

Pain Management Course

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4 CE Credit / Contact Hours

Important Note: We recommend printing the test and completing it as you read to prepare for the online post-test. As you go through the course, hover over or click the yellow 'sticky notes' to reveal helpful study tips. Enjoy the course!

Introduction

Pain. The word almost hurts to think about. We all experience pain of some kind, nearly every day. But it is the long-term, chronic pain that can be so debilitating.

The following is from the *National Center for Complementary and Integrative Health*. Here it lists some of the more common type of pain and potential natural pain relievers.

Chapter 1. Chronic Pain: In Depth

A. Complementary Health Approaches

How much do we know about the effectiveness of complementary health approaches for chronic pain?

A growing body of evidence suggests that some complementary approaches, such as acupuncture, *hypnosis*, massage, mindfulness meditation, spinal manipulation, tai chi, and yoga, may help to manage some painful conditions.

What do we know about the safety of complementary health approaches for chronic pain?

Although the mind and body practices studied for chronic pain have good safety records, that doesn't mean that they're risk-free for everyone. Your health and special circumstances (such as pregnancy) may affect the safety of these approaches. If you're considering natural products, remember that natural doesn't always mean safe and that some natural products may have side effects or interact with medications.

What Is Chronic Pain and Why Is It Important?

Chronic pain is pain that lasts more than several months (variously defined as 3 to 6 months, but longer than "normal healing"). It's a very common problem. Results from the 2012 National Health Interview Survey show that:

About 25.3 million U.S. adults (11.2 percent) had pain every day for the previous 3 months.

Nearly 40 million adults (17.6 percent) had severe pain.

Individuals with severe pain had worse health, used more health care, and had more disability than those with less severe pain.

Chronic pain becomes more common as people grow older, at least in part because health problems that can cause pain, such as osteoarthritis, become more common with advancing age. Military veterans are another group at increased risk for chronic pain; U.S. national survey data show that both pain in general and severe pain are more common among veterans than nonveterans.

Not all people with chronic pain have a health problem diagnosed by a health care provider, but among those who do, the most frequent conditions by far are low-back pain or osteoarthritis, according to a national survey. Other common diagnoses include rheumatoid arthritis, migraine, carpal tunnel syndrome, and fibromyalgia. The annual economic cost of chronic pain in the United States, including both treatment and lost productivity, has been estimated at up to \$635 billion.

Chronic pain may result from an underlying disease or health condition, an injury, medical treatment (such as surgery), inflammation, or a problem in the nervous system

(in which case it is called “neuropathic pain”); or the cause may be unknown. Pain can affect quality of life and productivity, and it may be accompanied by difficulty in moving around, disturbed sleep, anxiety, depression, and other problems.¹

What the Science Says About Complementary Health Approaches for Chronic Pain

The scientific evidence suggests that some complementary health approaches may help people manage chronic pain.

Some recent research has looked at the effects of complementary approaches on chronic pain in general rather than on specific painful conditions.

A 2017 review looked at complementary approaches with the opioid crisis in mind, to see which ones might be helpful for relieving chronic pain and reducing the need for opioid therapy to manage pain. There was evidence that **acupuncture, yoga, relaxation techniques, tai chi, massage, and osteopathic or spinal manipulation** may have some benefit for chronic pain, but **only** for acupuncture was there evidence that the technique could reduce a patient’s need for opioids.

Research shows that **hypnosis** is moderately effective in managing chronic pain, when compared to usual medical care. However, the effectiveness of hypnosis can vary from one person to another.

A 2017 review of studies of **mindfulness meditation** for chronic pain showed that it is associated with a small improvement in pain symptoms.

Studies have shown that **music** can reduce self-reported pain and depression symptoms in people with chronic pain.

A 2017 evaluation of the research on **acupuncture** found evidence that it has a small beneficial effect on acute low-back pain and a moderate beneficial effect on chronic low-back pain. Based on this evaluation, a 2017 clinical practice guideline (guidance for

health care providers) from the American College of Physicians (ACP) included acupuncture among the nondrug treatment options for management of both acute and chronic low-back pain.

Massage therapy might provide short-term relief from low-back pain, but the evidence is not of high quality. Massage has not been shown to have long-term benefits for low-back pain. The 2017 ACP guideline included massage therapy as an option for acute but not chronic low-back pain.

A 2017 research review concluded that **mindfulness-based stress reduction** is associated with improvements in pain intensity and physical functioning in low-back pain, compared to usual care, but the effect may be small and short term. The 2017 ACP guideline included mindfulness-based stress reduction as an option for chronic but not acute low-back pain.

There is some evidence that **progressive relaxation** may help relieve low-back pain, but studies on this topic have been small and not of the highest quality. The 2017 ACP guideline included progressive relaxation as an option for chronic but not acute low-back pain.

Spinal manipulation appears to be as effective as other therapies commonly used for chronic low-back pain, such as physical therapy, exercise, and standard medical care. The 2017 ACP guideline included spinal manipulation as an option for both acute and chronic low-back pain.

A 2018 evaluation of the research on **yoga** for low-back pain by the Agency for Healthcare Research and Quality (AHRQ) found that it has improved the pain and function in both the short term (1 to 6 months) and intermediate term (6 to 12 months). The effects of yoga were similar to those of exercise. The 2017 ACP guideline included yoga as an option for chronic but not acute low-back pain.

A 2016 evaluation of the research on herbal products for low-back pain found evidence that **cayenne**, administered topically (applied to the skin) can reduce pain. Two other herbal products used topically, **comfrey** and **lavender essential oil**, and two herbs used orally, **white willow bark** and **devil's claw**, may also be helpful, but the evidence for these herbs is not as strong as that for cayenne.

Studies of **prolotherapy** (a treatment involving repeated injections of irritant solutions) for low-back pain have had inconsistent results.

For more information, see the National Center for Complementary and Integrative Health (NCCIH) webpage on [low-back pain](#).

Update:

Recent large-scale surveys and integrative reviews further affirm the growing role of complementary health approaches (CHAs) in chronic pain management. In a 2024 JAMA analysis, the use of CHAs among U.S. adults increased from ~19.2 % in 2002 to ~36.7 % in 2022; moreover, nearly half of CHA users report using them for pain relief (Nahin, Rhee, & Stussman, 2024). Complementing that, a 2025 scoping review found increasing evidence, though still of modest strength, for modalities such as acupuncture, massage, mindfulness, and yoga in alleviating chronic noncancer pain (Crosier et al., 2025). Another 2025 review emphasized that integrative approaches combining conventional pharmacologic and complementary methods may yield synergistic benefits when delivered in multidisciplinary settings (Evidence of Commonly Used Integrative Approaches, 2024). However, methodological heterogeneity and small trial sizes remain significant challenges (Zhang, 2025). Clinicians should continue to present these modalities as adjuncts, aligned with patient preferences and guided by evidence transparency.

B. Complementary Health Approaches for Specific Pain

Osteoarthritis

There's evidence that **acupuncture** has short-term benefits in relieving knee pain caused by osteoarthritis. Acupuncture hasn't been shown to be helpful for osteoarthritis of the hip.

A small amount of research suggests that **massage** may help reduce osteoarthritis symptoms.

A 2017 review of the evidence by the AHRQ concluded that **tai chi** has short-term (up to 12 weeks) and medium-term (12 to 26 weeks) benefits on pain for people with knee osteoarthritis. There hasn't been enough research to show whether it's helpful for longer periods of time. **Qi gong** may have similar benefits, but little research has been done on it.

Little research has been done on **yoga** for osteoarthritis; there's only weak evidence of a possible benefit.

The 2017 AHRQ report concluded that one type of **electromagnetic therapy**, called pulsed electromagnetic field therapy, may have a short-term beneficial effect on knee osteoarthritis pain, but the strength of the evidence for an effect was low.

The 2017 AHRQ report evaluated **whole-body vibration** (an approach in which a person does exercises on a vibrating platform) for knee osteoarthritis and found that its effects on pain were inconsistent.

Studies of **glucosamine**, **chondroitin**, and **S-adenosyl-L-methionine (SAME)** for knee osteoarthritis pain have had conflicting results.

There isn't enough research on **dimethyl sulfoxide (DMSO)** or **methylsulfonylmethane (MSM)** for osteoarthritis pain to allow conclusions to be reached.

Rheumatoid arthritis

The amount of research on **mind and body practices** for rheumatoid arthritis pain is too small for conclusions to be reached about their effectiveness.

Dietary supplements containing **omega-3 fatty acids**, **gamma-linolenic acid (GLA)**, or the herb **thunder god vine** may help relieve rheumatoid arthritis symptoms.

Headache

There's moderate-quality evidence that *acupuncture* may reduce the frequency of migraines and moderate-to-low quality evidence that it may reduce the frequency of tension headaches.

Because not much research has been done or because research results are inconsistent, it's uncertain whether biofeedback, *massage*, *relaxation techniques*, *spinal manipulation*, *tai chi*, and *yoga* are helpful for headaches.

Guidelines from the American Academy of Neurology and the American Headache Society classify *butterbur* as effective; *feverfew*, *magnesium*, and *riboflavin* as probably effective; and *coenzyme Q10* as possibly effective for preventing migraines.

Neck pain

Acupuncture hasn't been studied as extensively for neck pain as for some other pain conditions. However, the studies that have been done suggest that acupuncture is helpful for neck pain, although its effect may not persist for long.

Massage therapy may provide short-term relief from neck pain, especially if massage sessions are relatively lengthy and frequent, but it doesn't appear to be more effective than other therapies.

Spinal manipulation may be helpful for short-term relief of neck pain, but the evidence favoring it is not of high quality.

Fibromyalgia

It's uncertain whether **acupuncture** is helpful for fibromyalgia pain.

Although some studies of *tai chi*, *yoga*, *mindfulness*, and *biofeedback* for fibromyalgia symptoms have had promising results, the evidence is too limited to allow definite conclusions to be reached about whether these approaches are helpful.

There is insufficient evidence that any **natural products** can relieve fibromyalgia pain, with the possible exception of vitamin D supplements, which may reduce pain in people with fibromyalgia who have low vitamin D levels.

Studies of **homeopathy** have not demonstrated that it is beneficial for fibromyalgia.

Irritable bowel syndrome

Hypnotherapy may be helpful for irritable bowel syndrome, but the quality of the evidence is not high.

Probiotics may be helpful for irritable bowel syndrome, but it's still uncertain which types of probiotics are most likely to be effective and which symptoms they may relieve. The small amount of research on **peppermint oil** suggests that at least some formulations might be helpful for irritable bowel symptoms.

Studies of **acupuncture** for irritable bowel syndrome have not found actual acupuncture to be more helpful than simulated acupuncture.

For more information, see the NCCIH fact sheet on [irritable bowel syndrome](#).

Other types of pain

Various complementary approaches have been studied for other types of chronic pain, such as **nerve pain**, **chronic pelvic pain**, **pain associated with endometriosis**, **carpal tunnel syndrome**, **pain associated with gout**, and **cancer pain**. There's promising evidence that some complementary approaches may be helpful for some of these types of pain, but the evidence is insufficient to clearly establish their effectiveness.

Other complementary approaches

There's some evidence that **cannabis (marijuana)-based medicines** (i.e., cannabinoids) may be helpful for chronic nerve (neuropathic) pain and perhaps other types of chronic pain, but it's unclear whether the potential benefits are greater than the potential harms. Further research is needed that meets U.S. Food and Drug Administration (FDA) requirements for determining the safety and efficacy of cannabinoids for the management of pain.

It's unclear whether **kratom** has an effect on chronic pain because of a lack of studies of this substance in people.

There's a lack of high-quality research to definitively evaluate whether **Reiki** is of value for pain relief.

Although **static magnets** are widely marketed for pain control, the evidence does not support their use.

Update:

Newer evidence is refining where CHAs contribute most in discrete pain conditions. For musculoskeletal and low back pain, acupuncture, yoga, and manual therapy persist among the better supported nonpharmacologic options (Zhang, 2025). In neuropathic pain, while first-line pharmacologic interventions remain critical, integrative modalities are gaining interest for addressing associated sleep disturbance, mood symptoms, or central sensitization (Crosier et al., 2025). For fibromyalgia, mindfulness-based stress reduction and gentle mind-body movement (e.g. tai chi) continue to show modest effect sizes in recent trials, but findings emphasize the necessity of multimodal combinations (Zhang, 2025). Importantly, not all complementary strategies have robust backing, and clinicians should be cautious about recommending unstandardized supplements or high-risk manipulations without clear evidence (Evidence of Commonly Used Integrative Approaches, 2024; Zhang, 2025).

C. Guidelines for the Treatment of Chronic Pain Conditions

National health professional organizations have issued guidelines for treating several chronic pain conditions. Some mention ways in which certain complementary health approaches can be incorporated into treatment plans. Others discourage the use of certain complementary approaches.

More information

A clinical practice guideline from the American College of Physicians encourages the use of nonpharmacologic approaches as initial treatment for chronic low-back pain. The options they suggest include several complementary approaches—acupuncture, mindfulness-based stress reduction, tai chi, yoga, progressive relaxation, biofeedback, and spinal manipulation—as well as conventional methods such as exercise and cognitive behavioral therapy.

The American College of Rheumatology mentions several complementary approaches in its guidelines for the management of osteoarthritis of the hip or knee. For

osteoarthritis of the knee, the guidelines mention tai chi as one of several nondrug approaches that might be helpful. The same guidelines, however, discourage using the dietary supplements glucosamine and chondroitin for osteoarthritis of the hip or knee. The American College of Gastroenterology (ACG) included probiotics/prebiotics, peppermint oil, and hypnotherapy in its evaluation of approaches for managing irritable bowel syndrome. The ACG found only weak evidence that any of these approaches may be helpful.

Update:

Guideline and policy environments continue evolving in ways that emphasize nonpharmacological care, individualized decision-making, and harm mitigation. The FDA's Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS) is being modified such that, beginning March 2025, pharmacies may order mail-back envelopes for patient disposal of unused opioids—a strategy expected to enhance safe disposal practices (FDA OA REMS Update, 2025). The CDC's 2022 opioid prescribing guideline remains foundational, urging lowest effective dosing, caution with dose escalation, regular review of benefits vs. harms, and use of PDMPs and naloxone where appropriate (CDC Guideline Recommendations, 2024). Meanwhile, in 2024 the Federation of State Medical Boards adopted updated strategies emphasizing individualized, patient-centered opioid prescribing decisions and shared decision-making (AMA, 2024). These guidance shifts align with emerging real-world data suggesting that nonopioid therapies (e.g. physical therapy) are modestly associated with reduced risk of opioid misuse, whereas certain prescribing combinations (e.g. opioids + gabapentinoids or benzodiazepines) elevate that risk (Responsible Controlled Substance and Opioid Prescribing, 2024). Overall, current guideline trends support earlier initiation of nonpharmacologic therapies, tighter oversight of opioid use, and emphasizing patient values in therapeutic decisions.

Chapter Update:

Chapter 1: Key Advances & Trends

Over the most recent biennium, several notable cross-cutting movements are shaping chronic pain care:

1. Widening uptake of complementary approaches

The prevalence of complementary health approach use has nearly doubled in two decades (Nahin et al., 2024), and integrative care models are increasingly feasible in pain clinics (Crosier et al., 2025). These modalities are being framed not as stand-alone cures but as strategic adjuncts when harmonized with standard care.

2. Sharper emphasis on evidence quality and transparency

New reviews and integrative summaries attempt to stratify modalities by strength of evidence, stressing methodological limitations (Zhang, 2025). Clinicians are encouraged to communicate uncertainty, effect sizes, and trade-offs when offering CHAs.

3. Regulatory and systems changes toward safety and stewardship

The FDA's OA REMS revision (mail-back envelopes) offers patients more accessible disposal options (FDA OA REMS Update, 2025). Meanwhile, state medical boards' adoption of patient-centered prescribing strategies (AMA, 2024) reflects a shift from rigid limits toward individualized risk-benefit balancing.

4. Reinforcing nonopioid strategies earlier in disease trajectory

Emerging data indicate that earlier use of physical therapy or structured nonpharmacologic care may modestly reduce downstream opioid-related risk, whereas certain drug combinations raise danger (Responsible Controlled Substance and Opioid Prescribing, 2024). This supports guideline momentum to frontload low-risk modalities.

5. Persistent evidence gaps and methodological caution

While momentum is positive, many newer studies remain small, heterogeneous, or weakly controlled (Crosier et al., 2025; Evidence of Commonly Used Integrative Approaches, 2024). As such, adoption of complementary strategies should be tempered with critical appraisal and ongoing monitoring.

In sum, the field is progressing: complementary therapies are more accepted, regulatory tools are evolving to enhance safety, and the focus is increasingly on early, multimodal,

individualized care. But the clinician's role in interpreting evidence and guiding patients remains essential.

Chapter 2. Prescription Opioids

A common but dangerous treatment for pain is prescription opioids. How addictive can they be. On a personal note, I had a friend who has since taken his life as a result of his addiction to Opioids. He was so addicted; he got a job which involved using a nail gun. He shot his hand with the nail gun just so he could get more pain killers.

The following is from the National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services. Updated June 2019

A. What are prescription opioids?

Opioids are a class of drugs naturally found in the opium poppy plant. Some prescription opioids are made from the plant directly, and others are made by scientists in labs using the same chemical structure. Opioids are often used as medicines because they contain chemicals that relax the body and can relieve pain. Prescription opioids are used mostly to treat moderate to severe pain, though some opioids can be used to treat coughing and diarrhea. Opioids can also make people feel very relaxed and "high" – which is why they are sometimes used for non-medical reasons. This can be dangerous because opioids can be highly addictive, and overdoses and death are common. Heroin is one of the world's most dangerous opioids and is never used as a medicine in the United States.

Popular slang terms for opioids include Oxy, Percs, and Vikes.

What are common prescription opioids?

- hydrocodone (Vicodin®) oxycodone (OxyContin®, Percocet®)
- oxymorphone (Opana®)

- morphine (Kadian®, Avinza®)
- codeine
- fentanyl

How do people misuse prescription opioids?

Prescription opioids used for pain relief are generally safe when taken for a short time and as prescribed by a doctor, but they can be misused. People misuse prescription opioids by:

- taking the medicine in a way or dose other than prescribed
- taking someone else's prescription medicine
- taking the medicine for the effect it causes—to get high

When misusing a prescription opioid, a person can swallow the medicine in its normal form. Sometimes people crush pills or open capsules, dissolve the powder in water, and inject the liquid into a vein. Some also snort the powder.

How do prescription opioids affect the brain?

Opioids bind to and activate opioid receptors on cells located in many areas of the brain, spinal cord, and other organs in the body, especially those involved in feelings of pain and pleasure. When opioids attach to these receptors, they block pain signals sent from the brain to the body and release large amounts of dopamine throughout the body. This release can strongly reinforce the act of taking the drug, making the user want to repeat the experience.

What are some possible effects of prescription opioids on the brain and body?

In the short term, opioids can relieve pain and make people feel relaxed and happy. However, opioids can also have harmful effects, including:

- drowsiness
- confusion
- nausea
- constipation

- euphoria
- slowed breathing

Opioid misuse can cause slowed breathing, which can cause hypoxia, a condition that results when too little oxygen reaches the brain. Hypoxia can have short- and long-term psychological and neurological effects, including coma, permanent brain damage, or death.

Researchers are also investigating the long-term effects of opioid addiction on the brain, including whether damage can be reversed.

What are the other health effects of opioid medications?

Older adults are at higher risk of accidental misuse or abuse because they typically have multiple prescriptions and chronic diseases, increasing the risk of drug-drug and drug-disease interactions, as well as a slowed metabolism that affects the breakdown of drugs.

Sharing drug injection equipment and having impaired judgment from drug use can increase the risk of contracting infectious diseases such as HIV and from unprotected sex.

Updates

In recent years, the role of prescription opioids in the U.S. overdose epidemic has shifted. Prescribing rates for high-dose opioids have steadily declined since the CDC released its revised Clinical Practice Guideline for Prescribing Opioids for Pain (2022), which emphasizes non-opioid and non-pharmacologic treatments as first-line options (CDC, 2023). Despite these efforts, prescription opioids remain a serious public health concern: in 2023, more than 14,000 overdose deaths involved prescription opioids, often in combination with benzodiazepines or illicit fentanyl (CDC, 2024).

The formulations most frequently linked with misuse today are oxycodone, hydrocodone, and methadone, though diversion of fentanyl-containing prescriptions also plays a role. A key update is that prescribing practices are improving—overall opioid dispensing has declined nearly 50% since 2012—yet misuse and overdose

persist, reflecting the complexity of pain management, dependence, and polysubstance use (NIDA, 2024).

B. Prescription Opioids and Heroin

Prescription opioids and heroin are chemically similar and can produce a similar high. In some places, heroin is cheaper and easier to get than prescription opioids, so some people switch to using heroin instead. Data from 2011 showed that an estimated 4 to 6 percent who misuse prescription opioids switch to heroin^{1,2,3} and about 80 percent of people who used heroin first misused prescription opioids.^{1,2,3} More recent data suggest that heroin is frequently the first opioid people use. In a study of those entering treatment for opioid use disorder, approximately one-third reported heroin as the first opioid they used regularly to get high.⁴

Can I take prescription opioids if I'm pregnant?

If a woman uses prescription opioids when she's pregnant, the baby could develop dependence and have withdrawal symptoms after birth. This is called neonatal abstinence syndrome, which can be treated with medicines. Use during pregnancy can also lead to miscarriage and low birth weight.

It can be difficult for a person with an opioid addiction to quit, but pregnant women who seek treatment have better outcomes than those who quit abruptly. Methadone and buprenorphine are the standard of care to treat opioid-dependent pregnant women. Methadone or buprenorphine maintenance combined with prenatal care and a comprehensive drug treatment program can improve many of the adverse outcomes associated with untreated opioid addiction. If a woman is unable to quit before becoming pregnant, treatment with methadone or buprenorphine during pregnancy improves the chances of having a healthier baby at birth.

In general, it is important to closely monitor women who are trying to quit drug use during pregnancy and to provide treatment as needed.

Can a person overdose on prescription opioids?

Yes, a person can overdose on prescription opioids. An opioid overdose occurs when a person uses enough of the drug to produce life-threatening symptoms or death. When people overdose on an opioid medication, their breathing often slows or stops. This can decrease the amount of oxygen that reaches the brain, which can result in coma, permanent brain damage, or death.

How can an opioid overdose be treated?

If you suspect someone has overdosed, the most important step to take is to call 911 so he or she can receive immediate medical attention. Once medical personnel arrive, they will administer naloxone. Naloxone is a medicine that can treat an opioid overdose when given right away. It works by rapidly binding to opioid receptors and blocking the effects of opioid drugs. Naloxone is available as an injectable (needle) solution, a hand-held auto-injector (EVZIO®), and a nasal spray (NARCAN® Nasal Spray).

Some states have passed laws that allow pharmacists to dispense naloxone without a personal prescription. This allows friends, family, and others in the community to use the auto-injector and nasal spray versions of naloxone to save someone who is overdosing.

Tolerance vs. Dependence vs. Addiction

Long-term use of prescription opioids, even as prescribed by a doctor, can cause some people to develop **a tolerance**, which means that they need higher and/or more frequent doses of the drug to get the desired effects.

Drug dependence occurs with repeated use, causing the neurons to adapt so they only function normally in the presence of the drug. The absence of the drug causes several physiological reactions, ranging from mild in the case of caffeine, to potentially life threatening, such as with heroin. Some chronic pain patients are dependent on opioids and require medical support to stop taking the drug.

Drug **addiction** is a chronic disease characterized by compulsive, or uncontrollable, drug seeking and use despite harmful consequences and long-lasting changes in the brain. The changes can result in harmful behaviors by those who misuse drugs, whether prescription or illicit drugs.

Can use of prescription opioids lead to addiction?

Yes, repeated misuse of prescription opioids can lead to a substance use disorder (SUD), a medical illness which ranges from mild to severe and from temporary to chronic. Addiction is the most severe form of an SUD. An SUD develops when continued misuse of the drug changes the brain and causes health problems and failure to meet responsibilities at work, school, or home.

People addicted to an opioid medication who stop using the drug can have severe withdrawal symptoms that begin as early as a few hours after the drug was last taken.

These symptoms include:

- muscle and bone pain
- sleep problems
- diarrhea and vomiting
- cold flashes with goose bumps
- uncontrollable leg movements
- severe cravings

These symptoms can be extremely uncomfortable and are the reason many people find it so difficult to stop using opioids. There are medicines being developed to help with the withdrawal process, and the U.S. Food and Drug Administration (FDA) approved sale of a device, NSS-2 Bridge, that can help ease withdrawal symptoms. The NSS-2 Bridge device is a small electrical nerve stimulator placed behind the person's ear, that can be used for up to five days during the acute withdrawal phase. There are also medicines being developed to help with the withdrawal process. The FDA approved lofexidine, a non-opioid medicine designed to reduce opioid withdrawal symptoms.

What type of treatment can people get for addiction to prescription opioids?

A range of treatments including medicines and behavioral therapies are effective in helping people with opioid addiction.

Two medicines, buprenorphine and methadone, work by binding to the same opioid receptors in the brain as the opioid medicines, reducing cravings and withdrawal symptoms. Another medicine, naltrexone, blocks opioid receptors and prevents opioid drugs from having an effect.

Behavioral therapies for addiction to prescription opioids help people modify their attitudes and behaviors related to drug use, increase healthy life skills, and persist with other forms of treatment, such as medication. Some examples include, cognitive behavioral therapy which helps modify the patient's drug use expectations and behaviors, and also effectively manage triggers and stress. Multidimensional family therapy, developed for adolescents with drug use problems, addresses a range of personal and family influences on one's drug use patterns and is designed to improve overall functioning. These behavioral treatment approaches have proven effective, especially when used along with medicines. Read more about drug addiction treatment in our *Treatment Approaches for Drug Addiction DrugFacts*.

Points to Remember

- Prescription opioids are used mostly to treat moderate to severe pain, though some opioids can be used to treat coughing and diarrhea.
- People misuse prescription opioids by taking the medicine in a way other than prescribed, taking someone else's prescription, or taking the medicine to get high. When misusing a prescription opioid, a person may swallow, inject, or snort the drug.
- Opioids bind to and activate opioid receptors on cells located in the brain, spinal cord, and other organs in the body, especially those involved in feelings of pain and pleasure, and can strongly reinforce the act of taking the drug, making the user want to repeat the experience.
- People who use prescription opioids can feel relaxed and happy, but also experience drowsiness, confusion, nausea, constipation, and slowed breathing.

- Prescription opioids have effects similar to heroin. While prescription opioid misuse is a risk factor for starting heroin use, only a small fraction of people who misuse opioid pain relievers switch to heroin.
- A person can overdose on prescription opioids. Naloxone is a medicine that can treat an opioid overdose when given right away.
- Prescription opioid use, even when used as prescribed by a doctor can lead to a substance use disorder, which takes the form of addiction in severe cases. Withdrawal symptoms include muscle and bone pain, sleep problems, diarrhea and vomiting, and severe cravings.
- A range of treatments including medicines and behavioral therapies are effective in helping people with an opioid use disorder.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S.

