Health. *Antioxid Redox Signal.* 2017;28(9):837-851. doi:10.1089/ars.2017.7312
- ³¹⁵ Degenhardt L, Lintzeris N, Campbell G, et al. Experience of adjunctive cannabis use for chronic non-cancer pain: Findings from the Pain and Opioids IN Treatment (POINT) study. *Drug Alcohol Depend.* 2015;147:144-150. doi:10.1016/j.drugalcdep.2014.11.031
- ³¹⁶ Reisfield GM, Wasan AD, Jamison RN. The Prevalence and Significance of Cannabis Use in Patients Prescribed Chronic Opioid Therapy: A Review of the Extant Literature. *Pain Med.* 2009;10(8):1434-1441. doi:10.1111/j.1526-4637.2009.00726.x
- ³¹⁷ Echeverria-Villalobos M, Todeschini AB, Stoicea N, Fiorda-Diaz J, Weaver T, Bergese SD. Perioperative care of cannabis users: A comprehensive review of pharmacological and anesthetic considerations. *J Clin Anesth.* 2019;57:41-49. doi:10.1016/j.jclinane.2019.03.011
- ³¹⁸ Salottolo K, Peck L, Tanner II A, et al. The grass is not always greener: a multi-institutional pilot study of marijuana use and acute pain management following traumatic injury. *Patient Saf Surg.* 2018;12(1):16. doi:10.1186/s13037-018-0163-3
- ³¹⁹ Liu CW, Bhatia A, Buzon-Tan A, et al. Weeding Out the Problem: The Impact of Preoperative Cannabinoid Use on Pain in the Perioperative Period. *Anesth Analg.* 2019;129(3):874-881. doi:10.1213/ANE.0000000000003963
- ³²⁰ Khelemsky Y, Goldberg AT, Hurd YL, et al. Perioperative Patient Beliefs Regarding Potential Effectiveness of Marijuana (Cannabinoids) for Treatment of Pain: A Prospective Population Survey. *Reg Anesth Pain Med.* 2017;42(5):652-659. doi:10.1097/AAP.0000000000000654
- ³²¹ Beaulieu P, Boulanger A, Desroches J, Clark AJ. Medical cannabis: considerations for the anesthesiologist and pain physician. *Can J Anesth Can Anesth.* 2016;63(5):608-624. doi:10.1007/s12630-016-0598-x
- ³²² Alexander JC, Joshi GP. A review of the anesthetic implications of marijuana use. *Bayl Univ Med Cent Proc.* 2019;32(3):364-371. doi:10.1080/08998280.2019.1603034
- ³²³ Grotenhermen F. Pharmacokinetics and Pharmacodynamics of Cannabinoids. *Clin Pharmacokinet.* 2003;42(4):327-360. doi:10.2165/00003088-200342040-00003
- ³²⁴ United States Food and Drug Administration. Epidiolex Prescribing Information. Published 2018. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210365lbl.pdf

References continued

- ³²⁵ Stuyt E. The Problem with the Current High Potency THC Marijuana from the Perspective of an Addiction Psychiatrist. *Mo Med*. 2018;115(6):482-486.
- ³²⁶ Webb C. Marijuana Abuse: Increasing the Likelihood of the use of Harder Substances. *Smart Approaches to Marijuana*. Published Feb. 11, 2019. <https://learnaboutsam.org/guest-contribution-marijuana-abuse-increasing-the-likelihood-of-the-use-of-harder-substances/>
- ³²⁷ Batalla A, Bhattacharyya S, Yücel M, et al. Structural and Functional Imaging Studies in Chronic Cannabis Users: A Systematic Review of Adolescent and Adult Findings. *PLoS ONE*. 2013;8(2). doi:10.1371/journal.pone.0055821
- ³²⁸ Filbey FM, Aslan S, Calhoun VD, et al. Long-term effects of marijuana use on the brain. *Proc Natl Acad Sci*. 2014;111(47):16913-16918. doi:10.1073/pnas.1415297111
- ³²⁹ Andréasson S, Engström A, Allebeck P, Rydberg U. CANNABIS AND SCHIZOPHRENIA A Longitudinal Study of Swedish Conscripts. *The Lancet*. 1987;330(8574):1483-1486. doi:10.1016/S0140-6736(87)92620-1
- ³³⁰ Zammit S, Allebeck P, Andreasson S, Lundberg I, Lewis G. Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. *BMJ*. 2002;325(7374):1199. doi:10.1136/bmj.325.7374.1199
- ³³¹ van Os J, Bak M, Hanssen M, Bijl RV, de Graaf R, Verdoux H. Cannabis Use and Psychosis: A Longitudinal Population-based Study. *Am J Epidemiol*. 2002;156(4):319-327. doi:10.1093/aje/kwf043