Department of Health and Human Services.

Updated June 2019

Updates

The relationship between prescription opioid misuse and heroin use continues to be a major concern, though patterns have evolved. Early in the epidemic, many individuals initiated heroin use after misusing prescription opioids. Current data, however, show that most new heroin users now start directly with heroin or illicit fentanyl, while prescription opioid misuse remains a risk factor for transitioning to these drugs (SAMHSA, 2024).

The danger today lies less in prescription-to-heroin “gateway” pathways alone and more in the highly toxic drug supply. Heroin is frequently adulterated with illicit fentanyl and other synthetic opioids, making overdose much more likely. In fact, synthetic opioids other than methadone (primarily illicit fentanyl) were involved in over 74,000 deaths in 2023, compared to 14,000 involving prescription opioids and 10,000 involving heroin (CDC, 2024).

These trends highlight the need for nuanced prevention and treatment strategies: reducing unnecessary prescribing, expanding access to medications for opioid use

disorder (MOUD) such as buprenorphine and methadone, and addressing the increasing overlap of opioid use with stimulants like methamphetamine and cocaine (NIDA, 2024).

Polysubstance Use and Emerging Trends

A critical development in recent years is the dramatic rise of **polysubstance use** in opioid-related overdoses. While opioids remain the leading driver of overdose deaths, most fatalities now involve **multiple substances** rather than opioids alone. In 2023, the CDC reported that nearly **half of fentanyl-involved overdose deaths also included stimulants such as methamphetamine or cocaine** (CDC, 2024). Benzodiazepines, alcohol, and xylazine—a veterinary sedative increasingly found in the illicit drug supply—further complicate overdose risk and clinical management (NIDA, 2024). This shift has profound implications for treatment and prevention. Traditional opioid-focused strategies are no longer sufficient. Providers must anticipate **co-occurring substance use patterns**, screen for stimulant and benzodiazepine misuse, and integrate harm reduction practices that address the realities of today’s drug supply. Expanding access to **naloxone** remains essential, but overdose reversal can be more difficult in polysubstance cases, particularly when sedatives like xylazine are involved (SAMHSA, 2024).

Clinical best practice now emphasizes comprehensive, **whole-person approaches**: combining medications for opioid use disorder (MOUD) with behavioral health treatment, trauma-informed care, and coordinated management of co-occurring mental health or substance use conditions. Recognition of polysubstance use as the “new normal” is essential for effective care and prevention.

The following section materials come from the following source:

U.S. Department of Health and Human Services (2019, May). Pain Management Best Practices Inter-Agency Task Force Report: Updates, Gaps, Inconsistencies, and Recommendations. Retrieved from U. S. Department of Health and Human Services website: <https://www.hhs.gov/ash/advisory-committees/pain/reports/index.html>

Chapter 3. Pain Management Best Practices

Executive Summary

Patients with acute and chronic pain in the United States face a crisis because of significant challenges in obtaining adequate care, resulting in profound physical, emotional, and societal costs. According to the Centers for Disease Control and Prevention, 50 million adults in the United States have chronic daily pain, with 19.6 million adults experiencing high-impact chronic pain that interferes with daily life or work activities. The cost of pain to our nation is estimated at between \$560 billion and \$635 billion annually. At the same time, our nation is facing an opioid crisis that, over the past two decades, has resulted in an unprecedented wave of overdose deaths associated with prescription opioids, heroin, and synthetic opioids.

The Pain Management Best Practices Inter-Agency Task Force (Task Force) was convened by the U.S. Department of Health and Human Services in conjunction with the U.S. Department of Defense and the U.S. Department of Veterans Affairs with the Office of National Drug Control Policy to address acute and chronic pain in light of the ongoing opioid crisis. The Task Force mandate is to identify gaps, inconsistencies, and updates and to make recommendations for best practices for managing acute and chronic pain. The 29-member Task Force included federal agency representatives as well as nonfederal experts and representatives from a broad group of stakeholders. The Task Force considered relevant medical and scientific literature and information provided by government and nongovernment experts in pain management, addiction, and mental health as well as representatives from various disciplines. The Task Force also reviewed and considered patient testimonials and public meeting comments,

including approximately 6,000 comments from the public submitted during a 90-day public comment period and 3,000 comments from two public meetings.

The Task Force emphasizes the importance of individualized **patient-centered care in the diagnosis and treatment** of acute and chronic pain. This report is broad and deep and will have sections that are relevant to different groups of stakeholders regarding best practices. See the table of contents and the sections and subsections of this broad report to best identify that which is most useful for the various clinical disciplines, educators, researchers, administrators, legislators, and other key stakeholders.

The report emphasizes the development of an effective pain treatment plan after proper evaluation to establish a **diagnosis**, with **measurable outcomes that focus on improvements, including quality of life (QOL), improved functionality, and activities of daily living (ADLs)**. Achieving excellence in acute and chronic pain care depends on the following:

An emphasis on an **individualized, patient-centered** approach for diagnosis and treatment of pain is essential to establishing a **therapeutic alliance** between patient and clinician.

Acute pain can be caused by a variety of conditions, such as trauma, burn, musculoskeletal injury, and neural injury, as well as pain from surgery/procedures in the perioperative period. A **multimodal approach that includes medications, nerve blocks, physical therapy, and other modalities should be considered for acute pain conditions**.

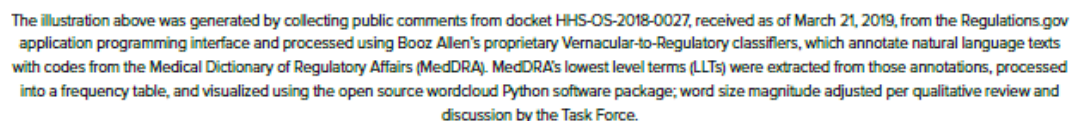
A **multidisciplinary** approach for chronic pain across various disciplines, using one or more treatment modalities, is encouraged when clinically indicated to improve outcomes. These include the following five broad treatment categories, which have been reviewed with an identification of gaps/inconsistencies and recommendations for best practices: **Medications: Various classes of medications**, including non-opioids and opioids, should be considered for use. The choice of medication should be based on the pain diagnosis, the mechanisms of pain, and related co-morbidities following a

thorough history, physical exam, other relevant diagnostic procedures and a **risk-benefit assessment that demonstrates that the benefits of a medication outweigh the risks**. The goal is to limit adverse outcomes while ensuring that patients have access to medication-based treatment that can enable a better QOL and function. Ensuring **safe medication storage** and **appropriate disposal of excess medications** is important to ensure best clinical outcomes and to protect the public health.

- Restorative Therapies, including those implemented by physical therapists and occupational therapists (e.g., physiotherapy, therapeutic exercise, and other movement modalities) are valuable components of multidisciplinary, multimodal acute and chronic pain care.
- Interventional Approaches, including image-guided and minimally invasive procedures, are available as diagnostic and therapeutic treatment modalities for acute, acute on chronic, and chronic pain when clinically indicated. A list of various types of procedures, including trigger point injections, radio-frequency ablation, cryo-neuroablation, neuromodulation, and other procedures are reviewed.
- Behavioral Approaches for psychological, cognitive, emotional, behavioral, and social aspects of pain can have a significant impact on treatment outcomes. Patients with pain and behavioral health comorbidities face challenges that can exacerbate painful conditions as well as function, QOL, and ADLs.
- Complementary and Integrative Health, including treatment modalities such as acupuncture, massage, movement therapies (e.g., yoga, tai chi), and spirituality, should be considered when clinically indicated.
- Effective multidisciplinary management of the potentially complex aspects of acute and chronic pain should be based on a biopsychosocial model of care.
- Health systems and clinicians must consider the pain management needs of the special populations that are confronted with unique challenges associated with acute and chronic pain, including the following: children/youth, older adults, women, pregnant women, individuals with chronic relapsing pain conditions such as sickle cell disease, racial and ethnic populations, active duty military and reserve service members and Veterans, and patients with cancer who require palliative care.

- Risk assessment is one of the four cross-cutting policy approaches necessary for best practices in providing individualized, patient-centered care. A thorough patient assessment and evaluation for treatment that includes a risk-benefit analysis are important considerations when developing patient-centered treatment. Risk assessment involves identifying risk factors from patient history; family history; current biopsychosocial factors; and screening and diagnostic tools, including prescription drug monitoring programs, laboratory data, and other measures. Risk stratification for a particular patient can aid in determining appropriate treatments for the best clinical outcomes for that patient. The final report and this section in particular emphasize safe opioid stewardship, with regular reevaluation of the patient.
- Stigma can be a barrier to treatment of painful conditions. Compassionate, empathetic care centered on a patient-clinician relationship is necessary to counter the suffering of patients with painful conditions and to address the various challenges associated with the stigma of living with pain. Stigma often presents a barrier to care and is often cited as a challenge for patients, families, caregivers, and providers.
- Improving education about pain conditions and their treatment for patients, families, caregivers, clinicians, and policymakers is vital to enhancing pain care. Patient education can be emphasized through various means, including clinician discussion, informational materials, and web resources. More effective education and training about acute and chronic pain should occur at all levels of clinician training, including undergraduate educational curricula, graduate professional training, and continuing professional education, with the use of proven innovations such as the Extension for Community Healthcare Outcomes (Project ECHO) model. Education for the public as well as for policymakers and legislators is emphasized to ensure that expert and cutting-edge understanding is part of policy that can affect clinical care and outcomes.
- Addressing barriers to access to care is essential in optimizing pain care. Recommendations include addressing the gap in our workforce for all disciplines involved in pain management. In addition, improved insurance coverage and payment for different pain management modalities is critical to improving access to effective clinical care and should include coverage and payment for care coordination, complex opioid management, and telemedicine. It is also important to note that in many parts of

- **Research and Development:** Continued medical and scientific research is critical to understanding the mechanisms underlying the transition from acute to chronic pain; to translating promising scientific advances into new and effective diagnostic, preventive and therapeutic approaches for patients; and to implementing these approaches effectively in health systems.



Definitions

Physical dependence is not the same as addiction and occurs because of physiological adaptations to chronic exposure to a drug. Someone who is physically dependent on medication will experience withdrawal symptoms when the use of the medicine is suddenly reduced or stopped or when an antagonist to the drug is administered. These symptoms can be minor or severe and can usually be managed medically or avoided by using a slow drug taper.^{2,3}

Tolerance is present when the same dose of a drug when given repeatedly produces a reduced biological response. Stated another way, it takes a higher dose of the drug to achieve the same level of response achieved initially.^{2,3}

Misuse of prescription drugs means taking a medication in a manner or dose other than prescribed; taking someone else's prescription, even if for a medical complaint such as pain; or taking a medication to feel euphoria (i.e., to get high). The term *nonmedical use* of prescription drugs also refers to these categories of misuse.^{2,3}

Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors. Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.⁴

Opioid use disorder (OUD) is defined in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) as a problematic pattern of opioid use leading to clinically significant impairment or distress. OUD was previously classified as Opioid Abuse or Opioid Dependence in DSM-IV. OUD has also been referred to as "opioid addiction."

Hyperalgesia is a condition where patients have a hypersensitivity to pain caused by pain medications. Healthcare providers may consider opioid induced hyperalgesia when

an opioid treatment effect dissipates and other explanations for the increase in pain are absent, particularly if found in the setting of increased pain severity coupled with increasing dosages of an analgesic.^{2,3}

Introduction

The experience of pain has been recognized as a national public health problem with profound physical, emotional, and societal costs.⁵ Although estimates vary depending on the methodology used to assess pain, it is estimated that chronic pain affects 50 million U.S. adults, and 19.6 million of those adults experience high-impact chronic pain that interferes with daily life or work activities.⁶ The cost of pain to our nation is estimated at between \$560 billion and \$635 billion annually.⁷ Pain management stakeholders have been working to improve care for those suffering from acute and chronic pain in an era challenged by the opioid crisis.⁸

An unprecedented rise in the number of deaths from overdose in the past two decades is associated with prescription opioids, heroin, and synthetic opioids.⁹ The practice of pain management and the opioid crisis have influenced one another as each has evolved in response to different influences and pressures. It is imperative to ensure that patients with painful conditions can work with their health care providers to develop integrative pain treatment plans that balance a focus on optimizing function, quality of life (QOL), and productivity while minimizing risks for opioid misuse and harm.

This report is the product of the Pain Management Best Practices Inter-Agency Task Force (Task Force) and is intended to guide the public at large, federal agencies, and private stakeholders. The field of pain management began to undergo significant changes in the 1990s, when pain experts recognized that inadequate assessment and treatment of pain had become a public health issue.⁵ Recommendations for improving the quality of pain care¹⁰ were followed by initiatives that recognized patients' reported pain scores as "The 5th Vital Sign."¹¹ Hospital administrators and regulators began to focus on pain scores, encouraging and incentivizing clinicians to aggressively treat pain

to lower pain scores. In addition, increasing administrative burdens (e.g., required quality measures, electronic health records [EHRs], data management, and government regulation requirements) led to less time for direct patient care. The administrative burden of using EHRs has contributed significantly to physicians' burnout, likely affecting their capacity to manage the complexity of pain care.^{12–14} As the mandate for improved pain management has increased, there was and is a need for better education and training of clinicians as well as more time and resources to respond to the unmet needs of patients with painful conditions.^{8,15} It is also important to note that in many parts of the country, patients have access only to their primary care provider (PCP). Support for education, time, and financial resources for PCPs is essential to managing patients with painful conditions.

Converging efforts to improve pain care led to an increased use of opioids in the late 1990s through the first decade of the 21st century.¹⁶ These initiatives included an overall effort for lowering pain scores, the more liberal use of opioids, and the aggressive marketing of new opioid formulations coupled with the continued limited coverage of non-opioid options. These trends resulted in a liberalization of opioid prescribing.^{3,11} Prescription opioids can and are used to treat acute and chronic pain and are often prescribed following surgery or injury and for a subset of patients with chronic pain from medical conditions such as cancer and inflammatory, neurological, and musculoskeletal conditions. Multidisciplinary and multimodal approaches to acute and chronic pain are often not supported with time and resources, leaving clinicians with few options to treat often challenging and complex underlying conditions that contribute to pain severity and impairment. As medical and policymaking organizations began to urge caution about the use of opioids for pain, the federal government has developed a multifaceted approach to the opioid epidemic, including the U.S. Department of Health and Human Services (HHS) 5-Point Strategy to Combat the Opioid Crisis.¹⁷ In addition, various efforts now address this public health problem across federal, state, and local governments as well as the community, private, and academic sectors, including the "Initiative to Stop Opioid Abuse and Reduce Drug Supply and Demand," issued in 2018 by President Donald J. Trump. A public health emergency was declared in October

2017 and subsequently renewed as a result of the continued consequences of the opioid crisis.

Significant public awareness through education and guidelines from regulatory and government agencies and other stakeholders to address the opioid crisis have in part resulted in reduced opioid prescriptions. Regulatory oversight has also led to fears of prescribing among clinicians, with some refusing to prescribe opioids even to established patients who report relief and demonstrate improved function on a stable opioid regimen.¹⁸ The Centers for Disease Control and Prevention published a pivotal article in the New England Journal of Medicine (NEJM) on April 24, 2019, specifically reiterating that the 2016 Guideline for Prescribing Opioids for Chronic Pain (CDC Guideline) has been, in some instances, misinterpreted or misapplied.¹ This increased vigilance of prescription opioids and the tightening of their availability have in some situations led to unintended consequences, such as patient abandonment and forced tapering. Some established patients with pain may transition to using illicit drugs for pain control, including illicit fentanyl and heroin — a separate group of patients distinguishable from those with substance use disorders (SUDs) (as evidenced by Task Force public comments). The CDC has recently noted that the opioid crisis is quickly moving to a fentanyl crisis.¹⁹ This has coincided with an increase in the demand for illicit synthetic opioids as well as other substances,^{20,21} including a four-fold increase in the rate of death from heroin since 2010.²² Nationwide, nearly half of all opioid overdose deaths in 2017 involved illicitly manufactured fentanyl. Fentanyl is an opioid 50 times more potent than morphine. Illicit fentanyl (manufactured abroad and distinct from commercial medical fentanyl approved for pain and anesthesia in the United States) is a potent synthetic opioid. Illicit fentanyl is sometimes mixed with other drugs (prescription opioids and illicit opioids, such as heroin, and other illegal substances, including cocaine) that further increase the risk of overdose and death.

A significant number of public comments submitted to the Task Force shared growing concerns regarding suicide due to pain as well as a lack of access to treatment.

According to a recent CDC report using data from the National Violent Death Reporting System, the percentage of people who died by suicide and had evidence of chronic pain increased from 7.4% in 2003 to 10.2% in 2014.²³ Numbers from this data set beyond

2014 are not yet available. These findings are made more concerning when one considers the rising trend of health care professionals opting out of treating pain, thus exacerbating an existing shortage of pain management specialists,⁵ leaving a vulnerable population without adequate access to care.

Comprehensive pain management can be a challenge for various reasons. In the current environment, patients with chronic pain — particularly those being treated with opioids — can be stigmatized, a tendency exacerbated when their pain condition is complicated by mental health co-morbidities such as anxiety and depression or by SUDs. Because opioids can produce opioid use disorder (OUD) in at-risk populations, risk assessment and periodic reevaluation and monitoring are required for all patients in these populations and should be a part of the complex care management they need, particularly when there is an intersection of chronic pain, opioids, mental health, and addiction. There is strong evidence that because of awareness of and education about these issues, prescription opioid misuse has been decreasing, from 12.8 million individuals in 2015 to 11.4 million individuals in 2017.²⁴

HHS is advancing a comprehensive approach that addresses improved pain management in both the acute and chronic pain setting. This effort is part of the 5-Point Strategy to Combat the Opioid Crisis.¹⁷ This work includes execution of mandates set forth by the Comprehensive Addiction and Recovery Act (CARA), which establishes “an interagency task force, convened by HHS, in conjunction with the Department of Defense (DoD), the Department of Veterans Affairs (VA), and the Executive Office of the President’s Office of National Drug Control Policy.”²⁵ The CARA legislation instructs the Task Force to “determine whether there are gaps in or inconsistencies between best practices for pain management” and “propose updates to best practices and recommendations on addressing gaps or inconsistencies.”²⁵

The Task Force recognizes that comprehensive pain management often requires the work of various health care professionals, including physicians of various disciplines, dentists, nurses, nurse practitioners (NPs), physician assistants (PAs), pharmacists, physical therapists, occupational therapists, behavioral health specialists, psychologists,

social workers, and integrative health practitioners. The complexity of some pain conditions requires multidisciplinary coordination among health care professionals; in addition to the direct consequences of acute and chronic pain, the experience of pain can exacerbate other health issues, including delayed recovery from surgery or worsen behavioral and mental health disorders. Achieving excellence in patient-centered care depends on a strong patient-clinician relationship defined by mutual trust and respect, empathy, and compassion, resulting in a strong therapeutic alliance.²⁶ As required by congressional legislation, HHS has convened the Task Force, which consists of 29 members who have expertise in pain management, patient advocacy, addiction, mental health, and minority health as well as other organizational representatives from state medical boards and Veteran service organizations, among others. The Task Force also includes representatives from federal agencies, including HHS, VA, DoD, and the Office of National Drug Control Policy.

In 2018, the Task Force convened two public meetings that included extensive public comments and critical patient testimonials from various patient groups, including various special population presentations. The Task Force reviewed and considered public comments, including approximately 6,000 comments from the public submitted during a 90-day public comment period and 3,000 comments from two public meetings.

Presentations to the Task Force included the Indian Health Services (IHS); the Defense Health Agency; VA officials; HHS officials from the National Institute on Drug Abuse, the National Institute on Neurological Disorders and Stroke, and the U.S. Food and Drug Administration (FDA); state health officials; private stakeholder organizations; and experts. The Task Force reviewed extensive public comments, patient testimonials, and existing best practices and considered relevant medical and scientific literature. Task Force discussion and analysis resulted in the identification of gaps and inconsistencies, updates, and recommendations for acute and chronic pain management best practices described in this report, consistent with the CARA legislation. In the context of this report, the term “gap” includes gaps across existing best practices, inconsistencies among existing best practices, the identification of updates needed to best practices, or a need to reemphasize vital best practices. Gaps and recommendations in the report

span five major treatment modalities that include medication, restorative therapies, interventional procedures, behavioral health approaches, and complementary and integrative health approaches. This report provides gaps and recommendations for special populations confronting unique challenges in pain management as well as gaps and recommendations for critical topics that are broadly relevant across treatment modalities, including stigma, risk assessment, education, and access to care. The report reviews the CDC Guideline as mandated by the statute.

In pain management, a critical part of providing comprehensive care is a thorough initial evaluation, including assessment of both the medical and the probable biopsychosocial factors causing or contributing to a pain condition. A second critical step is to develop a treatment plan to address the causes of pain and to manage pain that persists despite treatment. Quality pain diagnosis and management can alter opioid prescribing both by offering alternatives to opioids and by clearly stating when they may be appropriate.⁸ Several recent clinical practice guidelines (CPGs) for best practices for chronic pain management agree on specific recommendations for mitigating opioid-related risk through risk assessment, including screening for risks (e.g., depression, active or prior history of SUDs, family history of SUD, childhood trauma) prior to initiating opioids; medication dosing thresholds; consideration of drug-drug interactions, with specific medications and drug-disease interactions; risk assessment and mitigation (e.g., patient-provider treatment agreements); drug screening/testing; prescription drug monitoring programs; and access to nonpharmacologic treatments. Clinical practice guidelines for best practices that only promote and prioritize minimizing opioid administration run the risk of undertreating pain, especially when the cause of the pain is uncertain or cannot be reduced through non-opioid approaches.

To continue improving quality of pain care in the current environment of opioid-related risks, experts have noted several key challenges associated with clinical best practices (CBPs). First, there is the need to increase the use of CPGs, as indicated in specific patient groups delineated by their underlying diagnosis or cause of pain (e.g., arthritis, postoperative, neuropathic), comorbidities, psychosocial characteristics (e.g., social

support, stress), demographics, and settings (e.g., hospital, perioperative, primary care, emergency department [ED]). Second, access to effective pain management treatments must be improved through adoption of clinical best practices in medical and dental practice and clinical health systems.²⁸ Third, clinical best practices for pain management should be better incorporated into the routine training of clinicians,²⁹ with special attention to residency training to meet the needs of patients treated in each specialty.^{8,15} Finally, quality care must be adequately reimbursed.

Pain management experts have also identified specific research gaps that are impeding the improvement of pain management best practices, including synthesizing and tailoring recommendations across guidelines, diagnoses, and populations. In addition, gaps and inconsistencies exist within and between pain management and opioid prescribing guidelines.^{30–32} This finding is also the result of demographic and other variances, because CBPs are developed in different regions of the country. A recent review of clinical opioid prescribing guidelines by Barth et al.³³ notes several needs — including the development of postoperative pain management guidelines for different surgical procedures, with the understanding of patient variability in physiology, drug metabolism, and underlying disease processes. This research further emphasizes the need for an individualized, patient-centered approach focused on achieving improved function, activities of daily living (ADLs), and QOL as well as pain control. In light of these gaps, pain management providers should consider potential limitations to evidence-based clinical recommendations.³⁴

A systematic review of CPGs for neuropathic pain³⁵ identified shortcomings across four evaluation domains: (1) stakeholder involvement (i.e., the extent to which the guideline was developed by the appropriate stakeholders and represents the views of its intended users); (2) the rigor of development (i.e., the process used to gather and synthesize the evidence and the methods used to formulate the recommendations); (3) applicability (i.e., likely barriers and facilitators to implementation of the guideline, strategies to improve its uptake, and resource implications of applying it); and (4) editorial independence (i.e., bias in the formulation of the recommendations), not to mention the

knowledge and skill set of the clinician. Identified inconsistencies across guidelines for some painful conditions, such as fibromyalgia, have demonstrated a need for consensus in guideline development.³⁶ A review of state-level guidelines for opioid prescriptions found that a minority of states had guidelines specific to EDs.³⁷ Pain guidelines from the World Health Organization (WHO) are facing a lack of adoption, potentially because they lack incorporation of contemporary pain management practices.³⁸



EMILY'S STORY PATIENT TESTIMONIAL

For the past eight years, I have lived with debilitating chronic pain as the result of Klippel-Feil syndrome, a rare spinal defect. Over the years, I have tried every possible treatment. I've had neurosurgery. I get regular injections, massages, and acupuncture. I do physical therapy and yoga daily. I wear braces. I buy expensive pillows. I meditate. I eat well. I do all the things you're supposed to do. But I also need medications. For nearly a year after the pain began, I refused to take anything. I certainly had no interest in taking an opioid. But it was only after eight months of agonizing trial and error with other drugs that we tried Tramadol, as a last resort, and found that it worked. And yet despite taking one of the safest opioids available, and taking it responsibly for a legitimate problem, I faced restrictions that made me feel more like a criminal than a patient. Once, a doctor refused to refill my Tramadol prescription, even while acknowledging that I showed no signs of abuse. I ended up in the ER where they told me they could only treat withdrawal. It was the most horrific and dehumanizing experience of my life. Another example was the time I wanted to consult a second pain specialist about injections. Although I wasn't asking for medications, I was berated just for asking for a second opinion and left the appointment in tears. Most recently, my health insurance suddenly refused to cover Tramadol. After much back and forth, they wanted proof I had signed an opioid contract. I had in fact signed one, but the doctor had lost his copy. It took over three weeks to resolve. These stories may sound like minor inconveniences, but keep in mind what it would be like to deal with this on top of debilitating pain. I have sometimes wished I had cancer instead of a spine defect,

knowing I would be treated with more respect and compassion. And let's not overlook that I am a middle-class Caucasian female with a strong support system and a background in health care. I cannot imagine how these restrictions are affecting people of color, or the elderly, or those from a lower socioeconomic status.

A. APPROACHES TO PAIN MANAGEMENT

A multimodal approach to pain management consists of using treatments from one or more clinical disciplines incorporated into an overall treatment plan. This plan allows for different approaches to address the pain condition (acute and/or chronic), often enabling a synergistic approach that addresses the different aspects of the pain condition, including functionality. Multidisciplinary approaches address different aspects of chronic pain conditions, including biopsychosocial effects of the medical condition on the patient.^{39–41} The efficacy of such a coordinated, integrated approach has been documented to reduce pain severity, improve mood and overall QOL, and increase function.^{40,42–47}

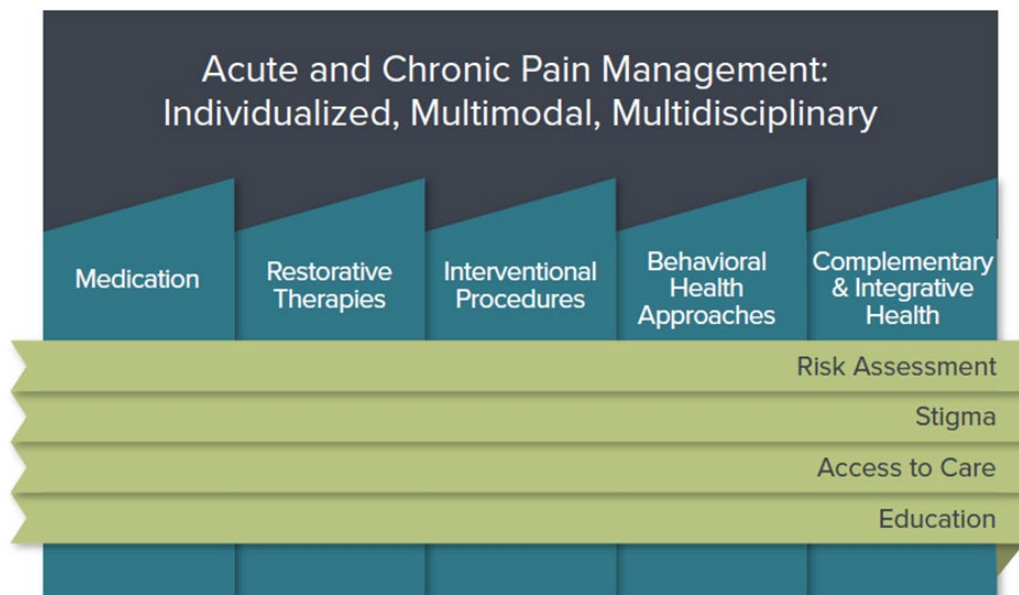


Figure 4: Acute and Chronic Pain Management Consists of Five Treatment Approaches Informed by Four Critical Topics

Recent clinical practice guidelines developed by the VA and DoD adopt the biopsychosocial model of pain.³² In this endeavor, they emphasize a collaborative, stepped care model.^{48,49} The biopsychosocial approach is applied clinically across pain experiences, including chronic pain,⁵⁰ and specifically to musculoskeletal pain,⁵¹ low-back pain,^{52,53} and HIV-related pain.⁵⁴ The development of a treatment plan should be preceded by a history and physical examination that aids in proper diagnosis. When clinically indicated, clinicians should consider an integrative and collaborative approach to care. Specialty interdisciplinary pain medicine team consultation, collaborative care, and (when indicated) mental health and addiction services should be readily available in the course of treatment of pain to help ensure the best patient outcomes. Medical organizations and advocacy groups are encouraged to be involved in the development of clinical practice guidelines for the treatment of particular pain conditions. When clinically indicated, these CPGs can be used within the context of the multimodal and multidisciplinary approach to pain care.

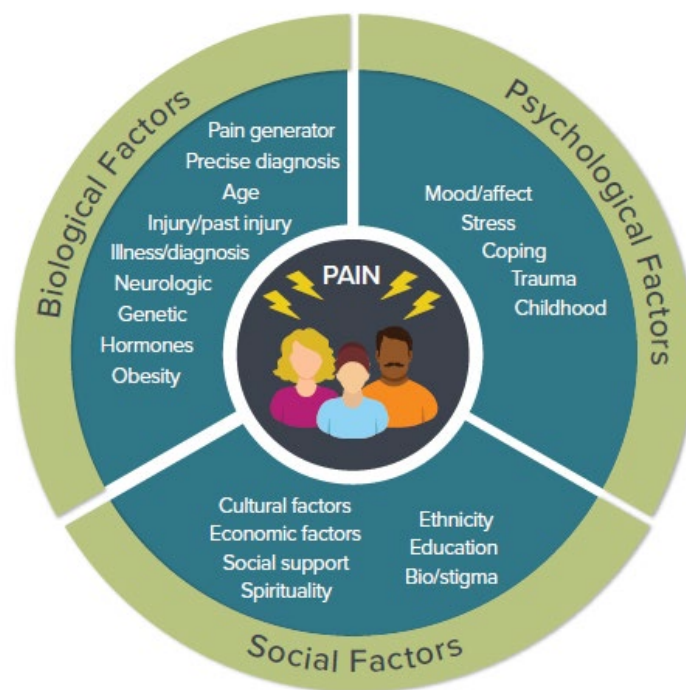


Figure 5: The Biopsychosocial Model of Pain Management

GAPS AND RECOMMENDATIONS

GAP 1: Current inconsistencies and fragmentation of pain care limit best practices and patient outcomes. A coherent policy for pain management for all relevant stakeholders is needed.

RECOMMENDATION 1A: Encourage coordinated and collaborative care that allows for best practices and improved patient outcomes, when clinically indicated.

RECOMMENDATION 1B: Encourage the use of guidelines that are informed by evidence and created by specialty organizations and associations that are experts in the treatment of certain pain conditions that result from a variety of medical conditions or in different special populations.

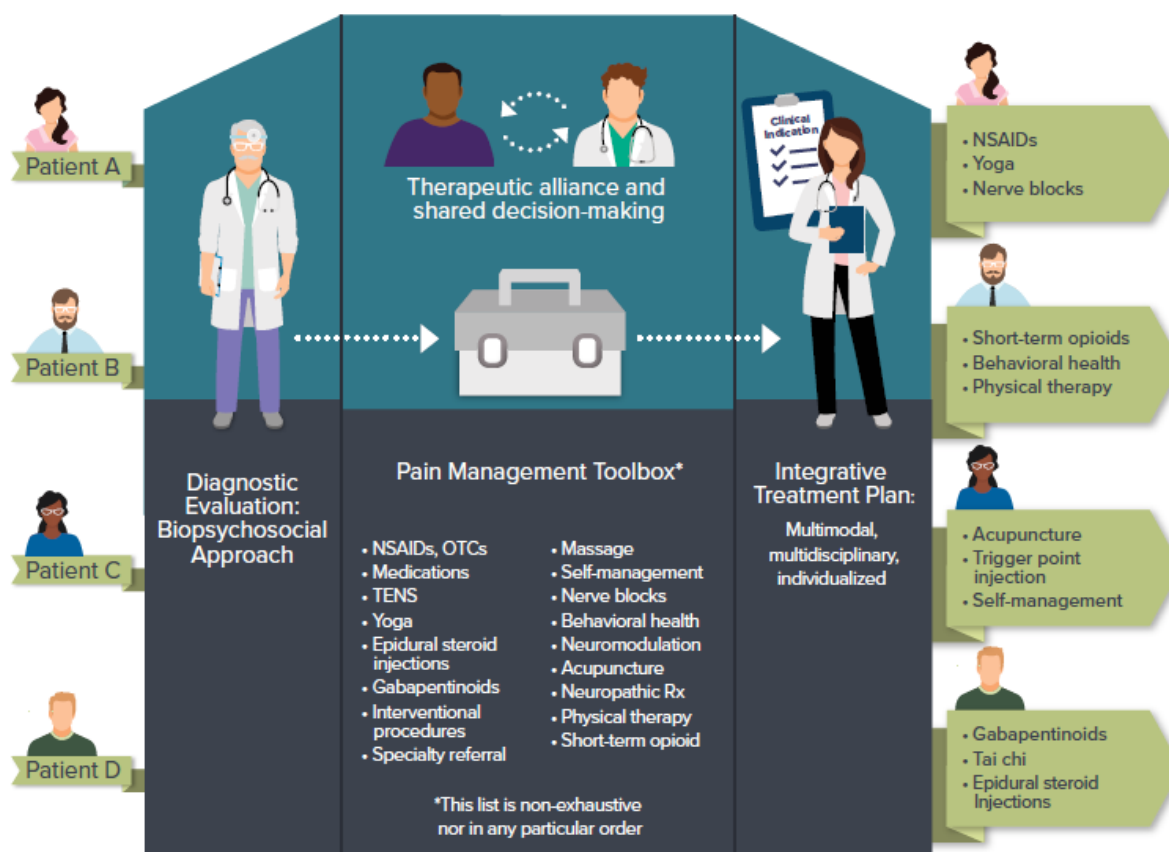


Figure 6: Individualized Patient Care Consists of Diagnostic Evaluation That Results in an Integrative Treatment Plan That Includes All Necessary Treatment Options

Acute and Chronic Pain

Acute pain is a ubiquitous human experience⁵⁵ — a physiologic response to noxious stimuli that is sudden in onset and time limited.⁵⁶ Acute pain can occur after a burn or trauma or following surgery in the perioperative period. Acute pain and chronic pain are often interlinked, with most cases of chronic pain beginning as acute pain.⁵⁷ Acute pain flares may recur periodically in chronic medical problems, including arthritis,⁵⁸ neuropathies,⁵⁹ spinal conditions, low-back pain,⁶⁰ sickle cell disease (SCD),⁶¹ migraine,⁶² multiple sclerosis (MS),⁶³ trigeminal pain or neuralgia,⁶⁴ and complex regional pain syndrome (CRPS).⁶⁵ As with acute pain flares in these and other conditions, it is important to perform a thorough evaluation that leads to a presumed diagnosis or differential diagnosis. The goal is to facilitate diagnostic accuracy and effective therapeutic plans, including a continuum of care plans into the non-acute care setting.⁶⁶ It is vital to consider a risk-benefit analysis to provide the best possible patient-centered outcome while mitigating unnecessary opioid exposure (see Section 3.1: Risk Assessment). To avoid the side effects associated with prescription opioids (e.g., nausea, vomiting, constipation, sedation, OUD), it is important to exploit the benefits of multimodal, non-opioid approaches in acute pain management in conjunction with possible opioid therapy.⁶⁷ Reevaluation of patients is critical in this setting because the use of medications to control acute pain should be for the shortest time necessary while also ensuring that the patient is able to mobilize and restore function. Opioids are effective in treating acute pain, but patients can be at risk of becoming new chronic opioid users in the postsurgical setting. As one large study illustrated, among a population of opioid-naïve patients who were given a course of opioids to treat pain following surgery, about 6% became new chronic users. Patients who were at higher risk for becoming chronic opioid users were those with a history of tobacco use, alcohol and substance abuse disorders, anxiety, depression, other pain disorders, and comorbid conditions.⁶⁸ This finding further underscores the value and importance of initial clinician-patient time together as well as appropriate follow-up to better assess risk and provide appropriate treatment for these complex pain conditions.

GAPS AND RECOMMENDATIONS

GAP 1: Multimodal, non-opioid therapies are underutilized in the perioperative, inflammatory, musculoskeletal, and neuropathic injury settings.

RECOMMENDATION 1A: Use procedure-specific, multimodal regimens and therapies when indicated in the perioperative period, including various non-opioid medications, ultrasound-guided nerve blocks, analgesia techniques (e.g., lidocaine, ketamine infusions), and psychological and integrative therapies to mitigate opioid exposure.

RECOMMENDATION 1B: Use multidisciplinary and multimodal approaches for perioperative pain control in selected patients at higher risk for opioid use disorder (e.g., joint camps, Enhanced Recovery After Surgery [ERAS], Perioperative Surgical Home [PSH]).^{69,70} Key components for optimal pre-habilitation may include preoperative physical therapy (PT), nutrition, and psychology screening and monitoring; preoperative and postoperative consultation and planning for managing pain of moderate to severe complexity; preventive analgesia with preemptive analgesic non-opioid medications; and regional anesthesia techniques, such as continuous catheter-based local anesthetic infusion.

RECOMMENDATION 1C: Encourage Centers for Medicare & Medicaid Services (CMS) and private payers to develop appropriate reimbursement policies to allow for a multimodal approach to acute pain in the perioperative setting and the peri-injury setting, including preoperative consultation to determine a multimodal plan for the perioperative setting.

RECOMMENDATION 1D: Use treatment regimens in the peri-injury setting that include various non-opioid and nonpharmacologic therapies to mitigate opioid exposure, when clinically indicated.

GAP 2: Guidelines for the use of multimodal clinical management of acute pain are needed.

RECOMMENDATION 2A: Encourage public and private stakeholders to develop acute pain management guidelines for common surgical procedures and trauma

management, carefully considering how these guidelines can serve both to improve clinical outcomes and to avoid unintended negative consequences.

RECOMMENDATION 2B: Emphasize the following in guidelines, which provide an initial pathway to facilitate clinical decision making:

- Individualized treatment as the primary goal of acute pain management, accounting for patient variability with regard to factors such as comorbidities, severity of conditions, psychosocial characteristics, surgical variability, geographic considerations, and community/hospital resources.
- Improved pain control, faster recovery, improved rehabilitation with earlier mobilization, less risk for blood clots and pulmonary embolus, and mitigation of excess opioid exposure.

To reflect multidisciplinary approaches and the biopsychosocial model of acute and chronic pain management, the following sections are organized by five major approaches to pain management: medication, restorative therapies, interventional procedures, behavioral health approaches, and complementary and integrative health.

Perioperative Management of Chronic Pain Patients

Perioperative pain management in patients with chronic pain presents unique challenges,^{71,72} particularly for patients with opioid tolerance or those vulnerable to opioid-associated risks. It can be more challenging to manage patients on long-term opioid therapy in the perioperative period compared with patients who are opioid naive. Considerations for managing these patients include the use of multimodal approaches as well as preoperative consultation and planning. In addition, behavioral interventions show promise for use in the pre- and perioperative periods for the management of postsurgical pain.^{73–76} Other experts have suggested use of perioperative surgical homes for this patient population.⁷⁷ Patients with chronic pain whose pain is managed by a pain management clinician should have this clinician consulted and involved in the planning of their pain control during and after surgery.

GAPS AND RECOMMENDATIONS

GAP 1: Patients with chronic pain who undergo a surgical procedure often have complex issues that go unaddressed and may lead to suboptimal care.

RECOMMENDATION 1A: The perioperative team should be consulted to form a treatment plan that addresses the various aspects that would be necessary for best outcomes in this patient population.



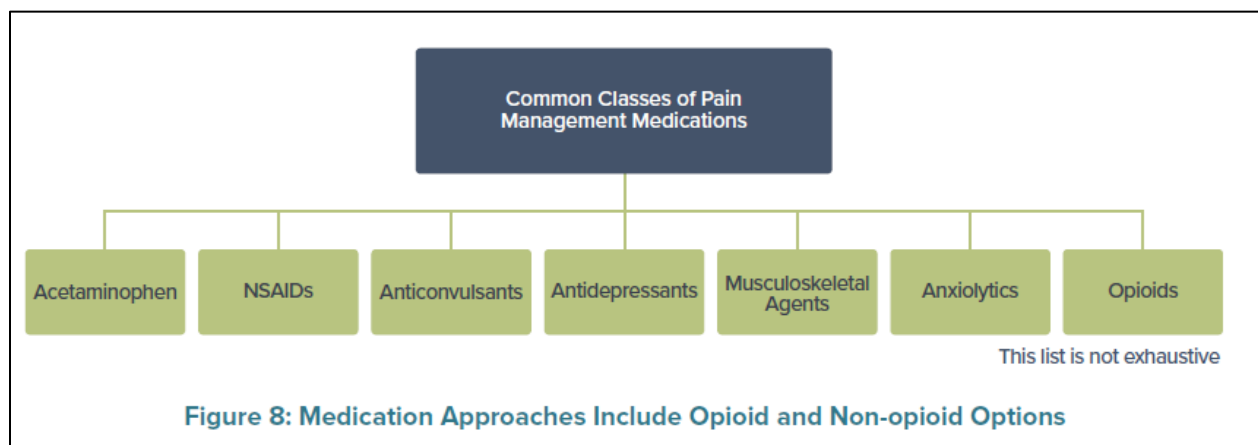
Figure 7: Medication Is One of Five Treatment Approaches to Pain Management

B. MEDICATION

Effective pain management, particularly for chronic pain, is best achieved through a patient-centered, multidisciplinary approach that may include harmacotherapy.^{49,52,78} In general, two broad categories of medications are used for pain management: non-opioids and opioid classes of medications.^{79,80}

In response to the public health crisis resulting from the current opioid epidemic, there is a surge of interest in non-opioid pharmacotherapies for chronic pain.^{81–83} Non-opioid medications that are commonly used include acetaminophen, nonsteroidal anti-

inflammatory drugs (NSAIDs), antidepressants (e.g., serotonin-norepinephrine reuptake inhibitors [SNRIs], tricyclic antidepressants [TCAs]), anticonvulsants, musculoskeletal agents, biologics, topical analgesics and anxiolytics.^{83–86} Non-opioid medications can mitigate and minimize opioid exposure. Each medication has its own risks and benefits as well as mechanism of action. Different medications can complement one another, and their effects can be synergistic when used in combination. A risk-benefit analysis is always recommended based on the individual patient’s medical, clinical, and biopsychosocial circumstances (see Section 3.1: Risk Assessment).



The following paragraphs briefly describe non-opioid medications. This list is not inclusive or exhaustive; rather, it provides examples of common non-opioid medications. As a general rule, caution should be taken, particularly for over-the-counter medicine, to ensure that patients are aware of the individual side effects and risks of these medications. Over-the-counter analgesic medications can be present in or components of common cold and cough medicine; clinicians must ensure that patients are aware of and discuss all their medications with their doctor or pharmacist.

Acetaminophen can be effective for mild to moderate pain. Risks of acetaminophen include dose-dependent liver toxicity, especially when the drug is taken at high doses, with alcohol, or by those with liver disease.⁸⁷ This risk further illustrates why patients should be aware of the presence of acetaminophen in both over-the-counter and prescribed combination medications.

NSAIDs such as aspirin, ibuprofen, and naproxen can provide significant pain relief for inflammation, such as from arthritis, bone fractures or tumors, muscle pains, headache, and acute pain caused by injury or surgery. Nonselective NSAIDs (those that inhibit the activity of both the cyclooxygenase [COX]-1 and COX-2 enzymes) can be associated with gastritis, gastric ulcers, and gastrointestinal (GI) bleeding. Conversely, COX-2 inhibitors have fewer GI adverse effects. The use of NSAIDs may be associated with renal insufficiency, hypertension, and cardiac-related events.

Anticonvulsants are medications originally developed to treat seizures, but they are also commonly used to treat different pain syndromes, including postherpetic neuralgia, peripheral neuropathy, and migraine.^{88,89} They are often used as part of a multimodal approach to the treatment of perioperative pain. Some of these agents can effectively treat the neuropathic components of pain syndromes. Anticonvulsants, which include gabapentinoids such as gabapentin and pregabalin, may cause significant sedation and have recently been associated with a possible risk of misuse.⁹⁰

Antidepressants are commonly used in various chronic pain conditions.^{88,91} TCAs are effective in a variety of chronic pain conditions, including neuropathic pain. As with other medications, they have risks and adverse effects, including dry mouth, dizziness, sedation, memory impairment, orthostatic hypotension, urinary retention, and cardiac conduction abnormalities. Trials with different TCAs (e.g., desipramine, nortriptyline, amitriptyline) should be initiated at a low dose and gradually titrated to optimal effect. SNRIs, such as venlafaxine and duloxetine, are effective for a variety of chronic pain conditions, including musculoskeletal pain, fibromyalgia, and neuropathic pain conditions, but have markedly fewer adverse effects (e.g., lower risk of drowsiness, memory impairment, and cardiac conduction abnormalities) than TCAs. There have been some reports of withdrawal reactions when these medications are suddenly stopped.⁹² Although selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, sertraline, citalopram, and paroxetine, are effective antidepressants; they have less analgesic effect compared with other antidepressant classes. Overall, the analgesic actions of antidepressants occur even in patients who are not clinically depressed, and

their analgesic effect typically occurs sooner and at lower doses than those required for the treatment of depression.

Musculoskeletal agents commonly used for pain treatment include baclofen, tizanidine, and cyclobenzaprine. Carisoprodol is metabolized to meprobamate, which is both sedating and possibly addictive, so the use of carisoprodol is not recommended, particularly because alternatives are available.⁹³

Antianxiety medications are often prescribed to treat the anxiety that accompanies acute pain as well as anxiety resulting from fluctuations in chronic pain. They may also be prescribed for co-morbid anxiety disorders such as generalized anxiety disorder, panic disorder, post-traumatic stress disorder (PTSD), and agoraphobia, which as a group have a prevalence estimated in the range of 30% in patients with chronic pain.^{94,95} SSRIs and SNRIs may also help manage the anxiety associated with co-morbid depression. It is important to recognize and treat anxiety effectively because it can worsen the severity of pain as well as interfere with a patient's coping skills for managing his or her pain. Several classes of medications can be used to treat anxiety. Benzodiazepines do not have independent analgesic effects but may have indirect pain-relieving effects.⁹⁶ Thus, they can be helpful when used briefly for the anxiety associated with pain in an acute medical setting (e.g., injury, hospitalization), but benzodiazepines should generally be avoided for regular or long-term use for three reasons. First, benzodiazepines increase the risk of substance use disorder. Second, co-prescription of benzodiazepines and opioids is associated with enhanced risks of overdose, respiratory depression, and death.^{97–99} Third, the cognitive effects of benzodiazepines, when used chronically, may interfere with a patient's development of new coping skills needed to manage a chronic pain condition.¹⁰⁰ For chronic anxiety disorders, usually a combination of medications indicated for that specific condition plus evidence-based psychotherapy, such as cognitive-behavioral therapy (CBT) (see Section 2.5: Behavioral Health Approaches), works best.^{101,102} SSRIs and SNRIs are the medications most frequently used for the generalized anxiety that often accompanies chronic pain conditions. Buspirone is another choice. SSRIs, because of

their lower side effect profile, are generally the first choice for panic disorder, but TCAs can also be used. Venlafaxine ER and prazosin are used for PTSD. For more severe cases of co-morbid anxiety disorders, psychiatric consultation for medication regimens is advised. (see Section 2.5: Behavioral Health Approaches and Section 4: Review of the CDC Guideline, Gap 6, Recommendations 6a and 6b). It should be noted that gabapentinoids have been useful in treating anxiety in patients with pain.¹⁰³

The following paragraphs briefly describe opioid medications.

Opioids are a controlled substance group of broad-spectrum analgesics that provide pain relief for a variety of conditions. Administration of opioid medication can include short- or long-acting formulations¹⁰⁴ and different delivery modalities, such as oral, buccal, sublingual, spray, intravenous, intramuscular, intrathecal, suppository, transdermal patches,¹⁰⁵ and lozenge formulation. Opioids bind to opioid receptors in the brain, spinal cord, and other sites, activating analgesic and reward pathways.¹⁰⁶ It is important to point out that opioid medications vary in the ratio of their analgesic potency and their potential for respiratory depression, the major cause of opioid overdose death.¹⁰⁷ For example, synthetic fentanyl and fentanyl analogues (e.g., carfentanil) are particularly potent for respiratory depression. Illicit fentanyl-related overdoses are now a leading cause of deaths from overdose in the United States, often because of its use in combination with alcohol or illicitly obtained heroin, cocaine, diverted prescription opioids, and other drugs such as benzodiazepines. Common prescription opioid medications that can be considered for management of acute and chronic pain include hydromorphone, hydrocodone, codeine, oxycodone, methadone, and morphine.^{108–111} Although effective for moderate to severe acute pain, the effectiveness of opioids beyond three months requires more evidence (see Section 4: Review of the CDC Guideline).¹¹² A recent study demonstrated that treatment with opioids alone was not superior to treatment with trials of various combinations of non-opioid medications for improving pain-related function over 12 months; the authors concluded that the results do not support initiation of opioid therapy alone for moderate to severe chronic back pain or hip or knee osteoarthritis pain.¹¹³ There are challenges to completing long-term studies of any therapy for moderate to severe pain, particularly patient drop-out from intolerable pain.¹¹⁴ Opioid medications can be associated with

significant side effects, including constipation, sedation, nausea, vomiting, irritability, pruritis, and respiratory depression.^{115–117} Opioid medications can be associated with OUD¹¹⁸ and can be diverted.¹¹⁹ Buprenorphine, an opioid medication that the FDA has approved for clinical use, is a partial agonist at the mu opioid receptor and therefore has a reduced potential for respiratory depression; it is thus safer than full agonists such as morphine, hydrocodone, and oxycodone.^{120,121} Buprenorphine also acts as an antagonist at the kappa receptor, an effect shown in experimental studies to reduce anxiety, depression, and the unpleasantness of opioid withdrawal. Buprenorphine is widely used and encouraged for treating patients with OUD and is approved for the treatment of pain. In some states, there is a significant challenge, however, for prescribing clinicians to get authorization for using buprenorphine for chronic pain management (see Section 2.2: Medication, Gap 4 and Recommendations).

Tapentadol is structurally similar to tramadol, and both have a dual mode of action as an agonist at the mu opioid receptor and as a serotonin and norepinephrine reuptake inhibitor. Tapentadol is at least equivalent to oxycodone in terms of analgesia, with better GI tolerability.¹²²

As outlined in recent guidelines, including the VA/DoD Clinical Practice Guidelines for Opioid Therapy for Chronic Pain, the CDC Guideline, and the American Society of Interventional Pain Physicians guidelines, risk assessment, close follow-up, and pain reevaluation are important aspects of the treatment plan prior to and throughout the duration of opioid therapy for pain management.^{32,123,124} Initiation of opioid therapy, when the patient and the clinician deem the benefits to outweigh the risks, should be at a low dose and titrated upward to find the lowest dose required to optimally control the pain or improve function and QOL. Opioid treatment should be maintained for a period no longer than necessary for adequate pain control.^{32,49,123} Similarly, assessing for tolerance and consideration of adjunctive therapies, opioid rotation, tapering, and discontinuation should be considered.^{32,123,125} Safe opioid stewardship involves a proper history and examination, periodic reevaluation, and risk assessment, with a

focus on measurable outcomes, including function, QOL and ADLs.^{32,49,123} Accurate dose adjustment is critical because patients vary widely in the dose required for analgesic efficacy.^{126,127}

The idea of a ceiling dose of opioids has been recommended, but establishing such a ceiling is difficult, and the precise level for such a ceiling has not been established.¹²⁸ The risk of overdose increases with the dose, but the therapeutic window varies considerably from patient to patient. For example, the CDC Guideline identified a dose limit of 90 morphine milligram equivalents (MMEs) per day. A more recent study evaluated the risk of death related to opioid dose in 2.2 million North Carolinians and found that the overall death rate was 0.022% per year.¹²⁹ The researchers noted that:

“Dose-dependent opioid overdose risk among patients increased gradually and did not show evidence of a distinct risk threshold. Much of the risk at higher doses appears to be associated with co-prescribed benzodiazepines. It is critical to account for overlapping prescriptions and justifies taking a person-time approach to MME calculation with intent-to-treat principles.”

DEA has classified medications according to categories, or “schedules,” based on the perceived risk of addiction. These scheduled medications require prescribers to register with DEA. Opioids are mainly category CIII (relatively lower risk) or CII (higher risk). CIII medications include acetaminophen with codeine and buprenorphine, while CII medications include hydrocodone (recently changed from a CIII to a CII classification), oxycodone, morphine, fentanyl, and methadone. CIV drugs are defined as drugs with a low potential for abuse and low risk of dependence, such as Tramadol. CI medications are those that are considered not to have medicinal value, including heroin, methamphetamine, and cannabis. (Although marijuana/cannabis is legal for medical use in several states, it is illegal at the federal level.)