- ³³² Henquet C, Krabbendam L, Spauwen J, et al. Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. *BMJ*. 2004;330(7481):11. doi:10.1136/bmj.38267.664086.63
- ³³³ Arseneault L, Cannon M, Poulton R, Murray R, Caspi A, Moffitt TE. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ*. 2002;325(7374):1212-1213. doi:10.1136/bmj.325.7374.1212
- ³³⁴ Fergusson DM, Horwood LJ, Swain-Campbell NR. Cannabis dependence and psychotic symptoms in young people. *Psychol Med*. 2003;33(1):15-21. doi:10.1017/S0033291702006402
- ³³⁵ Stefanis NC, Dragovic M, Power BD, Jablensky A, Castle D, Morgan VA. The effect of drug use on the age at onset of psychotic disorders in an Australian cohort. *Schizophr Res*. 2014;156(2):211-216. doi:10.1016/j.schres.2014.04.003
- ³³⁶ Moore TH, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *The Lancet*. 2007;370(9584):319-328. doi:10.1016/S0140-6736(07)61162-3
- ³³⁷ Libuy Hidalgo N, Angel V de, Ibáñez Berríos C, Murray RM, Mundt AP. The relative prevalence of schizophrenia among cannabis and cocaine users attending addiction services. *Schizophr Res*. Published online 2018. doi:10.1016/j.schres.2017.04.010
- ³³⁸ Di Forti M, Sallis H, Allegrì F, et al. Daily Use, Especially of High-Potency Cannabis, Drives the Earlier Onset of Psychosis in Cannabis Users. *Schizophr Bull*. 2014;40(6):1509-1517. doi:10.1093/schbul/sbt181
- ³³⁹ National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division, Board on Population Health and Public Health Practice, Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. National Academies Press (US); 2017. Accessed March 9, 2020. <http://www.ncbi.nlm.nih.gov/books/NBK423845/>
- ³⁴⁰ Lev-Ran S, Roerecke M, Foll BL, George TP, McKenzie K, Rehm J. The association between cannabis use and depression: a systematic review and meta-analysis of longitudinal studies. *Psychol Med*. 2014;44(4):797-810. doi:10.1017/S0033291713001438
- ³⁴¹ Borges G, Bagge CL, Orozco R. A literature review and meta-analyses of cannabis use and suicidality. *J Affect Disord*. 2016;195:63-74. doi:10.1016/j.jad.2016.02.007
- ³⁴² Wolff V, Zinchenko I, Quenardelle V, Rouyer O, Geny B. Characteristics and Prognosis of Ischemic Stroke in Young Cannabis Users Compared With Non-Cannabis Users. *J Am Coll Cardiol*. 2015;66(18):2052-2053. doi:10.1016/j.jacc.2015.08.867
- ³⁴³ Rumalla K, Reddy AY, Mittal MK. Association of Recreational Marijuana Use with Aneurysmal Subarachnoid Hemorrhage. *J Stroke Cerebrovasc Dis*. 2016;25(2):452-460. doi:10.1016/j.jstrokecerebrovasdis.2015.10.019
- ³⁴⁴ Tashkin DP. Effects of Marijuana Smoking on the Lung. *Ann Am Thorac Soc*. 2013;10(3):239-247. doi:10.1513/AnnalsATS.201212-127FR
- ³⁴⁵ Moir D, Rickert WS, Levasseur G, et al. A Comparison of Mainstream and Sidestream Marijuana and Tobacco Cigarette Smoke Produced under Two Machine Smoking Conditions. *Chem Res Toxicol*. 2008;21(2):494-502. doi:10.1021/tx700275p
- ³⁴⁶ Wilson KM, Torok MR, Wei B, et al. Detecting biomarkers of secondhand marijuana smoke in young children. *Pediatr Res*. 2017;81(4):589-592. doi:10.1038/pr.2016.261
- ³⁴⁷ Gurney J, Shaw C, Stanley J, Signal V, Sarfati D. Cannabis exposure and risk of testicular cancer: a systematic review and meta-analysis. *BMC Cancer*. 2015;15(1):897. doi:10.1186/s12885-015-1905-6
- ³⁴⁸ Liu C, Sadat SH, Ebisumoto K, et al. Cannabinoids promote progression of HPV positive head and neck squamous cell carcinoma via p38 MAPK activation. *Clin Cancer Res*. Published online Jan. 1, 2020. doi:10.1158/1078-0432.CCR-18-3301
- ³⁴⁹ Fish EW, Murdaugh LB, Zhang C, et al. Cannabinoids Exacerbate Alcohol Teratogenesis by a CB1-Hedgehog Interaction. *Sci Rep*. 2019;9(1):1-16. doi:10.1038/s41598-019-52336-w