JONATHAN'S STORY

PATIENT TESTIMONIAL

I am a soon to be 50-year-old man that has sickle-cell anemia. And it runs in my family. I come from a family of 12 siblings. And out of the 12, five of us have sickle-cell anemia. I'm not an advocate by any way for opioids. But they are a part of our toolbox that helps us maintain a quality of life. We get labeled as drug seekers. They don't think of us as fathers, husbands, sons, grandfathers. They just look at us as another number or as those patients coming in seeking drugs. In my life, opioids help me have a quality of life. I know how now not to get stressed out. I have all sorts of other things that I try before just taking medication. OxyContin is one of the medications that I take. And, yes, you have to take it every 12 hours daily. So, yes, that's part of my regimen. But I also do other things-- vitamins, try to eat healthy, try not to be stressed out-- just all sorts of things to help myself. I am a grandfather. I have two children. I have three grandkids. Please look at each case individually because everybody can't be lumped into one barrel together. I've been taking this medication since '95 and I take a really high amount. But I only take enough to be able to function. I'm not trying to get loopy and be out of my mind. That was never my intention. I take it because of the pain. But the main thing is, we need opioid medications to be an option in the toolbox.

Opioids: Additional Considerations

The following paragraphs briefly describe additional considerations relevant to medications used for pain management.

Medicines play an important role in treating certain conditions and diseases, but they must be taken with care and stored securely where they cannot be misused by a third party or accidentally ingested by children or pets.¹³⁰ Unused portions of these

medicines must be disposed of properly to avoid harm. Patients and caregivers can remove expired, unwanted, or unused medicine from their home as soon as they are no longer needed to help reduce the chance that others accidentally or intentionally misuse the unneeded medicine and to help reduce drugs from entering the environment. There are various take-back options such as DEA National Takeback Days, pharmacy takeback (in some locations), drop boxes in many local law enforcement offices, drug deactivation systems, and mail-back options. The FDA maintains a list of medicines that are potentially dangerous if diverted and should be flushed in the toilet (see Federal Resource Center).¹³⁰ Practicing safe medication storage is important; patients, caretakers, providers, and pharmacists should be educated in the various ways to keep them safe at home (<https://www.cdc.gov/features/medicationstorage/index.html>).¹³¹

Synthetic opioids other than methadone (a category that includes prescribed and illicit fentanyl and fentanyl analogues) are now the leading opioids involved in overdose deaths in the United States.^{108–110} The source of illicit fentanyl and its analogues has been identified as international and rarely from diverted fentanyl pharmaceuticals in the United States. These sources currently come through the U.S. Postal Service, borders, ports of entry, and other means. The illicit fentanyl analogues used are not necessarily the same product that is legally prescribed and used during surgeries or in the transdermal and mucosal fentanyl preparations provided for moderate to severe pain. One illicit analogue that has been seen is called carfentanil, which is 100 times more potent than fentanyl. The availability of naloxone as well as patient and family education about naloxone can mitigate the risks of fentanyl-related overdose.¹³²

Prescribers may offer a naloxone prescription to patients who are prescribed opioids (co-prescription) or to those with an addiction history who may be at risk for relapse. In many states, people may obtain naloxone without seeing their provider by obtaining a prescription through standing-order programs with pharmacies. Timely administered naloxone can reverse overdose from opioids whether the opioid is prescribed or illicitly obtained (see Section 2.2.1: Overdose Prevention Education and Naloxone).

Interaction among multiple medications prescribed to patients (polypharmacy) can have significant clinical and symptomatic effects. **Poison control centers** are available 24/7 to health care professionals and the public to answer questions about medication interactions and adverse effects and to assess the need for emergency health care resources.^{133,134} Poison control center engagement is associated with significant reductions in unnecessary use of emergency medical services, EDs, and hospital resources, resulting in significant cost savings for the U.S. health care system.^{135,136} Increased provider and patient awareness and education on the complex and variable interactions of prescribed medications as well as homeopathic, supplemental, and/or over-the-counter medications is needed.¹³⁷

Abuse-deterrent technologies are being developed with the goal of preventing alterations of prescription opioid formulations and the extraction of the active ingredients by users.¹³⁸ For example, some abuse-deterrent formulations (ADFs) have a hardened tablet surface that prevents crushing, while others turn into a gooey substance upon crushing; both formulations are designed to limit the potential for injecting the core substance.¹⁴⁰ ADFs also include the addition of pharmaceutical or chemical compound to the opioid to decrease the user's response to the abused substance or to provide an adverse reaction when the medication is altered.¹³⁹ To address misuse of prescription opioids, the FDA released guidance in 2015 for the development of opioids formulated to meaningfully deter abuse.¹³⁸ A challenge to the development of opioid ADFs is the need to maintain the same safety and efficacy profile as the opioid without the ADF for FDA approval.^{139,141,142} ADFs are not widely used, and more research is needed for better product development to reduce opioid misuse. (The review of ADFs is mentioned specifically for review in the CARA legislation.)

GAPS AND RECOMMENDATIONS

GAP 1: Clinical policies tend to treat the large population of patients with multiple conditions that cause chronic pain with simple medication rules. Guidelines for

medication use for specific populations of patients (e.g., different ages, genders, medical conditions, comorbidities) with chronic pain need to be developed for each specialty group and setting.

RECOMMENDATION 1A: Develop condition-specific treatment guidelines that guide physicians to have a more individualized approach to common pain syndromes and conditions. A multidisciplinary approach that integrates the biopsychosocial model is recommended when clinically indicated.

RECOMMENDATION 1B: Primary care and non-pain specialists should have timely, early consultation with pain specialists and other members of the pain management team for the assessment of patients with complex pain to prevent complications and loss of function and to improve QOL, as clinically indicated.

RECOMMENDATION 1C: Develop a collaborative, multimodal treatment plan as clinically indicated among the referring physician, the pain medicine team, and the patient.

RECOMMENDATION 1D: Pharmacies should collaborate with area health care providers to develop more effective and patient-friendly delivery systems to meet the needs of their patients.

GAP 2: Opioids are often used early in pain treatment. There has been minimal pain education in medical school and residency programs, and little guidance for PCPs on appropriate pain treatment approaches (see Section 3.3.3: Provider Education; see Section 3.4: Access to Pain Care).

RECOMMENDATION 2A: Non-opioids should be used as first-line therapy whenever clinically appropriate in the inpatient and outpatient settings.

RECOMMENDATION 2B: If an opioid is being considered, clinicians should use evidence-informed guidelines.

RECOMMENDATION 2C: The type, dose, and duration of opioid therapy should be determined by treating clinicians according to the individual patient's pain condition while using the opioid medication at the lowest effective dosage and shortest duration appropriate to achieve adequate pain control for improved function and QOL.

RECOMMENDATION 2D: Opioid therapy should be initiated only when the benefits outweigh the risks; the patient is experiencing significant acute or chronic pain that interferes with function and QOL; and the patient is willing to continue to engage with the team on a comprehensive multidisciplinary treatment plan, as clinically indicated, with established clear and measurable treatment goals, along with close follow-up and regular risk assessment and reevaluation.

RECOMMENDATION 2E: CMS and private payers should provide reimbursement that aligns with the medication guidelines the Task Force has described. Private payers and CMS should provide more flexibility in designing reimbursement models.

RECOMMENDATION 2F: Pharmacy Benefit Managers (PBM) and payers should be more transparent about non-opioid pharmacologic options in their formulary, and the Task Force encourages state and federal regulators to review payer and PBM formularies to ensure that non-opioid options are on low-cost tiers.

GAP 3: There is often a lack of understanding and education regarding the clinical indication and effective use of non-opioid medications for acute and chronic pain management. Chronic pain is often ineffectively managed for a variety of reasons, including clinician training, patient access, and other barriers to care (see Section 3.3: Education):

RECOMMENDATION 3A: Clinicians who treat chronic pain should understand the full complement of options, including the use of non-opioid medications and their mechanism-based pharmacology for managing different components of pain syndromes. (See Section 2.3: Restorative Therapies, Section 2.4: Interventional Procedures; Section 2.5: Behavioral Health Approaches; and Section 2.6: Complementary and Integrative Health.)

RECOMMENDATION 3B: For neuropathic pain, as a first-line therapy, consider anticonvulsants (e.g., gabapentin, pregabalin, carbamazepine, oxcarbazepine), SNRIs (e.g., duloxetine, venlafaxine), TCAs (e.g., nortriptyline, amitriptyline), and topical analgesics (e.g., lidocaine, capsaicin). Regardless of the route of medication, education

regarding the side effects as well as risks and benefits is vital in terms of understanding clinical indications and patient outcomes.

RECOMMENDATION 3C: For non-neuropathic, noncancer pain, use NSAIDs and acetaminophen as first-line classes of medications, following standard dosing schedules when clinically appropriate. Other classes of medication can be used depending on the patient's response and may include (depending on specific pain syndromes) anti-spasticity medications (e.g., tizanidine, baclofen) and topical preparations of various classes of medication in addition to other multimodal approaches. Additional consideration may be given to SNRIs or TCAs.

GAP 4: Barriers include lack of coverage and reimbursement for buprenorphine as well as the lack of education and training on the proper usage of buprenorphine. There has been a lack of access to buprenorphine treatment for chronic pain.¹⁴³

RECOMMENDATION 4A: Make buprenorphine treatment for chronic pain available for specific groups of patients and include buprenorphine in third-party payer and hospital formularies.

RECOMMENDATION 4B: Encourage CMS and private payers to provide coverage and reimbursement for buprenorphine treatment, both for OUD and for chronic pain. Encourage primary use of buprenorphine rather than use only after failure of standard mu agonist opioids such as hydrocodone or fentanyl, if clinically indicated.

RECOMMENDATION 4C: Encourage clinical trials using buprenorphine for chronic pain to better understand indication, usage, and dosage.

GAP 5: Education is currently inadequate for patients and clinicians regarding safe medication storage and appropriate disposal of excess medications targeted at reducing outstanding supplies of opioids that others can misuse or that children and other vulnerable members of the household can inadvertently access.

RECOMMENDATION 5A: Increase public awareness of poison control center services as a resource that provides educational outreach programs and materials; referral to treatment facilities; links to take-back facilities; and resources for safe drug storage, labeling, and disposal.

RECOMMENDATION 5B: HHS, in partnership with DEA and other federal and state agencies, should increase opportunities for safe drug disposal and drug disposal sites (e.g., pharmacies, police departments).

RECOMMENDATION 5C: Adopt neutralization technologies and methods that may make safe disposal more readily available for opioids and other relevant medications.

RECOMMENDATION 5D: Educate all providers, including veterinarians, on the importance of safe storage and disposal of opioid medications in their practice. In addition, educate patients and pet owners about the importance of safe storage and disposal of opioid pain medication prescribed for their pets.



Figure 9: Value of Poison Control Centers

2.2.1 Overdose Prevention Education and Naloxone

Naloxone is a medication designed to rapidly reverse opioid overdose.^{144,145} It is an opioid antagonist that binds to opioid receptors and can reverse and block the effects of other opioids. It can quickly restore normal respiration to a person whose breathing has slowed or stopped as a result of overdosing with illicit fentanyl, heroin, or prescription opioid pain medications.

The use of naloxone to treat those who have overdosed on opioids by family members, bystanders, and first responders can save lives,¹⁴⁶ and both intramuscular and nasal formulations are available. Widespread, rapid availability of bystander and take-home naloxone rescue kits, coupled with enhanced education on naloxone's proper use, is essential, particularly in cases where higher doses of opioids are to be prescribed or there is evidence of underlying OUD, as emphasized by the Surgeon General of the U.S. Public Health Service, Vice Adm. Jerome Adams', advisory on naloxone and opioid overdose.^{147,148}

GAPS AND RECOMMENDATIONS

GAP 1: Bystander/take-home naloxone distribution is associated with a cost-effective reduction in mortality; however, its optimal use is not widely understood, and it is not widely distributed.

RECOMMENDATION 1A: Provide naloxone co-prescription/dispensing and education for certain patients and family members/caregivers when the patient is on chronic opioid therapy.

RECOMMENDATION 1B: Increase naloxone distribution programs and education for first responders.

RECOMMENDATION 1C: Encourage the FDA and other entities to research the potential risks and benefits of making naloxone available over the counter.

RECOMMENDATION 1D: Educate health care providers and the public on the importance of identifying individuals at higher risk of overdose harm because of their history or findings consistent with substance abuse, co-prescription or illicit use of drugs

or substances that cause sedation or respiratory depression, or evidence of respiratory compromise



Figure 10: Restorative Therapies Are One of Five Treatment Approaches to Pain Management

C. RESTORATIVE THERAPIES

Restorative therapies include treatments provided by PT and occupational therapy (OT) professionals, physiotherapy, therapeutic exercise, and other movement modalities that are provided as a component of interdisciplinary, multimodal pain care. Restorative therapies play a significant role in acute and chronic pain management, and positive clinical outcomes are more likely if restorative therapy is part of a multidisciplinary treatment plan following a comprehensive assessment. Restorative therapies can be administered by physical therapists, occupational therapists, and others in a variety of settings. Patient outcomes related to restorative and physical therapies tend to emphasize improvement in outcomes, but there is value in restorative therapies to help maintain functionality. Use of restorative therapies is often challenged by incomplete or inconsistent reimbursement policies. The Task Force asks health care reimbursement policymakers to closely evaluate and advocate for payers to improve access to a range of restorative therapies.

The following paragraphs briefly describe restorative therapies, which can be considered singularly or combined with other therapies as part of a multimodal

approach to the management of chronic and acute pain, depending on the patient and his or her medical conditions. This list is not inclusive or exhaustive but instead provides examples of common restorative therapies.

Therapeutic exercise and its role in the treatment of pain is tied to the underlying diagnosis for the pain. Bed rest was scientifically recognized and prescribed as a treatment for low-back pain as recently as the 1980s,¹⁴⁹ but high-quality scientific evidence has since emerged establishing the superiority of movement therapies over rest.¹⁵⁰ The majority of pain-related PT guidelines exist for the treatment of spinal pain. In addition to improving physical functioning, a more contemporary biopsychosocial treatment approach to therapeutic exercise helps patients understand and overcome “secondary pathologies,” including fear of movement and anxiety that contribute to pain and disability.”⁵¹

Transcutaneous electric nerve stimulation (TENS) has been applied to treat pain, but studies of its efficacy are lacking in number and design, with high risks of bias commonly reported.¹⁵¹ An evaluation of 49 systematic reviews, randomized controlled trials (RCTs), and observational studies found insufficient evidence to assess the effectiveness of TENS for acute low-back pain.¹⁵² More recent individual studies have investigated the effectiveness of TENS for postpartum pain,¹⁵³ phantom limb pain,¹⁵⁴ and knee osteoarthritis.¹⁵⁵ Despite the overall limited evidence of efficacy, partially stemming from a lack of large RCTs, TENS is considered a safe self-care option for patients (with appropriate education).¹⁵⁶

Massage therapy can be effective in reducing pain.¹⁵⁷ There are a variety of types of massage therapy, including Swedish, shiatsu, and deep tissue (myofascial release).^{158,159} In Swedish massage, the therapist uses long strokes, kneading, and deep circular movements. Shiatsu massage uses the fingers, thumbs, and palm to apply pressure. Deep tissue massage focuses on myofascial trigger points, with attention on the deeper layers of tissues.

Traction is a PT technique used to treat spinal pain. Review of the evidence has failed to demonstrate the clinical effectiveness of traction as an effective, evidence-based best practice; however, the field in general lacks high-quality RCTs that examine

effectiveness of traction as an isolated treatment modality for low-back^{152,160} or neck pain.

Cold and heat have been used in the treatment of symptoms of a variety of acute and chronic pain conditions. The application of cold has long been a component of the RICE (rest, ice, compression, elevation) paradigm for the treatment of acute pain syndromes. Because it treats only symptoms, the effects and duration of this therapy are mitigated by the initial cause of the pain. For instance, cold therapy has been shown to decrease the pain of hip arthroplasty on the second but not the first or third day after surgery and did not decrease blood loss from the surgery.¹⁶² Evidence is not robust for all locations and types of pain, but significant evidence exists for the efficacy and safety of heat wraps in specific conditions, most notably for acute low-back pain. In fact, a review of non-pharmacologic therapies found that superficial heat had good evidence of efficacy for treatment of acute low-back pain.¹⁶³ Another review found moderate evidence for heat wraps for both symptom and functional improvements.¹⁵²

Therapeutic ultrasound (TU) is thought to deliver heat to deep tissues for improved injury healing.^{164,165} A 2001 review concluded that there was little evidence that TU is more effective than placebo for pain treatment in a range of musculoskeletal conditions.¹⁶⁶ More recent reviews of specific pain syndromes available through the Cochrane Database of Systematic Reviews reveal similar findings, although there is some evidence for TU in knee osteoarthritis.^{167,168}

Bracing has sometimes been discouraged in pain management because of fears of deconditioning and muscle atrophy. However, there is evidence that, for at least short periods of time, bracing (especially nonrigid bracing) may improve function and does not result in muscle dysfunction.¹⁶⁹ Bracing should be part of the clinician toolbox.

GAPS AND RECOMMENDATIONS

GAP 1: There is a lack of clarity on which restorative therapy or treatments are indicated in the various pain syndromes.

RECOMMENDATION 1A: Conduct further research to provide data on which restorative therapy or treatments are indicated as part of a multidisciplinary approach to specific pain syndromes.

RECOMMENDATION 1B: For those modalities for which clear indications of benefits in the treatment of chronic pain syndromes (e.g., treatments used by OT and PT professionals; aqua therapy; TENS; movement-based modalities, including tai chi, Pilates, and yoga), there should be minimal barriers to accessing these modalities as part of a recommended multidisciplinary approach to the specific pain condition.

RECOMMENDATION 1C: Make harm-free, self-administered therapies such as TENS freely available (e.g., over the counter) to support pain management treatment plans.

D. BEHAVIORAL HEALTH APPROACHES

In recent decades, pain management experts have recognized the important relationship between pain and psychological health.^{40,242,243} Psychological factors can play an important role in an individual's experience and response to pain^{244,245} and can affect treatment adherence, pain chronicity, and disability status.^{242,246}



Figure 13: Behavioral Health Is One of Five Treatment Approaches to Pain Management

Undiagnosed and untreated psychological concerns in individuals with pain are associated with increased health care utilization and readmissions, decreased treatment

adherence, and increased disability.^{247–249} Patients with chronic pain are at increased risk for psychological distress, maladaptive coping, and physical inactivity related to fear of reinjury.⁴⁰ Individuals with chronic pain are also more likely to have disabilities than patients with other chronic health conditions, such as stroke, kidney failure, cancer, diabetes, or heart disease.²⁵⁰ High-impact chronic pain is especially disruptive to multiple aspects of patients' life, including their relationships, work, physical activity, sleep, self-care, and self-esteem. Psychological interventions, following proper evaluation and diagnosis, can play a central role in reducing disability in these patients. Furthermore, preliminary evidence indicates that psychological interventions administered prior to surgery have been shown to reduce postsurgical pain and opioid use.^{74,251}

Behavioral health approaches as part of pain management should be considered a key component of the biopsychosocial model and multidisciplinary pain management. These approaches aim to improve the overall pain experience and restore function by addressing the cognitive, emotional, behavioral, and social factors that contribute to pain-related stress and impairment.^{242,246,252} They target a variety of domains, including physical functioning, pain medication use, mood, cognitive patterns, and QOL.²⁴²

The following paragraphs briefly describe behavioral health approaches. This list is not inclusive or exhaustive but instead provides examples of common behavioral health approaches.

Behavioral therapy (BT) for pain focuses largely on applying the principles of operant conditioning to identify and reduce maladaptive pain behaviors (e.g., fear avoidance) and increase adaptive or “well” behaviors. This improvement is achieved by minimizing reinforcement of maladaptive behaviors, providing reinforcement of well behaviors, and reducing avoidance behaviors through gradual exposure to the fear-provoking stimuli (e.g., exercise). The overall goal of BT in the treatment of pain is to increase function.^{253,254} BT has demonstrated effectiveness for reducing pain behaviors and distress and for improving overall function, and it can be more cost-effective than active physical treatment.^{254,255}

Cognitive behavioral therapy (CBT) aims to reduce maladaptive behavior and improve overall functioning. However, in addition to focusing on altering behavioral responses to pain, CBT focuses on shifting cognitions and improving pain coping skills.²⁵⁶ CBT includes psychoeducation about the relationship between psychological factors (e.g., thoughts, feelings) and pain; cognitive restructuring of maladaptive thought patterns; and training in a variety of pain coping strategies, including activity pacing and pleasant activity scheduling.²⁴² CBT is effective for a variety of pain problems²⁵⁷ and can help improve self-efficacy, pain catastrophizing, and overall functioning.^{258,259} The Agency for Healthcare Research and Quality (AHRQ) found that CBT can lead to long-term improvements in patients with low-back pain and fibromyalgia.²⁶⁰

Acceptance and commitment therapy (ACT) is a form of CBT that emphasizes observing and accepting thoughts and feelings, living in the present moment, and behaving in a manner that serves an individual's chosen values. Unlike traditional CBT approaches, ACT focuses on creating psychological flexibility through acceptance of psychological and physical experiences rather than by challenging them.^{261,262}

Mindfulness-based stress reduction (MBSR) is a mind-body treatment typically delivered in a group format. It focuses on improving patients' awareness and acceptance of their physical and psychological experiences through body awareness and intensive training in mindfulness meditation.²⁶³ Mindfulness meditation teaches patients to self-regulate their pain and pain-related comorbidities by developing nonjudgmental awareness and acceptance of present-moment sensations, emotions, and thoughts.^{264,265} Research suggests that MBSR is an effective intervention for helping individuals cope with a variety of pain conditions, including rheumatoid arthritis, low-back pain, and MS.^{266,267} MBSR also has a positive impact on pain intensity, sleep quality, fatigue, and overall physical functioning and well-being.^{263,268–270}

Emotional awareness and expression therapy (EAET) is an emotion-focused therapy for patients with a history of trauma or psychosocial adversity who suffer from centralized pain conditions.²⁷¹ In this approach, patients are taught to understand that

their pain is exacerbated or maintained by unresolved emotional experiences that influence neural pathways involved in pain. Patients are taught to become aware of these unresolved experiences, which include suppressed or avoided trauma, adversity, and conflict, and to adaptively express their emotions related to these experiences. Patients learn that control over pain can be achieved through emotional awareness and expression. Enhancing the patient's capacity to approach an experience rather than inhibit or avoid important emotions and interpersonal interactions leads to increased engagement in life activities. Research indicates that EAET has a positive impact on pain intensity, pain interference, and depressive symptoms.²⁷²

Self-regulatory or psychophysiological approaches include treatments such as biofeedback, relaxation training, and hypnotherapy. These approaches use the mind-body connection to help patients with pain develop control over their physiologic and psychological responses to pain.²⁴² **Biofeedback** entails monitoring and providing real-time feedback about physiologic functions associated with the pain experience (e.g., heart rate, muscle tension, skin conductance). The overall goal of biofeedback is to improve awareness and voluntary control over bodily reactions associated with pain exacerbations.²⁷³ Biofeedback training has proven effective for chronic headache and migraine in adults and children.²⁷⁴ **Relaxation training** and **hypnotherapy** involve altering attentional processes and heightening the experience of physical and psychological relaxation. Relaxation training is often used in conjunction with biofeedback to increase physiological awareness and enhance relaxation skills.²⁴² Both of these approaches have empirical support in pain management.^{275,276} Empirical evidence also supports the use of hypnotherapy to manage cancer pain, low-back pain, arthritis, pain from SCD, temporomandibular joint pain, fibromyalgia, and other pain conditions.²⁷⁵ Similar to relaxation training, hypnotherapy induces an altered state of consciousness guided by a hypnotherapist that focuses the individual's attention to alter his or her experience of pain.

Behavioral health interventions can be effective in improving clinical outcomes for pain,^{246,271,277} but treatment should be tailored to address patient preferences and

needs. This tailoring requires careful assessment of patients' pain perceptions, cognitive and emotional responses, coping skills, and social and environmental status.²⁷⁸ It also requires accurate diagnosis of comorbid psychosocial concerns.

Access to Psychological Interventions

Despite widespread understanding of the importance of psychological interventions in the management of pain, many patients with pain receive inadequate care.^{279,280} Many factors contribute to this problem, including clinical barriers (e.g., treatment accessibility, knowledge gaps, provider attitudes), health care system-related barriers (e.g., cost and reimbursement issues), and patient-related barriers (e.g., stigma, attitudinal variables). When access to providers and costs are limiting factors, evidence-based low-cost and scalable approaches delivered through telehealth and internet technologies may provide a low-burden, effective alternative to traditional treatment approaches.^{73,281} Research suggests that brief telehealth and digitally delivered treatments allow for broad patient access and yield outcomes similar to traditional in-person psychological interventions for chronic pain.²⁸²

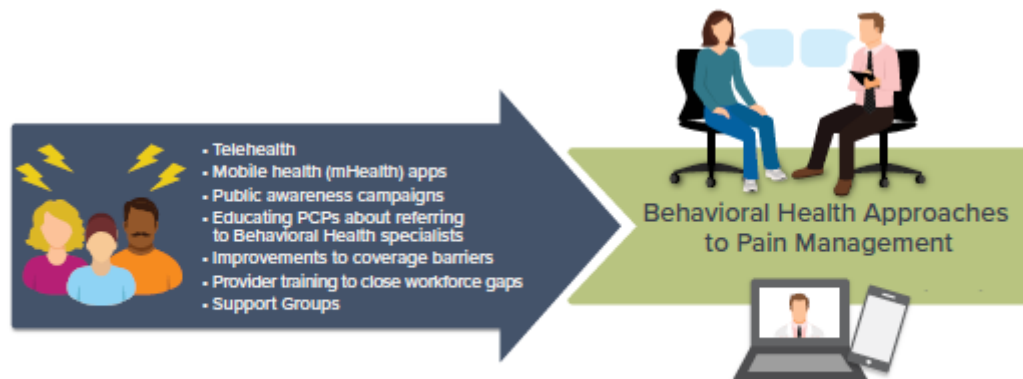


Figure 14: Overcoming Barriers to Behavioral Health Approaches

To further enhance patient acceptance and engagement in psychological treatment, patients and providers need to know about psychological treatments. Health professionals should have sufficient understanding of the biopsychosocial model of pain

and how to appropriately assess and refer patients for behavioral health treatment.^{252,283} This can be accomplished by improving training and education in pain management^{26,284,285} and initiating public campaigns to reduce stigma and enhance public awareness of the biopsychosocial aspects of pain.²⁸⁶

As noted in other sections of this report, the lack of health insurance coverage for psychological services has also been cited as a significant barrier to adequate pain management (see Section 3.4.2: Insurance Coverage for Complex Management Situations). Both a need for trained pain psychologists and appropriate incentives are required to fill the work gap. Although several organizations have identified policy recommendations to close gaps in access to pain management services,^{287,288} coverage barriers persist. These barriers continue to hinder patients' access to skilled behavioral health providers, integrated and multidisciplinary care, and (for OUD and SUD) co-morbid treatment, as required.^{289–292}

GAPS AND RECOMMENDATIONS

GAP 1: Access to evidence-based psychological and behavioral health approaches for treating chronic pain and mental health comorbidities (e.g., PTSD, depression, anxiety, mood disorders, SUD) is limited by geography, reimbursement, and education in primary care and specialty care settings.

RECOMMENDATION 1A: Increase access to evidence-based psychological interventions, including the full range of treatment deliveries (e.g., in-person, telehealth, internet self-management, mobile applications, group sessions, telephone counseling) and hub-and-spoke models.

RECOMMENDATION 1B: Educate physicians, dentists, and health care providers on the benefits of psychological and behavioral health treatment modalities in the multidisciplinary approach to acute and chronic pain management.

RECOMMENDATION 1C: Improve reimbursement policies for integrated, multidisciplinary, multimodal treatment approaches that include psychological and behavioral health interventions through traditional and nontraditional delivery methods

(e.g., in-person, telehealth, internet self-management, mobile applications, group sessions, telephone counseling).

Patients With Chronic Pain as well as Mental Health and Substance Use Comorbidities

The occurrence of pain and mental health comorbidities, including depression, PTSD, and SUD, is well documented.^{293–297} Psycho-social distress can contribute to pain intensity, pain-related disability, and poor response to treatment. Untreated psychiatric conditions and current or historical SUD also increase the risk of both unintentional and intentional medication mismanagement, OUD, and overdose.²⁹⁸ Given the intersection between psychiatric/psychological symptoms and chronic pain, it is important that the behavioral health needs of patients with pain be appropriately and carefully evaluated and treated with the concurrent physical pain problem.

Although the literature exploring the effectiveness of interventions for patients with painful conditions and comorbid psychiatric concerns is limited, research suggests that regular monitoring and early referral and intervention can improve pain and psychiatric outcomes and prevent negative opioid-related outcomes.^{74,242,290,299} Many CBPs recommend screening and regularly monitoring the psychological health concerns and substance misuse risk of all patients with pain, using multidisciplinary approaches and referring patients to behavioral health and substance use specialists as clinically indicated (see Section 3.1.2: Screening and Monitoring).^{40,300} Technological advances in the delivery of clinical tools (e.g., mobile applications) may improve assessment, monitoring, and treatment delivery,³⁰¹ although further research is needed.

GAPS AND RECOMMENDATIONS

GAP 1: CBPs for chronic pain do not adequately address how to treat individuals with comorbid psychological health concerns.

RECOMMENDATION 1A: Screen for psychological health and SUDs in patients with acute or chronic pain and consider early referral to behavioral health providers when clinically indicated.

RECOMMENDATION 1B: Use an integrated multidisciplinary approach that may include existing evidence-based psychological and behavioral interventions (e.g., CBT, coping skills, stress reduction, mindfulness-oriented recovery) to address chronic pain when clinically indicated.

RECOMMENDATION 1C: Refer patients to both pain and addiction specialists when OUD is suspected and ensure an integrative approach to health care.

RECOMMENDATION 1D: Buprenorphine may be considered appropriate for pain treatment in this population when clinically indicated.

RECOMMENDATION 1E: When considering buprenorphine and other opioids, use the lowest effective dose in conjunction with non-opioid treatment modalities, with enhanced monitoring and collaboration with addiction specialists. Conduct regular reevaluation and assessment, with a treatment plan and established goals, to achieve optimal patient outcomes.

GAP 2: Many CBPs for chronic pain do not adequately address barriers to acceptance of psychological treatments.

RECOMMENDATION 2A: Enhance and inform patient, clinician, and public understanding of the importance of a biopsychosocial model approach for chronic pain conditions.

GAP 3: Research gaps exist in the effectiveness of existing psychological interventions for the treatment of psychological health and substance use in the subpopulation of patients with chronic pain and psychological health comorbidities.

RECOMMENDATION 3A: Conduct research on the applications and indications of existing evidence-based psychological health interventions for patients with chronic pain and psychological health or substance use comorbidities.

RECOMMENDATION 3B: Conduct research on the efficacy of novel and innovative psychological and behavioral health treatments (e.g., biofeedback, hypnosis, relaxation therapies).

GAP 4: There has not been sufficient validation of mobile and electronic health applications (apps) used for clinical treatment of patients with pain with comorbid psychological conditions.

RECOMMENDATION 4A: Conduct peer-reviewed validation research to guide the use of mobile and electronic health (e health) applications within the context of the biopsychosocial treatment modalities for chronic pain.

RECOMMENDATION 4B: Add a category for electronic and mobile treatments to the Substance Abuse and Mental Health Services Administration's (SAMHSA's) Evidence-Based Practices (EBP) Resource Center and a designation for pain for target audiences when evidence of benefit exists.

RECOMMENDATION 4C: Establish a validation process for apps used for biopsychosocial treatments to better inform physician, provider, and patient users of these apps that are evidence-based and effective for the management of various chronic pain syndromes.



Figure 15: Complementary and Integrative Health Is One of Five Treatment Approaches to Pain Management

E. COMPLEMENTARY AND INTEGRATIVE HEALTH

Clinical best practices may recommend a collaborative, multimodal, multidisciplinary, patient-centered approach to treatment for various acute and chronic pain conditions to achieve optimal patient outcomes. For improved functionality, activities of daily living, and quality of life, clinicians are encouraged to consider and prioritize, when clinically indicated, nonpharmacologic approaches to pain management.^{54,302–307}

Complementary and integrative health approaches for the treatment or management of pain conditions consist of a variety of interventions, including mind-body behavioral interventions, acupuncture and massage, osteopathic and chiropractic manipulation, meditative movement therapies (e.g., yoga, tai chi), and natural products.³⁰⁸ The National Institutes of Health (NIH) National Center for Complementary and Integrative Health defines “complementary approaches” as those nonmainstream practices that are used together with traditional medicine; it defines “alternative approaches” as those used in place of conventional medicine, noting that most patients who use nonmainstream approaches do so with conventional treatments.³⁰⁹ There are many definitions of “integrative” health care, but all involve bringing together conventional, complementary, and integrative health approaches in a coordinated way.



CORY'S STORY

PATIENT TESTIMONIAL

I joined the Marines in 2005 and was deployed to Afghanistan. In 2009, my team was hit by an IED. I was about 10 feet away and it launched me in the air. I sustained numerous shrapnel injuries. My right arm was ripped open down to my hand and I had some shrapnel in both of my legs and my left arm. Overall, I had 26 surgeries over 3 1/2 years in the hospital, where I started receiving alternative therapy. After I got out of being an inpatient, I told myself I was going to get off of all my meds and I did that. I watched too many fellow service members, comrades, turn into zombies just being pumped full of medications. It was not something that I wanted to do with my life. So, I wanted to try something new. I tried acupuncture and it seemed to work very well. Recently I received a different type of therapy called digital medicine. I was having some pain in my foot. If my foot stays down for a long period of time, it gets swollen, and I have limited feeling from my left knee down to my foot. I went through a form of visual and audio therapy and somehow that triggered those nerves to kick back in. Within 15 minutes, I had regained feeling in my leg and foot. It was a 30-minute session. We did three sessions. That lasted for about a month. It's not forever, but in my opinion, it beats taking medications. I think a combination of acupuncture and digital medicine is, in a sense, the way of the future. That's what I've been doing, and it's worked for me and it's worked for many other people.

The current opioid crisis has spurred intense interest in identifying effective nonpharmacologic approaches to managing pain. The use of complementary and integrative health approaches for pain has grown within care settings across the United States over the past decades. As with other treatment modalities, complementary and integrative health approaches can be used as stand-alone interventions or as part of a multidisciplinary approach, as clinically indicated and based on patient status. Examples of complementary and integrative health approaches to pain include acupuncture, hands-on manipulative techniques (e.g., osteopathic or chiropractic manipulation, massage therapy), mindfulness, yoga, tai chi, biofeedback, art and music therapy, spirituality, and the use of natural or nutritional supplements. These therapies can be provided or overseen by licensed professionals and trained instructors. The use of complementary and integrative health approaches should be communicated to the pain management team.

Overall, most complementary and integrative health approaches can provide improved relief, when clinically indicated, when used alone or in combination with conventional therapies such as medications, behavioral therapies, and interventional treatments, although more research to develop evidence-informed treatment guidelines is needed.³⁰⁸

Improved reimbursement policies for complementary and integrative health approaches as well as improved education for medical professionals and a greater workforce of pain management specialists can address key barriers to acceptance and implementation of complementary and integrative health approaches for pain.³⁰⁸ Additional research, greater patient and clinician education — including clinical guidance and indications for use — and expanded coverage of complementary and integrative health approaches are essential for a comprehensive solution to reduce the reliance on opioids.

The following paragraphs briefly describe complementary and integrative health approaches, which can be considered singularly or as part of a multimodal approach to the management of chronic and acute pain, depending on the patient and his or her medical conditions. This list is not inclusive or exhaustive but instead provides examples of common complementary and integrative health approaches.



Figure 16: Complementary and Integrative Health Approaches for the Treatment or Management of Pain Conditions Consist of a Variety of Interventions

Acupuncture is a recognized form of therapy that has its origins in ancient Chinese medicine. It involves manipulating a system of meridians where “life energy” flows by

inserting needles into identified acupuncture points. An estimated 3 million American adults receive acupuncture each year.³¹⁰ It is generally considered safe when performed by a licensed, experienced, well-trained practitioner using sterile needles, and although there are risks as with any intervention, the risks are minimal. The therapeutic value of acupuncture in the treatment of various pain conditions, including osteoarthritis; migraine; and low-back, neck, and knee pain has growing evidence in the form of systematic reviews and meta-analyses.^{311–318} Existing CPGs concerning the use of acupuncture for pain are inconsistent and often differ regarding the evidence-based science and accepted mechanisms by which acupuncture has persisting effects on chronic pain.^{54,302–307,314,319–322} As with all medicine, a risk-benefit analysis, consideration of clinical indications, and patient acceptance need to be considered.

Massage and manipulative therapies, including osteopathic and chiropractic treatments, are commonly used for pain management. Such interventions may be clinically effective for short-term relief^{323,324} and are best accomplished in consultation with the primary care and pain management teams. Studies on massage have considered various types, including Swedish, Thai, and myofascial release, but these studies do not provide adequate details of the type of massage provided. Systematic reviews note that the few studies looking at the effect of massage on pain use rigorous methods and large sample sizes.^{157,325} Other reviews recognize positive clinical effects on various pain conditions, including postoperative pain; headaches; and neck, back, and joint pain.^{326–329}

MBSR, also discussed above in the Behavioral Health Approaches section, is a program that incorporates mindfulness skills training to enhance one's ability to manage and reduce pain. Mindfulness enables an attentional stance of removed observation and is characterized by concentrating on the present moment with openness, curiosity, and acceptance. This approach allows for a change in one's point of view on the pain experience. Studies support statistically significant beneficial effects for low-back pain.^{330,331} A meta-analysis demonstrated that mindfulness meditation significantly reduces the intensity and frequency of primary headache pain.³³²

Yoga, a practice rooted in ancient Hindu tradition and a way of life that incorporates mind, body, and a spiritual approach, has shown improved outcomes for a variety of medical and nonmedical conditions. Yoga has become popular in Western cultures as a form of mind and body exercise that incorporates meditation and chants. Yoga's use of stretching, breathing, and meditation has also been therapeutic in the treatment of various chronic pain conditions, especially low-back pain.^{333–337} Although there have been limited reports of pain symptoms becoming more severe with yoga, overall, the risk-benefit analysis suggests that yoga is generally safe, beneficial, and cost-effective, especially when administered in the group setting.³³⁸

Tai chi originated as an ancient Chinese martial art used to balance the forces of yin and yang. Modern tai chi has become popular for core physical strengthening through its use of slow movements and meditation. It has demonstrated long-term benefit in patients with chronic pain caused by osteoarthritis and other musculoskeletal pain conditions.^{339,340} Like yoga, tai chi appears to be safe; demonstrates positive results, especially over the long term; and can also be cost-effective in the group setting. Both yoga and tai chi can be delivered remotely via telemedicine/telehealth.

Spirituality is a broad concept and generally includes a sense of connection to something bigger than the individual. It typically involves a search for meaning in life. Spiritual or religious beliefs can influence a person's lifestyle, attitudes, and feelings about pain. People living with pain may use religious or spiritual forms of coping, such as prayer and meditation, to help manage their pain. Growing evidence indicates that spiritual practices and resources are beneficial for people with pain.³⁴¹ As a result, clinicians may consider the role of spirituality in pain management.

GAPS AND RECOMMENDATIONS

GAP 1: A large variety of complementary and integrative health approaches are often overlooked in the management of pain.

RECOMMENDATION 1A: Consider complementary and integrative health approaches, including acupuncture, mindfulness meditation, movement therapy, art therapy, massage therapy, manipulative therapy, spirituality, yoga, and tai chi, in the treatment of acute and chronic pain, when indicated.

RECOMMENDATION 1B: Develop CPGs for the application of complementary and integrative health approaches for specific indications.

GAP 2: There is a gap in the understanding of complementary and integrative health approaches.

RECOMMENDATION 2A: Conduct further research on complementary and integrative health approaches to determine their therapeutic value, risk and benefits, and mechanisms of action.

RECOMMENDATION 2B: Consider the inclusion of various complementary and integrative health approaches as part of an integrated approach to the treatment of chronic pain.

RECOMMENDATION 2C: Conduct further research on nutritional supplements such as alpha lipoic acid, L-carnitine transferase, and vitamin C and their effect on acute and chronic pain management.

F. SPECIAL POPULATIONS

Painful conditions and pain management are complex in part because various populations have unique issues that affect acute and chronic pain. Special populations in pain management that the Task Force identified include children, older adults, women, pregnant women, individuals with SCD, individuals with other chronic relapsing pain conditions, racial and ethnic minority populations, active duty service members and Veterans, and patients with cancer and those in palliative care. The special populations section in this report was included to highlight several special populations' considerations for pain management. The populations highlighted here are not exhaustive, and the special populations section on chronic relapsing conditions is intended to serve as a general category that applies to many painful conditions not

specifically mentioned. No special population was purposefully excluded from the report.

Unique Issues Related to Pediatric Pain Management

Chronic pain is estimated to affect 5% to 38% of children and adolescents.^{342–344} These pain conditions can be from congenital diseases (e.g. sickle cell disease), where pain begins in the infant or toddler age period; chronic non-congenital diseases (e.g., juvenile idiopathic arthritis, fibromyalgia, inflammatory bowel disease); or primary chronic pain conditions (e.g., headaches, chronic abdominal pain, chronic musculoskeletal pain, CRPS). The origin of pain conditions in the pediatric age group is important because the developing pediatric nervous system can be especially vulnerable to pain sensitization and development of neuroplasticity.³⁴⁵ Data support the finding that early neonatal and childhood pain experiences can alter pain sensitivity in later life.³⁴⁶ Poor pain management in children can put them at risk for persistent pain and increased impairment as they transition into adulthood and may even be linked to the development of new chronic pain conditions.^{347,348} The application of the biopsychosocial model to pediatric pain care is therefore vital. Psychological conditions resulting from chronic disease and pain syndromes can contribute to long-term pain. These psychological conditions can include difficulty coping, anxiety, and depression. Incorporation of parents and family into pain care is especially important in the pediatric population because childhood pain can be affected by family and parental factors, including family functioning and parental anxiety, and depression.

Appropriate pain management in childhood is imperative because children's early pain experiences can shape their response to pain as adults. Overall, there is a substantial need for more trained pediatric pain specialists to address the often-complex aspects of pediatric pain. There is a greater challenge in attracting top physicians to further specialize in pediatric pain fellowships, and this aspect of medical education would address an ongoing gap in this area. It is of utmost importance to introduce

comprehensive pain care early in the pediatric age group to optimize patients' QOL now and in the future.³⁴⁹

GAPS AND RECOMMENDATIONS

GAP 1: The significant shortage of pediatric pain specialists and comprehensive pain service centers presents a barrier to addressing the needs of pediatric patients with acute and chronic pain. This limited access is further compromised by lack of reimbursement and coverage for services related to comprehensive pain management, including nonpharmacologic evidence-based pain therapies.

RECOMMENDATION 1A: Increase access to pediatric pain services with pain expertise, which can likely be achieved through an increase in the workforce and novel care delivery models.

RECOMMENDATION 1B: Deliver and appropriately reimburse and cover pediatric pain care in the context of comprehensive, multidisciplinary treatment.

GAP 2: Pediatric patients with chronic pain conditions eventually transition to adult care, during which time they may experience gaps in care, increased health care utilization, poor patient outcomes, and other health care vulnerabilities and morbidities.

RECOMMENDATION 2A: Develop models of care for appropriate transition for pediatric patients with acute or chronic pain conditions to ensure seamless care delivery as well as decreased morbidity and mortality.

GAP 3: Most physician pain specialists are not credentialed in pediatric pain and therefore are not permitted by their institutions to take care of children with chronic pain.

RECOMMENDATION 3A: Encourage and assist pain physicians in obtaining the necessary training for credentialing in pediatric pain. This is a significant step toward improving pediatric patient access.

GAP 4: Many current CBPs do not address pediatric opioid prescribing best practices. Further, RCTs and real-world evidence of non-opioid pharmacologic therapies in pediatric patients for chronic pain are lacking.

RECOMMENDATION 4A: Develop pediatric pain management guidelines that address appropriate indications for opioids and responsible opioid prescribing.

RECOMMENDATION 4B: Conduct pediatric pain research to inform national guidelines using multimodal approaches to optimize pain management for children and adolescents.

Older Adults

Chronic pain is one of the most common, costly, and incapacitating conditions in older adults.³⁵⁰ Managing pain in older adults can be complex because of age-related physiologic changes, associated medical and mental health comorbidities, polypharmacy, increases in pain thresholds, decreases in pain tolerance, and alterations in pharmacokinetics and pharmacodynamics that increase the risk of side effects from pharmacologic treatment.^{304,351} Effective pain management for older adults requires an understanding of the special considerations associated with the physiology of aging, validated assessment tools, common pain presentations in the older adult population,³⁵² and the use of evidence-informed CPGs for common conditions such as low-back pain.³⁵³ Older patients may have increased risk of GI bleeding and renal damage from NSAIDs.

GAPS AND RECOMMENDATIONS

GAP 1: There is a need for opioid prescribing guidelines for the aging population that provide the potential for increased risk of falls, cognitive impairment, respiratory depression, organ metabolism impairment, and age-related and non-age-related pain issues.

RECOMMENDATION 1A: Develop pain management guidelines for older adults that address their unique risk factors. However, a risk factor of a medication should not necessarily be an automatic reason not to give this medication to an elderly patient. Clinicians must assess the risk versus benefit of using medications while considering other modalities in this patient population.

RECOMMENDATION 1B: Consider using a multidisciplinary approach with nonpharmacologic emphasis given the increased risk of medication side effects in this population.

RECOMMENDATION 1C: Establish appropriate pain management education for physicians and health care providers who treat older adults.

Patients with Cancer-Related Pain and Patients in Palliative Care

Cancer pain affects millions of Americans.^{306,354} In addition, there are more than 14 million cancer survivors in the United States as a result of remarkable advances in cancer diagnosis and therapy. An estimated 40% of cancer survivors continue to experience persistent pain as a result of treatments such as surgery, chemotherapy, and radiation therapy. Persistent pain is also common and significant in patients with a limited prognosis, as often encountered in hospice and palliative care environments.³⁵⁵

GAPS AND RECOMMENDATIONS

GAP 1: These patient populations are frequently managed by practitioners who do not specialize in pain or palliative care. Many oncologists and primary care physicians are not trained to recognize or treat persistent pain associated with cancer or other chronic medical problems with limited prognosis.

RECOMMENDATION 1A: Clinicians should assess and address pain at each patient encounter. Causes of pain such as recurrent disease, second malignancy, or late-onset treatment effects should be evaluated, treated, and monitored.

GAP 2: Patients with persistent pain associated with cancer and/or cancer treatment or other chronic medical problems with limited prognosis in palliative care often receive less optimal care with restricted treatment modalities.

RECOMMENDATION 2A: When clinically indicated, use multimodal and multidisciplinary treatment as part of cancer-related pain management and palliative care.

Unique Issues Related to Pain Management in Women

Central to the unique issues women face in pain management are the differences between men and women with respect to pain sensitivity, response to pain medication, and predisposition to clinical pain conditions.³⁵⁶ Data and recent literature suggest that women experience more pain than men, have greater sensitivities to painful stimuli compared with men, and report experiencing more intense pain.^{357,358} In addition to the response to pain medication, there exist sex differences in the patterns of nonmedical use and abuse of prescription opioids.^{359,360} Research has identified that women are more likely than men to misuse prescription opioids.³⁶¹ Furthermore, from 1999 to 2010, the percentage increase in opioid-related overdose deaths was greater in women than in men.³⁶² Finally, women face unique pain management challenges in the pregnancy and postpartum periods. To mitigate the heightened risk associated with pain management in these periods, it is important to emphasize the importance of obstetricians and gynecologists (OB-GYNs) on the multidisciplinary pain management team.

GAPS AND RECOMMENDATIONS

GAP 1: Women face unique challenges regarding their physical and mental health, interactions with the health care system, and roles in society. Women use the health care system as patients, caregivers, and family representatives and can be

particularly affected by costs, access issues, and gender insensitivity from health care providers and staff. Several diseases associated with pain — in particular, chronic high-impact pain — have a higher prevalence in women or are sex specific, including endometriosis, musculoskeletal and orofacial pain, fibromyalgia, migraines, and abdominal and pelvic pain.

RECOMMENDATION 1A: Increase research to elucidate further understanding of the mechanisms driving sex differences in pain responses and research of mechanism-based therapies that address those differences.

RECOMMENDATION 1B: Raise awareness in the public and health care arenas to the unique challenges that women face during pregnancy and in the postpartum period, including various pain syndromes and psychosocial comorbidities.

GAP 2: Women may experience increased pain sensitivity. Of note, OB-GYNs may be one of the first health care providers a woman with pain encounters, yet they are not often included as part of a multidisciplinary care team.

RECOMMENDATION 2A: Include OB-GYNs as part of multidisciplinary care teams because they are likely to play an important role in the treatment of pain for women.

Pregnancy

Managing pain in pregnant women is uniquely challenging because clinical decision making must account for the pregnant mother and the developing fetus.³⁶³ Further complicating pain management in the peripartum period is the lack of CPGs for nonpharmacologic treatments that may decrease the potential adverse outcomes for newborns associated with opioid therapy, such as neonatal abstinence syndrome. Greater research into chronic pain management in pregnancy is needed.^{364–366}

GAPS AND RECOMMENDATIONS

GAP 1: There is a need for evidence-based CPGs for the use of analgesics during pregnancy and the postpartum period.

RECOMMENDATION 1A: Improve evidence for pain management of pregnant and postpartum women with greater research and innovation, in collaboration with the national specialty societies (the American College of Obstetricians and Gynecologists, neonatologists, obstetricians, perinatal pediatricians, and other specialists).

RECOMMENDATION 1B: Counsel women of childbearing age on the risks of opioids and non-opioid medications in pregnancy, including risks to the fetus and newborns.

Chronic Relapsing Pain Conditions

Chronic pain with periods of remission and frequent relapses defines “chronic relapsing pain conditions.” Examples of such conditions include various degenerative, inflammatory, immune-mediated, rheumatologic, and neurologic conditions such as MS, trigeminal neuralgia, Parkinson’s disease, CRPS, porphyria, systemic lupus erythematosus, lumbar radicular pain, migraines, and cluster headaches. Acute pain flares on top of the chronic pain condition can be a common occurrence that may affect daily routines and overall functionality, resulting in additional morbidity and the need for comprehensive pain care.

GAPS AND RECOMMENDATIONS

GAP 1: There is sometimes a lack of partnership between the disease specialist (i.e., the hematologist, oncologist, rheumatologist, or neurologist) and providers of comprehensive multidisciplinary pain programs.

RECOMMENDATION 1A: Provide referrals to a comprehensive pain program early in the course of the chronic disease (e.g., MS, porphyria, systemic lupus erythematosus, migraine, Parkinson’s disease, neuropathic pain syndromes) to determine the optimal approach to managing acute or chronic pain exacerbations, including potential non-opioid, alternative therapies and nonpharmacologic therapies. Establish a partnership between the disease specialist (e.g., the hematologist, oncologist, neurologist, or rheumatologist) and the pain team to optimize care.



ANNE'S STORY

PATIENT TESTIMONIAL

My name is Anne. I'm a 19-year-old girl and college sophomore. I have struggled with sickle-cell disease my whole life. My dad always told me that sickle cell does not have me — I have sickle cell. I have learned to persevere through the pain. I found that my passions were the one thing that kept the pain away. Even though I would be in pain, I would still go out and dance. I would still sing. I was even a cheerleader at one point. I think that with sickle cell, it's also about what you can handle mentally. I struggled with depression for a while and as recently as last February, I went through a period of depression. It was the hardest thing, but I kept telling myself, OK Anne, you're going to get better. Just keep pushing. Just keep pushing. I have been through six surgeries in my 19 years. I have had brain surgery due to Chiari I malformation from sickle cell, which caused multiple migraines every day. I was shocked because I would still go to school. I would still get my homework done. I would still go out and have fun with my friends, even though I was still going through all this pain. My brother told me that I am one of the strongest people he's ever met. And that was so touching because at that time I didn't believe I was a strong person. It was hard because my parents never dealt with a child with sickle cell. I'm their last child. And I've seen them cry. I've seen them persevere with me. My family is one thing that keeps me going; I can't let anything stop me. I can't even let one little crisis stop me. I barely go to a hospital for my crisis now because I try to find ways at home to get rid of my pain.

Sickle Cell Disease

Sickle cell disease is a group of inherited disorders characterized by complex acute and chronic symptoms, including pain.³⁶⁷ An estimated 90,000 people in the United States have SCD, which disproportionately affects minority populations, particularly African Americans.³⁶⁸ Acute pain episodes, or “pain crises,” associated with SCD are abrupt in onset and unpredictable, and they drive patients to seek care in the ED and inpatient unit, with estimated health care costs of almost \$2 billion per year.^{369,370} Chronic, severe, daily pain also occurs in approximately 30% to 40% of adolescents and adults with SCD, significantly impairing their functioning and increasing in incidence and severity with age.^{371–373} Pain in SCD is unique in that it occurs throughout the patient’s lifespan, from infancy to adulthood, and develops directly from the disease.³⁷⁴ The biology of SCD pain is complex and varied; it likely arises from multiple mechanisms depending on whether an individual is suffering from acute or chronic pain.³⁷⁵ Pulmonary,³⁷⁶ orthopedic,³⁷⁷ psychosocial,³⁷⁸ and other comorbidities of SCD can also give rise to painful complications in adults and children.

GAPS AND RECOMMENDATIONS

GAP 1: There is a lack of evidence-based management guidelines for the treatment of acute and chronic pain in children and adults with SCD.

RECOMMENDATION 1A: Develop comprehensive, evidence-based guidelines for the treatment of acute and chronic SCD pain in children and adults.

RECOMMENDATION 1B: Conduct research to understand underlying mechanisms of acute and chronic pain and develop mechanistic non-opioid pharmacologic therapies and nonpharmacologic approaches for SCD pain management.

GAP 2: Unpredictable, episodic exacerbations of acute pain pose a challenge for SCD pain management, and the majority of patients have failed non-opioid pain medications prior to presentation for acute care. Constraints on opioid treatment duration can make individualization of pain management difficult. Further, limited

access to oral opioids at home for the treatment of unplanned acute pain can result in increased use of health care services that could have been avoided.

RECOMMENDATION 2A: Protect access to the appropriate and safe use of opioids for patients with SCD, with consideration for exemption from prescribing guidelines and state prescribing laws that do not specifically address patients with SCD because of the complex nature and mechanism of acute and chronic sickle cell pain.

RECOMMENDATION 2B: Consider the lowest effective dose of opioids to treat acute pain crises and prescribe within the context of close follow-up and comprehensive outpatient pain care.

RECOMMENDATION 2C: Develop an individualized approach to pain management that includes consideration of opioid and non-opioid therapies, such as behavioral health strategies and multimodal approaches.

RECOMMENDATION 2D: Provide patient education on the risks and benefits of opioids.

GAP 3: The SCD patient population faces significant health care disparities that affect access to and delivery of comprehensive pain care and mental health services. Further, stigma, negative provider attitudes, and perceived racial bias are associated with SCD pain,^{379,380} which may compromise care, thus leading to increased suffering from pain and pain care delivery.^{381–385}

RECOMMENDATION 3A: Develop comprehensive care delivery models for SCD pain management, including collaborative partnerships among pain medicine, SCD specialists and advocates, and multidisciplinary teams.

RECOMMENDATION 3B: Develop outpatient infusion clinics/day hospitals for SCD pain management to decrease reliance on the ED for pain treatment.

RECOMMENDATION 3C: Increase access to and reimbursement for mental health services for patients with SCD.

RECOMMENDATION 3D: Provide education focused on stigma, negative provider attitudes, and perceived racial bias at all levels of health care to optimize delivery of pain treatment to patients with SCD.

Health Disparities in Racial and Ethnic Populations, Including African-Americans, Hispanics/ Latinos, American Indians, and Alaska Natives

Considerable evidence exists documenting health disparities in racial and ethnic minority populations, particularly substantial disparities in the prevalence, treatment, progression, and outcomes of pain-related conditions.³⁸⁶ These disparities in care are attributed to factors related to social disadvantage as well as factors within health systems.³⁸⁷ Health disparities contributing to suboptimal pain management in these special populations may be related to such factors as barriers to accessing health care, lack of insurance, discrimination, lack of a PCP, lack of child care, a lower likelihood to be screened or receive pain treatment, and environmental barriers that impede effective self-management. Effective strategies and plans to address these issues specifically in these disparate communities are necessary to address these gaps to improve patient outcomes.

GAPS AND RECOMMENDATIONS

GAP 1: Socioeconomic and cultural barriers may impede patient access to effective multidisciplinary care. Evidence exists of racial and ethnic disparities in pain treatment and treatment outcomes in the United States, yet few interventions have been designed to address these disparities. Lower quality pain care may be related to many factors, including barriers to accessing health care, lack of insurance, discrimination, lack of a PCP, lack of childcare, lower likelihood to be screened or receive treatment, and environmental barriers that impede self-management.

RECOMMENDATION 1A: Develop intervention programs informed by the biopsychosocial model to reduce racial and ethnic disparities in pain.

GAP 2: Research shows that ethnic minorities may have greater pain sensitivity and are at increased risk for chronic pain, yet they remain underserved.

RECOMMENDATION 2A: Develop biopsychosocial interventions for pain that are scalable and culturally enhanced.

Military Active Duty, Reserve Service Members, and Veterans

The experience of pain is prevalent in military and Veteran populations.³⁸⁸ Pain management can be complex in military populations, who experience combat-related injuries (e.g., ballistic wounds, burns, over pressurization, blunt trauma) in addition to complications from accompanying conditions such as post-traumatic stress disorder and traumatic brain injury (TBI), both of which are more prevalent in Veterans than in the civilian population.^{48,389,390} Delayed pain treatment following injury can increase the likelihood of acute pain becoming chronic pain in service members and Veterans.⁴⁸

As a Nation, we must do better in fulfilling our solemn obligation to care for all those who have served our country and to improve the QOL of our Nation's Veterans, many of whom have risked their lives to protect our freedom while deployed, often multiple times, to areas of prolonged conflict. Veterans die by suicide at higher rates compared with civilians in the United States.³⁹¹ Among Veterans, pain conditions are associated with an increased risk of suicide.³⁹² Clinicians can discuss suicide risk with Veterans and recognize that public health approaches to suicide prevention include addressing pain.

GAPS AND RECOMMENDATIONS

GAP 1: Military active duty, reserve service members, and Veterans have unique physical and mental health challenges related to their military service that contribute to the development of or exacerbate acute and chronic pain conditions. Medical and mental health comorbidities such as TBI, PTSD, limb loss, and musculoskeletal injuries often interfere with successful treatment outcomes. Assessment and treatment of pain conditions in active duty service members and

Veterans require military-specific expertise and a coordinated, collaborative approach between medical and mental health providers.

RECOMMENDATION 1A: Physicians and clinical health care providers taking care of military service members and Veterans, regardless of practice setting, should consider in their pain care plan prior military history and service-related health factors that may contribute to acute or chronic pain, as relevant to the clinical presentation.

RECOMMENDATION 1B: Physicians and clinical health care providers should work collaboratively to deliver comprehensive pain care that is consistent with the biopsychosocial model of pain.

RECOMMENDATION 1C: Conduct research to better understand the biopsychosocial factors that contribute to acute and chronic pain in active duty service members and Veterans, with a focus on TBI, PTSD, other mental health issues, and SUDs.

RECOMMENDATION 1D: Conduct studies to better understand the contributing factors predisposing these patients to movement along the spectrum from acute to chronic pain.

GAP 2: The transition from active military service to Veteran status can be complicated. A multitude of factors may affect a successful transition, including incomplete integration of EHRs and imposed changes or delays in access to primary care, pain specialty, and mental health physicians and health care providers.

RECOMMENDATION 2A: The integration of the DoD and Veterans Health Administration (VHA) health systems is important for effective and timely pain care. This integration should include coordination of the transition from active duty to Veteran status and care coordination across the health care spectrum that includes a smooth transition to primary care, mental health and pain specialty physicians, and health care providers.

GAP 3: Active duty, reserve service members, and Veterans increasingly receive care in the community (including care provided through external payment systems and Department of Defense (DoD)- or VHA-purchased care). A fragmented health care system results in lack of coordinated care in the community, within the

Military Health System (MHS), and in VHA as well as differing care standards (such as the implementation of opioid risk-mitigation strategies). Within MHS, access to primary care and specialty care — and multidisciplinary pain specialty care in particular — is difficult for some Veterans because of geographical factors, limited availability of providers, and the need for specialized pain care treatment.

RECOMMENDATION 3A: To improve care coordination across health care systems, streamlined access to medical records and collaboration across systems are needed to provide more timely and effective pain care.

G. CROSS-CUTTING CLINICAL AND POLICY BEST PRACTICES

RISK ASSESSMENT

The selection of the most appropriate medication-based treatment approach for an individual with pain involves a careful analysis of risks and benefits. Risks of side effects and toxicity must be balanced against the benefits, including improved function with improved QOL, ADLs, and ability to work, as well as with improvement in medical condition. Clinicians evaluating pain, whether acute or chronic, must conduct a thorough history, physical exam, and risk assessment, especially when considering medications such as opioids in the treatment plan. Identifying patients at risk of SUD will help minimize potential adverse consequences and facilitate treatment or referral for treatment of active SUDs.

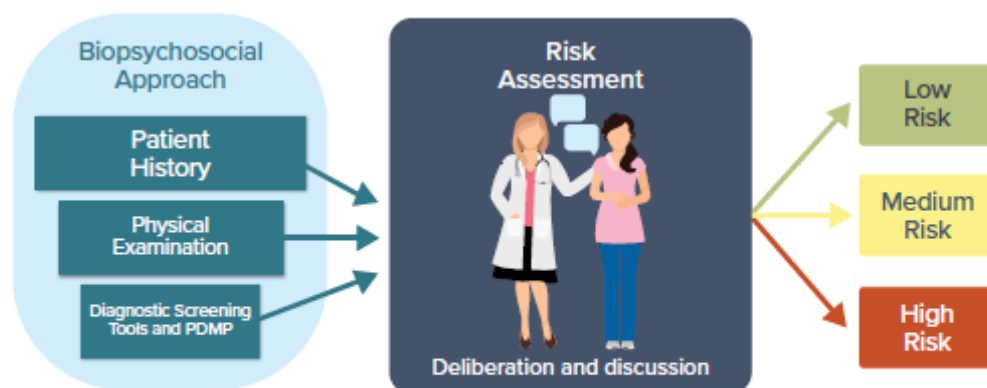


Figure 17: A Risk Assessment Is Critical to Providing the Best Possible Patient-Centered Outcome While Mitigating Unnecessary Opioid Exposure

Prescription Drug Monitoring Programs

Prescription drug monitoring programs (PDMPs) are state-managed electronic databases of controlled substances dispensed (typically schedule II-IV drugs), with the majority of the data being reported by community-based pharmacies.³⁹³ PDMPs enable prescribers and pharmacists (and in some states, insurers, researchers, and medical licensing boards) to access the data, monitor use by patients, monitor prescribing practices by practitioners, and check population-level drug use trends. Forty-nine states and most of Missouri and the District of Columbia have operational PDMPs.^{394,395}

Prescribers may be required to use PDMP data at the point of care, enabling them to identify patients who have had multiple provider episodes or potentially overlapping prescriptions that place them at risk. PDMPs can support safe prescribing and dispensing practices and help curb opioid prescription by detecting patterns that can alert clinicians to patients who may be at risk of an SUD. PDMPs can alert clinicians to provide potentially lifesaving information and interventions. The information found in the PDMP can prompt the clinician to take action to improve patient safety by having a conversation about safety concerns and understanding the patient's goals and needs. Providers who identify uncertain medication behavior can respond clinically, making referrals to mental health or substance abuse treatment.^{396,397} McAllister et al.³⁹⁸ found that all prescribers who were surveyed indicated that accessing PDMP data altered their prescribing patterns. Caution is needed when using PDMPs as a tool to aid in the proper dispensing of medications. However, PDMPs are not to be used as tools to stop dispensing medications appropriately to those in need. For example, it is important for pharmacists to know that doctors often work as teams and to ensure that the conclusion of inappropriate multiple provider use is made only after the pharmacist has communicated directly with the prescribing clinician. Concerns that physicians, nurses, dentists, and pharmacies may have should be communicated among one another or to the relevant state regulatory agencies, including state medical boards, nursing boards, dental boards, and pharmacy boards, when appropriate.

PDMPs can assist in determining whether a patient is obtaining medications from multiple providers and filling prescriptions at multiple pharmacies, especially when prescriptions are filled in quick succession or on the same day. As a tool to help inform clinical decisions, PDMPs' potential utility was highlighted in the CDC's Guideline for Prescribing Opioids for Chronic Pain Guideline.³⁹⁹ Clinicians should consider reviewing PDMP data when starting patients on opioid therapy and periodically during chronic opioid treatment.³⁹⁹

Prescribers are more likely to use PDMPs that present data in real time, are used by all prescribers, are technically easy to use without time constraints, and actively identify potential problems such as multiple prescribers or multiple prescriptions.⁴⁰⁰ Requiring PDMP checks also has a positive effect. Buchmueller and Carey⁴⁰¹ found stronger effects when providers are required to access the PDMP, and PDMPs significantly reduced measures of misuse in Medicare Part D. In contrast, they found that PDMPs without such provisions had no effect. PDMPs can also bolster provider confidence. For example, in one study, ED providers report feeling more comfortable prescribing controlled substances when they receive information from a PDMP.³⁹⁸

Baehren et al.⁴⁰² found that when PDMP data were used in an ED, 41% of cases had altered prescribing after the clinician reviewed PDMP data, with 61% of the patients receiving fewer or no opioid pain medications than the physician had originally planned prior to reviewing the PDMP data and 39% receiving more opioid medication than previously planned because the physician was able to confirm that the patient did not have a recent history of controlled substance use. The effective use of PDMP data is beneficial to both health care professionals and patients.

The need to modernize and enhance the functionality of PDMPs is widely acknowledged.^{403–406} For example, Colorado favors the integration of automatic queries and responses that obviate time-consuming manual data entry and also

recommends that PDMPs be optimized with improvements, links to ED registration, and data population in EHRs.⁴⁰⁷ EHRs should work to integrate PDMPs into their system design at minimal to no additional cost to providers (to eliminate barriers to accessing PDMP data), especially when these data points are mandated. States should individually provide links to their PDMPs from major, certified EHR platforms. Maryland also recommends enhanced user interfaces and interstate data sharing for PDMPs.⁴⁰⁴

Provider PDMP adoption has been shown to fall when interoperability is low, and use is not mandated.⁴⁰⁸ Accessing PDMP data also affects VA and IHS. VA physicians noted that incomplete or unavailable data was a significant barrier to increasing PDMP use.⁴⁰⁹ In 2016, HHS issued a policy requiring IHS prescribers to query the PDMP before prescribing opioids and pharmacists to report their dispensing activity to the PDMP; it also directed IHS to ensure that memorandums of understanding were signed with the appropriate state offices.^{49,410} Links to and use of PDMPs varies across IHS service areas.

GAPS AND RECOMMENDATIONS

GAP 1: PDMP use varies greatly across the United States, with variability in PDMP design; the state's health information technology infrastructure; and current regulations on prescriber registration, access, and use.

RECOMMENDATION 1A: Consider checking PDMPs, in conjunction with other risk stratification tools, upon initiation of opioid therapy, with periodic reevaluation.

RECOMMENDATION 1B: Provide clinician training on accessing and interpreting PDMP data.

RECOMMENDATION 1C: Clinicians should engage patients to discuss their PDMP data rather than making a judgment that may result in the patient not receiving appropriate care. PDMP data alone are not error proof and should not be used to dismiss patients from clinical practices.

RECOMMENDATION 1D: If already performed upon admission in the inpatient hospital setting, the health care team should not be mandated to repeatedly check the PDMP if already performed upon admission and pending discharge.

RECOMMENDATION 1E: Conduct studies to better identify where PDMP data are best used (e.g., inpatient versus outpatient settings). Adjust PDMP data use based on the findings of the recommended studies to minimize undue burdens and overuse of resources (i.e., streamline PDMP data use).

RECOMMENDATION 1F: States are encouraged to have interoperability between PDMP and EHR platforms (Code of Federal Regulations 170.315). EHR vendors should work to integrate PDMPs into their system design at minimal to no additional cost or burden to providers (to eliminate barriers to accessing PDMP data), especially when these data points are mandated.

RECOMMENDATION 1G: Enhance the interoperability of PDMPs across state lines to allow for more effective use, along with consistent reporting to PDMP by the VA and military health system.

RECOMMENDATION 1H: Clinicians within and outside federal health care entities should have access to each other's data to ensure safe continuity of care.

RECOMMENDATION 1I: Allow access to PDMPs by all opioid prescribers.

RECOMMENDATION 1J: Encourage funding programs to link interstate PDMP programs to each other.

Screening and Monitoring

Screening and monitoring in pain management seek to identify and reduce the risk of substance misuse, abuse, and overdose as well as improve overall patient care.

Evaluations of patient physical and psychological history can screen for risk factors and characterize pain to inform treatment decisions. Screening approaches include efforts to assess for concurrent substance use and mental health disorders that may place patients at higher risk for OUD and overdose. This includes screening for drug and

alcohol use and the use of urine drug testing, when clinically indicated.^{84,411} These approaches enable providers to identify high-risk patients so that they can consider substance misuse and mental health interventions, ADFs, and education materials to mitigate opioid misuse.⁴¹³

Screening tools can help clinicians identify risks and help determine which medication classes may be appropriate for the patient, including for long-term opioid therapy. Effective screening can include single questions, such as, “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”⁴¹³ Other validated screening tools include the Drug Abuse Screening Test⁴¹⁴ and the Alcohol Use Disorders Identification Test.⁴¹⁵ Clinicians must recognize the limits of screening tools in detecting prior or developing SUD or OUD.

Urine drug tests (UDTs) can provide information about drug use that the patient does not report, including not using prescribed medications as intended and unreported drug use. UDTs can also potentially inform treatment decisions by assessing an individual’s drug metabolism rate. However, according to a systematic review by Agency for Healthcare Research and Quality (AHRQ), evidence demonstrating the effectiveness of UDTs for risk mitigation during opioid prescribing for pain is lacking.^{416,417} UDT results can be subject to misinterpretation and may sometimes be associated with practices that can harm patients (e.g., stigmatization, inappropriate termination from care). Clinicians do not consistently use practices intended to decrease the risk for misuse, such as UDTs⁴¹¹ and opioid treatment agreements,⁴¹⁸ likely in part because of competing clinical demands, perceived inadequate time to discuss the rationale for UDTs and order confirmatory testing, and feeling unprepared to interpret and address results.⁴¹⁹

To mitigate the risks of prescription opioid misuse, medical societies, in conjunction with state and federal regulatory agencies, have recommended specific risk-reduction strategies, including written treatment agreements for patients with chronic pain who are

prescribed opioids.⁴¹⁸ Pain agreements or treatment agreements can be useful in defining the responsibilities of the patient and the provider, and they create a structure to guide and evaluate opioid use. The agreement should be viewed as an opportunity for ongoing dialogue about the risks of opioids and what the patient and clinician can expect from each other.³⁶³ The agreement should not be about simply getting a form signed or a means to “fire” a patient for breaking the terms of the agreement; rather, it is a tool for facilitating a conversation between the clinician and the patient.⁴¹⁸

56 Monitoring approaches should be applied transparently and consistently in a manner that emphasizes safety so that miscommunication and accidental stigmatization are minimized.⁴²⁰ At follow-up, doctors should assess benefits in function, pain control, and QOL using tools such as the three-item “average pain intensity (P), interference with enjoyment of life (E), and interference with general activity (G)” or PEG scale⁴²¹ or asking patients about progress toward functional goals that have meaning for them. Clinicians should also screen for factors that predict risk for poor outcomes and substance abuse, such as sleep disturbance, mood disorder, and stress, either by using a pain rating scale such as the Defense and Veterans Pain Rating Scale, which includes brief questions, or by routinely asking about these factors on clinical examination.⁴²² Clinicians should ask patients about their preferences for continuing opioids, given their effects on pain and function relative to any adverse effects they experience.³⁹⁹ These factors illustrate the importance of health care providers having sufficient time with the patient for a thorough evaluation.

GAPS AND RECOMMENDATIONS

GAP 1: Comprehensive screening and risk assessment of patients are time-consuming but vital for proper evaluation of their chronic pain conditions. Lack of sufficient compensation for time and payment for services have contributed to barriers in best practices for opioid therapy.

RECOMMENDATION 1A: Encourage CMS and private payers to provide sufficient compensation for time and payment for services to implement the various screening measures (e.g., extensive history taking, review of medical records, PDMP query, urine toxicology screenings, when clinically indicated). These are vital aspects of risk assessment and stratification for patients on opioids and other medications.

RECOMMENDATION 1B: Consider referral to pain, mental health, and other specialists, including addiction medicine-trained physicians when high-risk patients are identified.

GAP 2: UDTs are not consistently used as part of the routine risk assessment for patients on opioids.

RECOMMENDATION 2A: Use UDTs as part of the risk assessment tools prior to the initiation of opioid therapy and as a tool for reevaluating risk, using the clinical judgment of the treatment team.

RECOMMENDATION 2B: Clinicians should educate patients on the use of UDTs and their role in identifying both appropriate and potentially inappropriate use.

GAP 3: Variability exists in what is included in opioid treatment agreements, which should be based on common principles and reflect provider, practice, and patient demographics.

RECOMMENDATION 3A: Conduct studies to evaluate the effectiveness of the different components of opioid treatment agreements. Treatment agreements should include the responsibilities of both the patient and the provider.

RECOMMENDATION 3B: Use opioid treatment discussions as an educational tool between providers and patients to inform the patient about the risks and benefits of and alternatives to chronic opioid therapy.

STIGMA

Stigma associated with having chronic pain, especially when opioid therapy is used as a treatment modality, is a major concern and has far-reaching effects on patients and all

those involved in their care.⁴²³ The different facets of stigma — at the patient, provider, and social levels — collectively serve as a significant barrier to effective treatment of chronic pain.⁴²⁴ There is a growing body of empirical research into stigmatization and the resulting barriers to care. Studies suggest that patients who are receiving or who have previously received long-term opioid therapy for nonmalignant pain face both subtle and overt stigma from their family, friends, coworkers, the health care system, and society at large for their opioid treatment modality.^{423–426} Compassionate, empathetic care in a provider-patient partnership is best for countering the stigma, isolation, and psychosocial challenges of living with pain.



Figure 18: Public Comments to the Task Force Affirm the Barriers Stigma Creates

Feelings of guilt, shame, judgement, and embarrassment resulting from such stigma can increase the risk for behavioral health issues, such as anxiety and depression, which can further contribute to symptom chronicity.⁴²⁶ Reducing barriers to care that exist as a consequence of stigmatization is crucial for patient engagement and treatment effectiveness.⁴²⁴

Furthermore, the sub-population of patients with painful conditions and comorbid SUD face additional barriers to treatment because of stigmatization of both chronic pain and addiction.⁴²⁷ Chronic pain is common among individuals with SUD, including opioid misuse,⁴²⁸ yet stigma remains a significant barrier to implementation of programs and treatments for OUD, such as medication-assisted treatment^{429,430} and naloxone.⁴³¹

Patients with comorbid problematic opioid use and chronic noncancerous pain report significant perceived stigma associated with methadone and buprenorphine treatment.⁴²⁵ Clinicians who treat acute and chronic pain, particularly with opioids, may experience stigma from colleagues and society in general that — in addition to fear of scrutiny from state medical boards and the DEA — may also dissuade them from using opioids appropriately. Clinicians are overburdened with time constraints, EHR demands, and other administrative tasks, which has led to unprecedented levels of burnout among physicians. Stigma, combined with the enhanced time required to effectively evaluate and treat pain, leads to over-referral and patient abandonment.⁴³² According to one study, only 12.2% of individuals who require treatment for a SUD actually seek treatment. In addition, stigma is found to be a significant barrier, with 20.5% not seeking treatment because of negative consequences associated with their work and around 17% being concerned about negative judgements by friends or community.⁴³²



JULIE'S STORY

PATIENT TESTIMONIAL

Eight years ago, through a series of relatively minor events, I ended up with multiple herniated and bulging disks in my lumbar and cervical spine and nerve-root impingement in my neck. I also have two painful disc-spur complexes in my thoracic spine. This is how my nightmare began. I ended up going to multiple doctors to find help for my pain — orthopedists, physiatrists, a neurologist, and four top neurosurgeons. I was told that I was not a candidate for surgery, but few other solutions were given. I was accused of drug seeking, belittled for having a low pain threshold, which was not true, and dismissed as a patient. I was unable to work and take care of my family because of the constant pain. I was reduced to lying in bed, crying from the pain, and being emotionally devastated. It was as if I had to prove my pain. This was also the most vulnerable time for my family, who were my caregivers, because they had no knowledge or understanding or tools to deal with me and my pain. Understandably I became severely depressed. I had no prior psychiatric history and had never been to a psychiatrist in my life. I was hospitalized three times for suicidal ideation. Each time I would return home, but nothing had changed. My family didn't know what to do to help me and the situation caused a lot of family stress. My doctors at the time didn't help either. When I couldn't stand the pain anymore, I went to the ER several times and was treated like an addict. During one hospital stay, I was labeled chemically dependent and recommended for a 30-day drug-rehabilitation program. I refused to go because all I wanted was for the pain to stop and to go back to my normal life. About two years later, I finally ended up in a pain management clinic headed by fellowship-trained pain management anesthesiologists. I was treated with understanding and respect and given the medical care that I needed to help improve my quality of life

GAPS AND RECOMMENDATIONS

GAP 1: Patients with chronic pain may face barriers in access to pain care due to being stigmatized as people seeking medications to misuse. Contributing to this stigmatization are the lack of objective biomarkers for pain, the invisible nature of the disease, and societal attitudes that equate acknowledging pain with weakness.

RECOMMENDATION 1A: Increase patient, physician, clinician, nonclinical staff, and societal education on the underlying disease processes of acute and chronic pain to reduce stigma.

RECOMMENDATION 1B: Increase patient, physician, clinician, nonclinical staff, and societal education on the disease of addiction.

RECOMMENDATION 1C: Counter societal attitudes that equate pain with weakness through an awareness campaign that urges early treatment for pain that persists beyond the expected duration for that condition or injury.

RECOMMENDATION 1D: Encourage research aimed at discovering biomarkers for neurobiological mechanisms of chronic pain.

GAP 2: The national crisis of illicit drug use, with overdose deaths, is confused with appropriate therapy for patients who are being treated for pain. This confusion has created a stigma that contributes to barriers to proper access to care.

RECOMMENDATION 2A: Identify strategies to reduce stigma in opioid use so that it is never a barrier to patients receiving appropriate treatment, with all cautions and considerations, for the management of their chronic pain conditions.

EDUCATION

Public, patient, provider, and policymaker education are critical to the delivery of effective, patient-centered pain management and necessary for optimizing patient outcomes, promoting appropriate use of pain medication, and reducing the risk associated with prescription opioids. This common theme is underscored across many federal reports, including the Institute of Medicine's (IOM's) report, "Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research"; HHS's National Pain Strategy; and other pain management and opioid-related consensus documents.^{5,49,128,433} These reports consistently describe the extent to which pain and SUD education is insufficiently covered in medical education and training programs, which has a downstream impact on the extent to which patients are educated about pain and SUD.

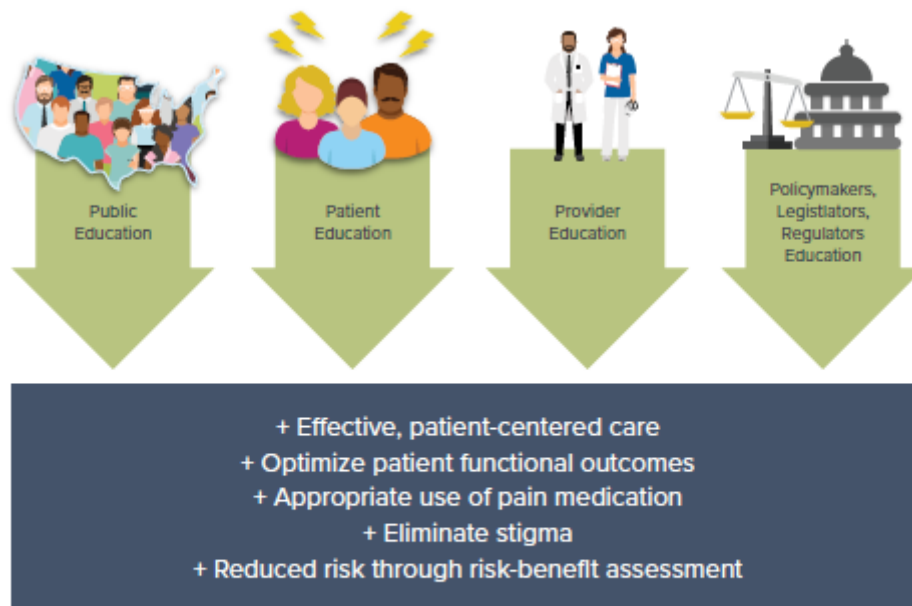


Figure 19: Education Is Critical to the Delivery of Effective, Patient-Centered Pain Care and Reducing the Risk Associated With Prescription Opioids

To begin to address the growing need for educational initiatives, multiple entities, including government agencies, nonprofit organizations, pharmaceutical manufacturers, academic institutions, and health systems, have developed and disseminated pain- and opioid-related patient education programs, toolkits, pamphlets, and other interventions. Similarly, state-level continuing education requirements have been established for several provider types (e.g., physicians, dentists, NPs, PAs, pharmacists) that mandate education about appropriate opioid prescribing and dispensing. Addressing multiple education gaps simultaneously will likely be necessary to optimize patient outcomes tied to public, patient, and provider education. Other programs that could be considered are the development and effectiveness testing of a reimbursable pain self-management training program that incorporates a pain educator, or evaluation of the role of a certified pain educator, in optimizing pain care and improving patient education.

Public Education

The evidence base for public education about pain is limited. Whereas some evaluation of mass media campaigns for low-back pain have been conducted in other countries,

analyses in the United States are lacking.^{434–436} The gaps and recommendations specific to public pain education, as outlined below, that will inform best practices in public pain education are consistent with those described elsewhere.⁴⁹ There is a significant need for improved public education on and understanding of the distinction ⁶⁰ between acute and chronic pain — notably, that chronic pain, regardless of its etiology, can become a chronic disease itself, with measurable changes in the nervous system, spinal cord, and brain. An estimated 50 million to 100 million people have chronic pain, making it the most prevalent, costly, and disabling health condition in the United States.^{5,6} Yet, despite its pervasiveness, it remains largely unknown to the broader public.

GAPS AND RECOMMENDATIONS

GAP 1: National public education about pain is needed.

RECOMMENDATION 1A: Develop a national evidence-based pain awareness campaign that emphasizes the public's understanding of acute and chronic pain syndromes.

RECOMMENDATION 1B: Establish a mechanism to finance a large-scale, systematic, coordinated public campaign to address pain awareness.

Patient Education

Patient education is another key component of any best practice model for outcomes. Patients benefit from a greater understanding of their underlying disease process and pain triggers as well as knowing how to seek appropriate professional care. It is important for patients to know that pain as a symptom is typically a warning of injury or disease that can affect the body and mind. Finding the precipitating and perpetuating causes of the pain and addressing them with appropriate multimodal therapy is considered the best management strategy for improving patient outcomes. It is also important for patients to understand that pain can be a disease in its own right, particularly when pain becomes chronic and loses its protective function. In this context, pain is often detrimental to the patient's health, functionality, and QOL. A category of

diseases is characterized by chronic debilitating pain (e.g., trigeminal neuralgia, CRPS, postherpetic neuralgia). In such conditions, there is rarely a cure, but appropriate assessment; accurate diagnosis; and patient-centered, multidisciplinary treatment can optimize pain relief, improve function, and enhance QOL. Self-management skills training may include relaxation, pacing, cognitive restructuring, maintenance planning, and relapse prevention.^{42,43,47,437} Innovative delivery systems, including telehealth and other Web-based applications, can offer technology-based education and self-management support to further engage and empower patients in their care plan.^{438–440}

GAPS AND RECOMMENDATIONS

GAP 1: Current patient education is lacking for both acute and chronic pain.

RECOMMENDATION 1A: Prioritize access to educational tools for patients, families, and their caregivers that include clinician visits, patient handouts, Web resources, and support groups to optimize patient outcomes.

RECOMMENDATION 1B: Explore and test innovative methods of delivering patient education and support for patients with acute or chronic pain using technology, particularly in rural areas that have limited access to multimodal treatment. Examples of means to provide patient access in such situations include telemedicine online support groups, networks of in-person support groups with training and guidance from leaders, and applications easily accessible on mobile devices.

GAP 2: Patient expectations for pain management in the perioperative arena are frequently not aligned with current surgical practices or procedures that require pain management.

RECOMMENDATION 2A: During the preoperative visit, discuss pain control after surgery. This discussion should be conducted by both the surgical team and the preoperative team.

RECOMMENDATION 2B: For major surgeries, use models such as the PSH or ERAS protocols to emphasize the importance of patient education in the management of pain and rehabilitation activities.

RECOMMENDATION 2C: CMS and private payers should recognize that the time spent educating and managing patients' expectations is cost-effective and provides a significant value that reduces the length of hospital stays and improves patients' postoperative pain management, allowing for faster recovery through earlier PT and mobility that decreases the risk for postoperative complications (e.g., blood clots). CMS and other payers should compensate according to physician-patient time spent.

GAP 3: Current educational materials and interventions for patients with chronic pain lack consistency, standardization, and comprehensive information.

RECOMMENDATION 3A: Establish an online resource of evidence-informed educational materials for common pain conditions and appropriate treatment modalities.

RECOMMENDATION 3B: Convene a chronic pain expert panel that includes experienced patients, patient advocates, and clinicians to develop a set of core competencies and other essential information specific to patient pain education. Provide grants for the creation of patient education programs and materials based on these core competencies, and disseminate them widely to patients, their family, and caregivers through clinics, hospitals, pain centers, and patient groups.

Provider Education

Experts have noted the benefits that could be realized from the development of a more comprehensive pain curriculum for training and continuing education of providers.¹⁵ Encouraging licensing and education practices that do more to emphasize safe and effective pain assessment and management has the potential to improve pain management and mitigate factors that contribute to the current opioid crisis.^{26,44}¹ Health care professionals who prescribe opioids are in a key position to balance the

benefits of analgesics against the risk of adverse clinical outcomes. It is estimated that “apart from federal prescribers who are required to be trained, fewer than 20% of the over one million health providers licensed to prescribe controlled substances have training on how to prescribe opioids safely and effectively.”⁴⁴² Providers can access educational resources, receive accreditation, or renew existing licenses through public- or private-sector enterprises.⁴⁰⁴ National stakeholders have recommended that accrediting organizations develop, review, promulgate, and regularly update core competencies for pain care education, licensure, and certification at the prelicensure (i.e., undergraduate professional) and post-licensure (i.e., graduate) levels.^{49,291}

Educational interventions for pain should be guided by core competencies and target both the training and practice levels.²⁶ Provider education research specific to patient outcomes is limited, but systematic reviews on continuing medical education (CME) programs indicate that interventions that include multimedia, multiple instructional techniques, and multiple exposures are associated with improved provider knowledge outcomes compared with alternatives (e.g., print materials, one-time interventions).^{443–445} Likewise, regardless of whether educational interventions are targeted at clinicians in training or in practice, aligning educational interventions with core competencies (i.e., outcomes) for pain care education^{15,441} is a best practice.⁴⁹ In addition, although Frank et al.⁴⁴⁶ demonstrated the effectiveness of a longitudinal distance learning approach that uses telemedicine to change clinical pain practice in primary care (e.g., Extension for Community Healthcare Outcomes [Project ECHO]), a recent systematic review by Rochfort et al.⁴⁴⁷ found a scarcity of studies on the effectiveness of educational interventions implemented by a PCP designed to promote optimal patient outcomes. Results do indicate that education and skills training of PCPs may positively affect patient performance of self-management pain-reduction activities, improve patient lifestyle behaviors, and increase perceived QOL. This finding underscores the importance of further training for health care professionals in patient self-management support as part of patient-centered care and as a mechanism for improving pain outcomes.

Chronic Pain and Headache Management TeleECHO (ECHO Pain), with Project ECHO, is a telehealth approach that supports clinicians’ education and training

regarding treating patients with chronic pain and safe opioid management.⁴⁴⁸ The model is based on workplace learning, with cases selected by participants from their patient panels combined with short lectures by experts (referred to as a “hub-and-spoke model”).

GAPS AND RECOMMENDATIONS

GAP 1: Gaps exist in pain management understanding and education throughout the health care provider community. There is a need for further education regarding acute and chronic pain for all health care providers in professional school curricula, postgraduate education, and further clinical specialty training.

RECOMMENDATION 1A: Further develop biopsychosocial educational models for clinicians at all levels of training.

RECOMMENDATION 1B: Develop effective educational resources for PCPs to improve the current understanding and knowledge of pain treatment modalities, initially available treatments, and early referral to pain specialists

RECOMMENDATION 1C: Explore intensive continuing pain education for PCPs, including telehealth, tele-mentoring, and the Project ECHO model, as a means of providing pain education for PCPs by pain specialists. Consider the State Targeted Response Technical Assistance Consortium model for pain training as it currently exists for addiction training.

GAP 2: Pain is generally treated as a symptom of another illness, disease, or injury; it is not commonly recognized as a separate category of disease.^{5,449} The lack of education on pain syndromes and pain mechanisms limits the ability to recognize chronic pain as a category of disease.

RECOMMENDATION 2A: The Task Force supports WHO’s recognition of chronic and acute pain as a category of disease, with its revisions to the “International Classification of Diseases, 11th Revision.”⁴⁵⁰

RECOMMENDATION 2B: Conduct further education on pain syndromes and mechanisms through clinician training, such as CME, the Project ECHO model, tele-mentoring, and other continuing education programs.

3.3.4 Policymaker, Regulator and Legislator Education

Policymakers, regulators, and legislators at both the federal and state levels play an important role in formulating policy, issuing guidelines and direction, and passing legislation on issues related to acute and chronic pain management, payment mechanisms, and the use and regulation of controlled medications. The issue of pain management is complicated, so every decision made, law passed, or guideline issued has a cascading effect on many aspects of pain management. As such, a deep understanding of the issues, especially the potential for unintended consequences of these decisions, is essential in formulating effective comprehensive policy.

GAPS AND RECOMMENDATIONS

GAP 1: Current education for policymakers at the state and federal levels has significant opportunities for improvement for both acute and chronic pain.

RECOMMENDATION 1A: Strongly encourage education by key and relevant expert stakeholders from the appropriate professional associations, clinicians, and patient advocacy groups prior to effecting policy on acute and chronic pain.

RECOMMENDATION 1B: Establish criteria for evaluating legislation and regulation based on the principles in the preamble of this report, ensuring an understanding of all potential unintended consequences of guidelines, policies, regulations, or legislation that is being considered.

ACCESS TO PAIN CARE

In the United States, the estimated number of patients with chronic daily pain is 50 million, with 19.6 million having chronic, high-impact pain.⁶ Several factors act as barriers to adequate care, including inadequate insurance coverage for pain

management services,²⁸⁰ shortages of medical and behavioral pain management specialists,⁵ provider underestimation of patients' reports of pain,⁴⁵¹ poorly functioning drug supply systems,⁴⁵² lack of research on innovative and effective pain management approaches,²⁸ and — more recently — widespread fear among providers of regulatory scrutiny. The recent advent of retail pharmacies limiting

the duration of prescriptions, making unrequested changes to dosages, or placing barriers to obtaining properly prescribed pain medications has had the unintended consequence of limiting access to optimal pain care. Without such access, many patients face significant medical complications, prolonged suffering, and increased risk of psychiatric conditions.⁴⁵³ Medical complications from inadequately treated acute pain may include prolonged recovery time, unanticipated hospital readmissions, and transition to chronic and persistent pain.⁴⁵⁴ Unremitting and inadequately treated pain is also associated with increased anxiety, depression, disability, unemployment, and lost income.²⁹⁵

In addition to experiencing medical and psychiatric consequences, individuals who receive inadequate pain treatment may transition to illicit opioid or other substance misuse. Although the pathway to illicit substance use in pain is not well understood, a small but growing number of individuals who misuse prescription opioids without the supervision or oversight of a medical provider transition to using illicit substances, such as heroin, within a year of use.⁴⁵⁵ The nonmedical and illicit use of opioids may increase an individual's risk for substance use problems, accidental or intentional overdose, or death.⁴⁵⁶ Heroin, fentanyl, and other illicit synthetic opioids continue to drive increasing numbers of overdose deaths.⁹ Understanding the indicators associated with inappropriate opioid use may improve the ability of health care providers to tailor treatments and surveillance without placing arbitrary limitations on all patients who are prescribed opioids. This understanding could also potentially improve access to effective care.

There is a concern as to the definition of what an “outlier prescriber” is and to avoid arbitrary limitations without taking into account the provider expertise and the patient demographic. Careful consideration of how outliers will be defined is needed to avoid patient harm. Patient care should be based primarily on the clinical context and the patient-clinician interaction. Opioid stewardship programs can provide a holistic, efficient, comprehensive, multidisciplinary approach to address safer opioid prescribing within a health system, thus empowering cross-disciplinary collaboration and inclusion with the development of measures to guide implementation and successful efforts. Quality measures should include function, QOL, and ADL. CMS is currently implementing sections of the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act (SUPPORT Act). The SUPPORT Act requires CMS to convene a technical expert panel; make recommendations regarding quality measures for opioids; identify outlier prescribers and furnish technical support regarding proper prescribing practices; and implement minimum standards for states’ Drug Utilization Review programs regarding opioid prescribing, including safety edits on refills and daily dosage policies. It is essential to ensure that careful consideration of clinical context is always considered.

Medication Shortage

Shortages of pharmacologic and biological products, including opioid and non-opioid analgesics, can have severe and immediate consequences for patient care. Appropriate treatment can be delayed or denied because of unavailability and, in other cases, result in the use of second-line, less effective alternatives.^{457,458} Several underlying factors have contributed to national shortages, including manufacturing problems that affect the drug supply chain and quality control, as well as regulatory changes in response to the opioid overdose public health crisis.^{452,458} Tracking data from the FDA show that drug shortages peaked in 2011, with more than 250 new drug shortages, and although the number has steadily declined, 2017 saw 39 new shortages and a failure to adequately address existing shortages.⁴⁵⁸

Health care systems and providers, with clinical pharmacists, are responding to the drug shortages by identifying therapeutic alternatives and prioritizing supplies. Patient safety events — namely, medication errors — are more likely to occur during times of shortages because of the increased prescribing of less familiar pharmacologic agents.^{452,459} Use of compounded products or alternative preparations is a common underlying cause of errors.⁴⁶⁰ An investigation by the Institute for Safe Medication

Practices into shortage-related patient safety events cited that use of an alternative drug or alternative dosage form/strength of a substitute drug accounted for up to 27% of reported harmful outcomes.^{459,461} Advance notice of shortages, communication and education, consultation with clinical pharmacists, and standardized management algorithms help mitigate the effects of drug shortages. For instance, a retrospective chart review of patients admitted to the pediatric intensive care unit during a 2011- 2012 peak shortage of injectable benzodiazepines (e.g., midazolam, lorazepam, diazepam) and fentanyl reported no significant increase in rates of prescribing error and adverse patient outcomes because of well-established guidelines for prioritized and alternative analgesic and sedative management protocols.⁴⁶²

64 Current widespread shortages of several key parenteral opioids used for fast and reliable analgesic effects, including morphine, hydromorphone, and fentanyl, are affecting hospitals and cancer centers nationwide, leading to compromised acute pain management in the critical care and postoperative settings. Morphine, hydromorphone, and fentanyl are the most commonly used opioid injectables because of their fast and reliable analgesic effects and because they offer a viable option for patients unable to tolerate oral administration.^{452,457} Other potential analgesic shortages include the NSAIDs ketoprofen and ketorolac tromethamine, methocarbamol, methadone, promethazine, and remifentanyl. In July 2018, the FDA established the Agency Drug Shortages Task Force, charged with identifying the causes of medication shortages and proposing solutions. The results will be summarized in a report to Congress, informed

by input from the pharmaceutical and health care industries, patient representatives, the FDA's federal partners, and Congress.⁴⁶³

GAPS AND RECOMMENDATIONS

GAP 1: Recurrent shortages in opioid and non-opioid pain medications have created barriers to the proper treatment in patients with pain.

RECOMMENDATION 1A: The Task Force strongly supports the FDA's ongoing efforts to monitor, report, and prioritize the availability of key opioid and non-opioid medications, including injectables such as local anesthetic agents.

RECOMMENDATION 1B: The FDA should make available alternative sources for these medications when critical shortages are anticipated.

RECOMMENDATION 1C: Support the Agency Drug Shortages Task Force in its endeavors to find solutions to the critical challenges of drug shortages.

Insurance Coverage for Complex Management Situations

Patients with complex and persistent pain often experience barriers to care related to nonexistent or insufficient insurance coverage and reimbursement for evidence-based medical, behavioral, and complementary pain management services. Although the HHS National Pain Strategy calls for greater coverage for pain management services, there is a lack of uniformity in insurance coverage and lack of coverage alignment with current practice guidelines for pain management.^{280,464} This is particularly true for nonpharmacologic²⁸⁰ and behavioral health interventions.^{280,465}

The process for determining insurance coverage for pain management services is lengthy and complex, often requiring product testing, assessment against evidence-based protocols, determination of medical necessity, evidence-based coverage determination processes, and review by physician networks and stakeholders. Moreover, there is substantial variability in the availability and structure of guidance

regarding the data needed to qualify for coverage provided to developers working on innovative nonpharmacologic treatments.²⁸⁰ For example, CMS uses national coverage determinations (NCDs) to determine whether to cover a particular item or service. In the absence of a national coverage policy, an item or service may be covered at the discretion of the Medicare contractors based on a local coverage determination. Such practice leads to variation in coverage of items and services that can affect medical care. In addition, CMS requires testing of products in the Medicare-aged population for NCDs. Guidance to medication and product developers working on alternatives to opioids and opioid-sparing technologies; procedures concerning data needed to qualify for CMS coverage determinations; and innovation payments under CMS programs, especially for Medicare-eligible Americans in pain, is limited to basic statutory language. In contrast, the FDA provides extensive guidance on data needed to qualify for labeling for products like “abuse deterrent” medicines.

The inconsistencies in insurance policies, the variability in guidance regarding coverage determinations, and the variability in utilization management tools that coverage providers use can cause delays in service delivery, provision of inadequate treatment, and added financial and psychosocial burden for patients with pain.²⁹⁰ Requiring patients and health care professionals to navigate burdensome and variable coverage policies may contribute to slow development, adoption, and implementation of timely and effective pain treatments and may force providers to treat patients in a less-than-optimal fashion. Consistently forcing providers to try a series of non-first-line treatments prior to authorizing treatment plans can be problematic, hindering appropriate patient care, creating tremendous inefficiency, and resulting in a loss of time and resources. This situation is problematic when patients change insurance coverage, requiring a new set of preauthorization rules to be followed and potentially leading to delays in critical, ongoing treatment.⁴⁶⁴

GAPS AND RECOMMENDATIONS

GAP 1: Time and resources are insufficient for complex and safe opioid management.

RECOMMENDATION 1A: Reimburse complex opioid and non-opioid management consistent with the time and resources required for patient education; safe evaluation; risk assessment; reevaluation; and integration of alternative, non-opioid modalities.

RECOMMENDATION 1B: CMS and private payers should investigate and implement innovative payment models that recognize and reimburse holistic, integrated, multimodal pain management, including behavioral health.

GAP 2: Many pain-related payer guidelines are outdated with respect to current clinical practice guidelines.

RECOMMENDATION 2A: CMS and private payers should align their reimbursement guidelines for acute and chronic multidisciplinary pain management with current CPGs.

GAP 3: Payers often do not reimburse for non-opioid pharmacologic therapies that are more expensive than opioids, such as long-acting local anesthetic injection/infusion and intravenous acetaminophen analgesia.

RECOMMENDATION 3A: CMS and other payers should align their reimbursement guidelines for non-opioid pharmacologic therapies with current CPGs.

GAP 4: Coordinated, individualized, multidisciplinary care for chronic pain management is a best practice, yet this model of care is difficult to achieve with current payment models.

RECOMMENDATION 4A: Payers should reimburse pain management using a chronic disease management model. CMS and private payers should reimburse for integrative, multidisciplinary pain care by using a chronic disease management model similar to that currently used to reimburse for cardiac rehabilitation and diabetes chronic care management programs. In addition, reimburse care team leaders for time spent coordinating patient care. A CPT code should be developed for pain care coordination as well as team and group conferences to enable multidisciplinary care.

RECOMMENDATION 4B: Payers should reimburse for pain management in a manner that facilitates access in underserved locations through telehealth or other technology-assisted delivery methods.

Workforce

A 2011 IOM report highlighted the current shortage of pain management specialists, citing that for every physician who is board certified in pain care, there are more than 28,500 Americans living with chronic pain.⁵ As of August 2018, there were 2,300 American Board of Pain Medicine-certified pain specialists⁴⁶⁶ and 6,595 physicians certified in pain management by the American Board of Medical Specialties⁴⁶⁷; many of these physicians have both certifications. Pain management specialists possess expertise and are specially trained in the evaluation, diagnosis, and treatment of acute and chronic pain.⁴⁶⁸ Because of an inadequate number of specialized pain physicians, PCPs are tasked with managing the majority of patients with painful conditions, often without adequate time and resources.⁴⁶⁹ This indicates the need for an increase in the pain specialist workforce to support PCPs while also ensuring that specialists and PCPs have adequate time, incentives, and resources to manage patients with painful conditions. Likewise, access to behavioral pain management is limited because financial incentives are lacking for psychologists and other providers to specialize in pain. Many insurance programs do not reimburse for behavioral pain treatments, or they reimburse at a much lower rate than for pharmacologic or interventional treatments. Because of the lack of incentives, not enough providers are trained in behavioral pain management.^{281,284} Taken together, the severe shortage of pain medicine specialists and under-resourced and insufficiently trained PCPs treating pain along with insufficient access to behavioral therapists, pharmacists, and other members of the pain management team has hindered the development of efficient, cost-effective health care delivery models to treat chronic pain.^{5,15,470}

GAPS AND RECOMMENDATIONS

GAP 1: There is a shortage of clinicians who specialize in pain. These clinicians include pain physicians, addiction psychiatrists, psychologists, pharmacists, nurses, NPs, PAs, physical therapists, social workers, and others who make up a multidisciplinary pain management team. Furthermore, there is a shortage of multidisciplinary pain management teams to care for patients with complex pain conditions and physical and psychological comorbidities.

RECOMMENDATION 1A: Expand clinician training in acute, chronic, or end-of-life pain evaluation and treatment. Enhancements should be made in professional school curricula, postgraduate training programs, and continuing education courses.

RECOMMENDATION 1B: Expand postgraduate (e.g., residency, fellowship) positions to train clinicians as pain specialists, especially positions that train clinicians to work on multidisciplinary pain management teams.

RECOMMENDATION 1C: Expand the availability of clinician specialists, including physicians, NPs, PAs, nurses, physical and occupational therapists, psychologists, behavioral health specialists, and social workers.

RECOMMENDATION 1D: Encourage and incentivize the creation of multidisciplinary pain management teams and programs as centers of excellence, where patients with diverse and complex pain conditions as well as physical and psychological comorbidities can be managed effectively and investigated for optimal outcomes.

Research

Research is fundamental to advancing both the understanding and treatment of acute and chronic pain. The NIH Help to End Addiction Long-term (HEAL) initiative is a trans-NIH effort to improve prevention and treatment strategies for opioid misuse and addiction and to enhance pain management. Resources include governance and guidance as well as research and funding opportunities. NIH launched the Acute to Chronic Pain Signatures program to investigate the biological characteristics underlying the transition from acute to chronic pain and to look at mechanisms that make some people susceptible and others resilient to the development of chronic pain.

New knowledge development is needed in various areas of pain research, with emphasis placed on molecular and cellular mechanisms of pain, the genetics of pain, bio-behavioral pain, and preclinical models of pain.^{5,471} Supporting research initiatives throughout these fields across the basic science, translational, and clinical research arenas will aid in addressing current research gaps. This will lead to understanding the mechanisms of pain and SUD, translating promising advancements into effective therapies, and identifying best practices to implement in the management of acute and chronic pain. As novel and proven treatment options emerge to improve acute pain and specific chronic pain conditions, they should be rapidly incorporated.

GAPS AND RECOMMENDATIONS

GAP 1: Incentives for innovations in the treatment of chronic and acute pain are necessary for the advancement of treatment.

RECOMMENDATION 1A: Support public-private partnerships for improved funding to support and accelerate basic science, translational, and clinical research of pain and implementation research in health care systems. Allocate funding to develop innovative therapies and build research capabilities for better clinical outcomes tracking and evidence gathering.

GAP 2: Sex as a biological variable as well as genetic, epigenetic, and experiential factors in the progression of pain are not well understood.

RECOMMENDATION 2A: Improve understanding of the specific interplay of sex as a biological variable as well as genetic and experiential contributions to pain, including identification of biomarkers; factors that play a role in persistent pain and eventually chronic pain; the role of comorbid conditions; and predictive risk factors.

GAP 3: There is a lack of understanding of contributing factors that predispose certain patients to SUD and addiction.

RECOMMENDATION 3A: Further evaluate the lifelong risk factors for the development of SUD rather than the isolated evaluation of prescription opioid use (e.g., adolescent substance use, early-life trauma).

RECOMMENDATION 3B: Conduct research to identify biomarkers, genetic predisposition, epigenetic mechanisms, and other patient factors to assist in improved and accurate identification of those patients at risk for SUD.

GAP 4: There is a lack of research on and funding of potentially innovative modes of health care delivery and treatment.

RECOMMENDATION 4A: Increase research into novel strategies that target the underlying mechanisms of chronic pain, including pharmacologic and biologic research and development; medical devices; medication delivery systems; neuromodulation; regenerative medicine; and complementary and integrative health approaches, including movement-based modalities.

RECOMMENDATION 4B: Increase the level of research on accelerating the development and implementation of integrated pain care.

H. REVIEW OF THE CDC GUIDELINE

In 2016, in response to growing concerns about overprescribing opioids for pain management and opioid-related overdose, CDC published a widely read guideline on opioid therapy for chronic pain.¹²⁸ Their recommendations focus on the use of opioids in treating chronic pain in patients 18 years or age or older. The “CDC Guideline for Prescribing Opioids for Chronic Pain” is not intended for patients who are in active cancer treatment, palliative care, or end-of-life care.

It is important to note that CDC reports that the recent acceleration in deaths from opioid overdose is largely driven by illicit opioids as opposed to prescribed opioids.⁴⁷² Illicit fentanyl has been found in a growing number of toxicology studies of overdose decedents. Furthermore, given the current state of the overdose crisis, further drastic

reduction of clinician prescribing alone may not have a large effect on decreasing opioid overdose deaths in the short term.^{473,474}

The CDC Guideline provides useful general guidance for prescribing opioids that is primarily intended for primary care providers. Various organizations, such as the American College of Physicians, supported the guideline when it was initially released, but clinicians, patients, professional organizations, and other stakeholders have highlighted important limitations since its publication. A commentary by Busse et al.⁴⁷⁵ identified several limitations related to expert selection, evidence inclusion criteria, method of evidence quality grading, selective support of some recommendations with low-quality evidence, and instances of vague recommendations. CDC cited the lack of clinical trials with a duration of one year or longer as lack of evidence for sustained clinical effectiveness of opioids in chronic pain. The Task Force respectfully points out that there is little clinical trial evidence showing that opioids lack clinical efficacy for such patients. Furthermore, Tayeb et al.¹¹⁴ found that lack of long-term efficacy is true for all common medication and behavioral therapy studies. Long-term studies of therapies for chronic, moderate, or severe pain are difficult to conduct because of patient drop-out for ineffective treatment.⁴¹⁷ One long-term study from VA assessed patients on opioids versus non-opioid medications over a 12-month study evaluation period.¹¹³ Both groups showed similar changes in pain severity and pain-related function over 12 months. The authors conclude that the results of this study do not support initiation of opioid therapy alone for moderate to severe chronic back pain or hip or knee osteoarthritis pain.¹¹³ Noting that the CDC Guideline focused primarily on patients initiating opioid treatment, Gordon and Connolly⁴⁷⁶ discussed application of the guideline to patients who are already receiving opioid maintenance therapy for chronic pain. Given that chronic pain is associated with many different underlying conditions, with great patient variability in analgesic drug metabolism, risk for abuse, and underlying comorbid medical condition, further studies are needed to assess the value of long-term opioids alone and in combination with other therapies, coupled with risk assessment and periodic reevaluation (see Section 3.1: Risk Assessment).

The Task Force recognizes the utility of the 2016 CDC Guideline for many aspects of pain management and its value in mitigating adverse outcomes of opioid exposure. Unfortunately, misinterpretation, in addition to gaps in the guideline, has led to unintended adverse consequences. Our report documented widespread misinterpretation of the CDC Guideline — specifically, the recommendation regarding the 90 morphine milligram equivalents (MME) dose. In November 2018, the American Medical Association issued a statement advocating against the misapplication of the CDC Guideline.⁴⁷⁷ Educating stakeholders about the intent and optimal application of this guideline and re-emphasis of its core beneficial aspects are essential. Instances have been reported where the CDC Guideline was misapplied to the palliative care and cancer populations with pain and to providers who care for these patient populations. It is important to recognize the need for an individualized approach to palliative care and cancer patients with pain, a population that typically requires higher doses of opioids for pain relief and function, often for long periods.^{306,355} The American Society of Clinical Oncology, the American Society of Hematology, and the National Comprehensive Cancer Network recently received a key clarification letter from the CDC (February 2019) that the guideline was developed to provide recommendations for primary care clinicians who prescribe opioids for patients with chronic pain outside of active cancer treatment, palliative care, and end-of-life care, and the guideline is not intended to deny clinically appropriate opioid therapy to any patients who suffer acute or chronic pain from conditions such as cancer and sickle cell disease.⁴⁷⁸

The 2016 CDC Guideline, which provided a comprehensive synthesis of scientific evidence on opioid prescribing, was intended as a tool primarily for PCPs to help inform their decisions about managing pain with opioids and to encourage dialogue and discussion of risks between providers and patients (shared decision making).¹ Although the CDC Guideline was not intended to be model legislation, at least 28 states have gone beyond the guidelines and enacted legislation related to opioid prescription limits. As a result, such unintended consequences have led health care providers to limit or not provide pain treatment due in part to concerns and undue burdens of investigation and prosecution by drug enforcement.¹⁸ Furthermore, many states and organizations

have implemented the guideline without recognizing that the intended audience was PCPs; have used legislation to override what should be medical decision making by health care professionals; and have applied them to all physicians, dentists, NPs, and PAs, including pain specialists.^{479–482} Some stakeholders have interpreted the guideline as intended to broadly reduce the amount of opioids prescribed for treating pain; some experts have noted that the guideline emphasizes the risk of opioids while minimizing the benefit of this medication class when properly managed.⁴⁸³

A major problematic unintended consequence of the guideline is the forced tapering, medication discontinuation, or abandonment that many patients with chronic pain on stable long-term doses of opioids have experienced.⁴⁸⁴ CDC published a pivotal article in *New England Journal of Medicine* on April 24, 2019, specifically reiterating that the CDC Guideline has been, in some instances, misinterpreted or misapplied. The authors highlight that the dose recommendations in the CDC Guideline do not address or suggest discontinuation of opioids prescribed at higher dosages. They note “policies invoking the opioid-prescribing guideline that do not actually reflect its content and nuances can be used to justify actions contrary to the guideline’s intent.”¹ This conclusion is supported by the comments the Task Force has received indicating that many patients have experienced access issues related to provider fears and concerns with how the guideline would be interpreted and have caused some to consider obtaining opioids from illicit sources or suicide (see Section 3.2: Stigma). The FDA recently issued a safety announcement recognizing harm reported from sudden discontinuation of opioid pain medicines, including serious withdrawal symptoms, uncontrolled pain, psychological distress, and suicide. They are requiring label changes to guide prescribers on gradual, individualized tapering.⁴⁸⁵ PCPs should be encouraged to refer to or seek input from pain specialists and (potentially) addiction specialists in complex or high-risk patient scenarios (see Section 2.5: Behavioral Health Approaches). In the expert opinion of the Task Force members, the CDC Guideline does not sufficiently emphasize that optimal pain management begins with identification of the cause of the pain and the biopsychosocial mechanisms that contribute to its severity and associated disability⁴⁸⁶

The CDC Guideline recommends that opioids prescribed for acute pain be limited to three or fewer days and that more than a seven-day supply is rarely necessary.¹²⁸ Various health insurance plans, retail pharmacies, and local and state governments are implementing the CDC Guideline as policy, limiting the number of days a patient can receive prescription opioids even when the seriousness of the injury or surgery may require opioids for adequate pain management for a longer period. A more even-handed approach would balance addressing opioid overuse with the need to protect the patient-provider relationship by preserving access to medically necessary drug regimens and reducing the potential for unintended consequences.⁴⁸⁷ The vast majority of medical organizations, in response to the 90-day public comment period to the Task Force draft report, supported this balanced approach. Policies should help ensure safe prescribing practices, minimize workflow disruption, and ensure that beneficiaries have access to their medications in a timely manner, without additional, cumbersome documentation requirements.⁴⁸⁷ In essence, clinicians should be able to use their clinical judgement to determine opioid duration for their patients while considering risk assessment recommendations as discussed in Section 3.1: Risk Assessment. Safe opioid stewardship involves a proper history and examination, periodic reevaluation, and risk assessment, with a focus on measurable outcomes, including function, QOL, and ADLs.

Recommendations noted in this section are organized into two groups:

UPDATE: Requires updated scientific evidence since the release of the CDC Guideline in March 2016.

EMPHASIZE OR EXPAND: Refers to content already in the CDC Guideline or areas to expand on.

UPDATE

1: There is an absence of high-quality data on the duration of opioid effectiveness for chronic pain, which has been interpreted as a lack of benefit.

RECOMMENDATION 1A: Support studies to determine the long-term efficacy of opioids in the treatment of chronic pain syndromes (primary and secondary) in different populations as determined by clinical context, clinical conditions, and comorbidities.

RECOMMENDATION 1B: Conduct clinical trials on specific disease entities, with a focus on patient variability and response to tissue injury and on the effectiveness of opioid analgesics. Design trials to be applicable in real-world settings (e.g., patients receiving trialed opioid medications while maintaining the usual multimodal therapy).

2: There is an absence of criteria for identifying the sub-population of patients for whom opioids may contribute significantly to improve their pain management and therefore their QOL and functionality.

RECOMMENDATION 2: Conduct clinical studies or complete systematic reviews to identify which chronic pain conditions and patient characteristics are appropriate for long-term opioid treatment in conjunction with the various non-opioid modalities.

EMPHASIZE OR EXPAND

3: There is wide variation in patient and disease factors that determine the dose of opioids that is optimal for pain relief and minimizes risk.

RECOMMENDATION 3A: Consider patient variables that may affect opioid dose in patients prior to initiation of opioid therapy, including respiratory compromise, individual patient metabolic variables, or differences between opioid medications that could affect plasma opioid concentrations.

RECOMMENDATION 3B: Perform comprehensive initial assessments for patient management, with an understanding of the need for periodic comprehensive reevaluation to adjust the medication dose.

RECOMMENDATION 3C: Careful consideration should be given to patients on an opioid pain regimen who have additional risk factors for OUD (see Section 3.1: Risk Assessment).

RECOMMENDATION 3D: The CDC Guideline, meant for primary care clinicians, should explicitly reemphasize that the 90 MME/day maximum dose recommendation is not mandatory but is a target that may be exceeded if clinically appropriate when benefits outweigh risks.

4: Specific guidelines addressing opioid tapering and escalation need further elucidation.

RECOMMENDATION 4A: Undertake opioid tapering or escalation only after a thorough assessment of the risk-benefit ratio. This assessment should be conducted in collaboration with the patient.

RECOMMENDATION 4B: Develop guidelines for tapering and dose escalation for the sub-populations of patients who have chronic pain conditions that includes consideration of their comorbidities.

RECOMMENDATION 4C: Consider maintaining therapy for patients who are stable on long-term opioid therapy and for whom the benefits outweigh the risks.

5: Multiple potential causes of worsening pain are often not recognized or considered. Nontolerance-related factors include iatrogenic causes such as surgery, flares of the underlying disease or injury, and increased ergonomic demands or emotional distress.

RECOMMENDATION 5A: When a stable dose has been established for at least two months, avoid increases in the dose until the patient has been reevaluated for the underlying causes of elevated pain or possible OUD risk.

RECOMMENDATION 5B: Considerations to avoid dose escalation should include opioid rotation, non-opioid medications, interventional strategies, cognitive behavioral strategies, complementary and integrative health approaches, and PT.

6: Although the risk of overdose by benzodiazepine co-prescription with opioids is well established, this combination may still have clinical value in patients who have chronic pain and comorbid anxiety, which commonly accompanies pain, and in patients who

have chronic pain and spasticity. However, initiating regular long-term use of benzodiazepines with opioids should be done with caution, because SSRIs, SNRIs, and psychotherapies are preferred treatments for anxiety disorders. (See Section 2.2: Medications for further discussion about anxiolytics as well as treatment of anxiety and chronic pain.)

RECOMMENDATION 6A: If clinically indicated, co-prescription should be managed and coordinated by physicians and clinician specialists who have knowledge, training, and experience in co-prescribing benzodiazepines with opioids. For those patients who have anxiety disorders or SUD who have been prescribed benzodiazepines, risk mitigation strategies and counseling, collaboration with experts in mental health, and the use of psychological modalities should be considered.

RECOMMENDATION 6B: Develop CPGs that focus on tapering for co-prescription of benzodiazepines and opioids.

7: The variability in effectiveness and safety (respiratory depression and abuse liability) at any given dose of an opioid is not clearly defined and may vary between different opioids and different patients. **Consequently, the risk-benefit balance for opioid management of pain may vary for individual patients.** Similarly, the balance of benefit and risk for doses above 90 MME/day may be acceptable in some patients. Failure to closely monitor patients when opioid dose is adjusted puts them at risk for either inadequate pain control or overdose toxicity.

RECOMMENDATION 7A: Use the lowest effective opioid dose and shortest duration appropriate for the pain condition that balances benefits, risks, and adverse reactions. Clinicians should individualize dose based on a carefully monitored medication trial. With each dose adjustment patients should be assessed at expected peak drug concentration for analgesic effectiveness and adverse effects, such as respiratory compromise and sedation.

RECOMMENDATION 7B: Additional factors influence risk and benefit that should be considered; therefore, guidance regarding dose should not be applied as strict limits.

Providers should use established and measurable goals such as functionality, ADLs, and QOL measures.

8: The duration of pain following an acute, severely painful event such as trauma, surgery, or burn is widely variable. For clarity, the CDC Guideline recommendation #6 refers to acute pain that is non-surgical, non-traumatic pain.

RECOMMENDATION 8A: Appropriate duration of therapy is best considered within guidelines, and then ultimately determined by the treating clinician. The CDC recommendation for duration of treatment should be emphasized as guidance only for a general approach, with individualized patient care as the primary goal, and the clinician then considering all modalities for best outcomes.

RECOMMENDATION 8B: Develop and/or update acute pain management guidelines for common surgical procedures and trauma management, as noted in Section 2.1.1: Acute and Chronic Pain, Recommendation 2a.

RECOMMENDATION 8C: To address this variability and provide an easy solution to the challenges of medication duration, consideration should be given to a partial refill system.

End of the course!

References For Chapter 3

1. Dowell D, Haegerich T, Chou R. No Shortcuts to Safer Opioid Prescribing. *N Engl J Med*. April 2019. doi:10.1056/NEJMp1904190
2. National Institute on Drug Abuse. Drugs, Brains, and Behavior: The Science of Addiction. <https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/preface>. Published 2018.

3. National Institute on Drug Abuse. Misuse of Prescription Drugs.
<https://www.drugabuse.gov/publications/misuse-prescription-drugs/overview>.
Published 2018.
4. American Society of Addiction Medicine. Public Policy Statement: Short Definition of Addiction. 2011. https://www.asam.org/docs/default-source/public-policy-statements/1definition_of_addiction_short_4-11.pdf?sfvrsn=6e36cc2_0.
5. Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington (DC): National Academies Press (US); 2011. <http://www.ncbi.nlm.nih.gov/books/NBK91497/>. Accessed January 7, 2018.
6. Dahlhamer J, Lucas J, Zelaya C, et al. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults - United States, 2016. *MMWR Morb Mortal Wkly Rep*. 2018;67(36):1001-1006. doi:10.15585/mmwr.mm6736a2
7. Gaskin DJ, Richard P. The economic costs of pain in the United States. *J Pain Off J Am Pain Soc*. 2012;13(8):715- 724. doi:10.1016/j.jpain.2012.03.009
8. National Academies. *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use*. Washington DC: National Academies of Sciences, Engineering, and Medicine.; 2017.
9. Ahmad F, Rossen L, Spencer M, Warner M, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>. Published 2018. Accessed August 31, 2018.
10. Max M, Donovan M, Miaskowski C. Quality improvement guidelines for the treatment of acute pain and cancer pain. American Pain Society Quality of Care Committee. *JAMA*. 1995;274(23):1874-1880.
11. Mularski RA, White-Chu F, Overbay D, Miller L, Asch SM, Ganzini L. Measuring pain as the 5th vital sign does not improve quality of pain management. *J Gen Intern Med*. 2006;21(6):607-612. doi:10.1111/j.1525-1497.2006.00415.x

12. Borg H. Electronic health records: agenda-based medicine. *J Am Physicians Surg.* 2017;22(2):48-54.
13. Huntoon L. The Disaster of Electronic Health Records. *J Am Physicians Surg.* 2016;21(2):35-37.
14. Shanafelt TD, Dyrbye LN, Sinsky C, et al. Relationship Between Clerical Burden and Characteristics of the Electronic Environment With Physician Burnout and Professional Satisfaction. *Mayo Clin Proc.* 2016;91(7):836-848.
doi:10.1016/j.mayocp.2016.05.007
15. Lippe PM, Brock C, David J, Crossno R, Gitlow S. The First National Pain Medicine Summit--final summary report. *Pain Med Malden Mass.* 2010;11(10):1447-1468.
doi:10.1111/j.1526-4637.2010.00961.x
16. Guy GP, Zhang K, Bohm MK, et al. Vital Signs: Changes in Opioid Prescribing in the United States, 2006–2015. *MMWR Morb Mortal Wkly Rep.* 2017;66(26):697-704.
doi:10.15585/mmwr.mm6626a4
17. U.S. Department of Health and Human Services. 5-Point Strategy To Combat the Opioid Crisis. [HHS.gov/opioids. https://www.hhs.gov/opioids/about-the-epidemic/hhs-response/index.html](https://www.hhs.gov/opioids/about-the-epidemic/hhs-response/index.html). Published August 7, 2018. Accessed October 21, 2018.
18. Comerci G, Katzman J, Duhigg D. Controlling the Swing of the Opioid Pendulum. *N Engl J Med.* 2018;378(8):691- 693. doi:10.1056/NEJMp1713159
19. Centers for Disease Control and Prevention. Rising Numbers of Deaths Involving Fentanyl and Fentanyl Analogs, Including Carfentanil, and Increased Usage and Mixing with Non-opioids. <https://emergency.cdc.gov/han/HAN00413.asp>. Published 2018. Accessed December 1, 2018.
20. Mackey TK. Opioids and the Internet: Convergence of Technology and Policy to Address the Illicit Online Sales of Opioids. *Health Serv Insights.* 2018;11:1178632918800995. doi:10.1177/1178632918800995

21. Martin J, Cunliffe J, Décary-Héту D, Aldridge J. Effect of restricting the legal supply of prescription opioids on buying through online illicit marketplaces: interrupted time series analysis. *BMJ*. 2018;361:k2270.
22. Hedegaard H, Warner M, Minino AM. Drug Overdose Deaths in the United States, 1999-2015. *NCHS Data Brief*. 2017;(273):1-8.
23. Petrosky E, Harpaz R, Fowler KA, et al. Chronic Pain Among Suicide Decedents, 2003 to 2014: Findings From the National Violent Death Reporting System. *Ann Intern Med*. September 2018. doi:10.7326/M18-0830
24. Substance Abuse and Mental Health Services Administration. *National Survey on Drug Use and Health*. Substance Abuse and Mental Health Services Administration; 2017. <https://www.samhsa.gov/data/nsduh/reports-detailed-tables-2017-NSDUH>.
25. 114th Congress. *Comprehensive Addiction and Recovery Act of 2016*.; 2016. <https://www.govtrack.us/congress/bills/114/s524>.
26. Fishman SM, Young HM, Lucas Arwood E, et al. Core competencies for pain management: results of an interprofessional consensus summit. *Pain Med Malden Mass*. 2013;14(7):971-981. doi:10.1111/pme.12107
27. 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*. Washington (DC): National Academies Press (US); 2017. <http://www.ncbi.nlm.nih.gov/books/NBK423845/>. Accessed April 24, 2019.
28. Gereau RW, Sluka KA, Maixner W, et al. A pain research agenda for the 21st century. *J Pain Off J Am Pain Soc*. 2014;15(12):1203-1214. doi:10.1016/j.jpain.2014.09.004

29. Fishman SM, Carr DB, Hogans B, et al. Scope and Nature of Pain- and Analgesia-Related Content of the United States Medical Licensing Examination (USMLE). *Pain Med Malden Mass*. 2018;19(3):449-459. doi:10.1093/pm/pnx336
30. Weinberg EL, Baer PA. Inconsistencies in the 2017 Canadian Guideline for Opioids for Chronic Noncancer Pain. *CMAJ Can Med Assoc J J Assoc Medicale Can*. 2017;189(39):E1233. doi:10.1503/cmaj.733244
31. Centers for Disease Control and Prevention. *Guideline for Prescribing Opioids for Chronic Pain*. Washington, DC: US Department of Health and Human Services; 2016.
32. U.S. Department of Veterans Affairs, U.S. Department of Defense. *Management of Opioid Therapy (OT) for Chronic Pain (2017) - VA/DoD Clinical Practice Guidelines*; 2017. <https://www.healthquality.va.gov/guidelines/Pain/cot/>. Accessed October 25, 2017.
33. Barth KS, Guille C, McCauley J, Brady KT. Targeting practitioners: A review of guidelines, training, and policy in pain management. *Drug Alcohol Depend*. 2017;173 Suppl 1:S22-S30. doi:10.1016/j.drugalcdep.2016.08.641
34. Carr DB. Evidence-Based Pain Medicine: Inconvenient Truths. *Pain Med Malden Mass*. October 2017. doi:10.1093/pm/pnx252
35. Deng Y, Luo L, Hu Y, Fang K, Liu J. Clinical practice guidelines for the management of neuropathic pain: a systematic review. *BMC Anesthesiol*. 2016;16:12. doi:10.1186/s12871-015-0150-5
36. Thieme K, Mathys M, Turk DC. Evidenced-Based Guidelines on the Treatment of Fibromyalgia Patients: Are They Consistent and If Not, Why Not? Have Effective Psychological Treatments Been Overlooked? *J Pain Off J Am Pain Soc*. 2017;18(7):747-756. doi:10.1016/j.jpain.2016.12.006
37. Broida RI, Gronowski T, Kalnow AF, Little AG, Lloyd CM. State Emergency Department Opioid Guidelines: Current Status. *West J Emerg Med*. 2017;18(3):340-344. doi:10.5811/westjem.2016.12.30854

38. Carlson CL. Effectiveness of the World Health Organization cancer pain relief guidelines: an integrative review. *J Pain Res.* 2016;9:515-534. doi:10.2147/JPR.S97759
39. Gatchel RJ, McGeary DD, McGeary CA, Lippe B. Interdisciplinary chronic pain management: past, present, and future. *Am Psychol.* 2014;69(2):119-130. doi:10.1037/a0035514
40. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull.* 2007;133(4):581-624. doi:10.1037/0033-2909.133.4.581
41. Staats PS, Hekmat H, Staats AW. The psychological behaviorism theory of pain: A basis for unity. *Pain Forum.* 1996;5(3):194-207. doi:10.1016/S1082-3174(96)80031-6
42. Gatchel RJ, Okifuji A. Evidence-based scientific data documenting the treatment and cost-effectiveness of comprehensive pain programs for chronic nonmalignant pain. *J Pain Off J Am Pain Soc.* 2006;7(11):779-793. doi:10.1016/j.jpain.2006.08.005
43. Oslund S, Robinson RC, Clark TC, et al. Long-term effectiveness of a comprehensive pain management program: strengthening the case for interdisciplinary care. *Proc Bayl Univ Med Cent.* 2009;22(3):211-214.
44. Stanos S. Focused review of interdisciplinary pain rehabilitation programs for chronic pain management. *Curr Pain Headache Rep.* 2012;16(2):147-152. doi:10.1007/s11916-012-0252-4
45. Takahashi N, Kasahara S, Yabuki S. Development and implementation of an inpatient multidisciplinary pain management program for patients with intractable chronic musculoskeletal pain in Japan: preliminary report. *J Pain Res.* 2018;11:201-211. doi:10.2147/JPR.S154171
46. Turk D, Swanson K. Efficacy and cost-effectiveness treatment of chronic pain: An analysis and evidence-based synthesis. In: *Chronic Pain Management: Guidelines for Multidisciplinary Program Development.* New York, NY: Informa Healthcare; 2007:15-38.

47. Weiner SS, Nordin M. Prevention and management of chronic back pain. *Best Pract Res Clin Rheumatol*. 2010;24(2):267-279. doi:10.1016/j.berh.2009.12.001
48. Gallagher RM. Advancing the Pain Agenda in the Veteran Population. *Anesthesiol Clin*. 2016;34:357-378. doi:10.1016/j.anclin.2016.01.003
49. U.S. Department of Health and Human Services. *National Pain Strategy*. Washington, DC: US Department of Health and Human Services; 2016.
https://iprcc.nih.gov/sites/default/files/HHSNational_Pain_Strategy_508C.pdf.
50. Cheatle MD. Biopsychosocial Approach to Assessing and Managing Patients with Chronic Pain. *Med Clin North Am*. 2016;100(1):43-53. doi:10.1016/j.mcna.2015.08.007
51. Booth J, Moseley GL, Schiltenswolf M, Cashin A, Davies M, Hübscher M. Exercise for chronic musculoskeletal pain: A biopsychosocial approach. *Musculoskeletal Care*. March 2017. doi:10.1002/msc.1191
52. Kamper SJ, Apeldoorn AT, Chiarotto A, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain: Cochrane systematic review and meta-analysis. *BMJ*. 2015;350:h444.
53. Marin TJ, Van Eerd D, Irvin E, et al. Multidisciplinary biopsychosocial rehabilitation for subacute low back pain. *Cochrane Database Syst Rev*. 2017;6:CD002193. doi:10.1002/14651858.CD002193.pub2
54. Bruce RD, Merlin J, Lum PJ, et al. 2017 HIVMA of IDSA Clinical Practice Guideline for the Management of Chronic Pain in Patients Living With HIV. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2017;65(10):e1-e37. doi:10.1093/cid/cix636
55. Free MM. Cross-cultural conceptions of pain and pain control. *Proc Bayl Univ Med Cent*. 2002;15(2):143-145.
- 56.
57. Kent ML, Tighe PJ, Belfer I, et al. The ACTION–APS– AAPM Pain Taxonomy (AAAPT) Multidimensional Approach to Classifying Acute Pain

Conditions. *Pain Med Off J Am Acad Pain Med*. 2017;18(5):947-958.
doi:10.1093/pm/pnx019

58. 57. Tighe P, Buckenmaier CC, Boezaart AP, et al. Acute Pain Medicine in the United States: A Status Report. *Pain Med Malden Mass*. 2015;16(9):1806-1826.

59. 58. Bonnet CS, Walsh DA. Osteoarthritis, angiogenesis and inflammation. *Rheumatol Oxf Engl*. 2005;44(1):7-16. doi:10.1093/rheumatology/keh344

60. 59. Artemiadis AK, Zis P. Neuropathic Pain in Acute and Subacute Neuropathies: A Systematic Review. *Pain Physician*. 2018;21(2):111-120.

61. 60. Suri P, Saunders KW, Von Korff M. Prevalence and Characteristics of Flare-ups of Chronic Non-specific Back Pain in Primary Care: A Telephone Survey. *Clin J Pain*. 2012;28(7):573-580. doi:10.1097/ AJP.0b013e31823ae173

62. 61. Matthie N, Ross D, Sinha C, Khemani K, Bakshi N, Krishnamurti L. A Qualitative Study of Chronic Pain and Self-Management in Adults with Sickle Cell Disease. *J Natl Med Assoc*. September 2018. doi:10.1016/j. jnma.2018.08.001

63. 62. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S. Pathophysiology of Migraine: A Disorder of Sensory Processing. *Physiol Rev*. 2017;97(2):553-622. doi:10.1152/physrev.00034.2015

64. 63. Jawahar R, Oh U, Yang S, Lapane KL. A systematic review of pharmacological pain management in multiple sclerosis. *Drugs*. 2013;73(15):1711-1722. doi:10.1007/ s40265-013-0125-0

65. 64. Renton T. Dental (Odontogenic) Pain. *Rev Pain*. 2011;5(1):2-7. doi:10.1177/204946371100500102

66. 65. Bruehl S. Complex regional pain syndrome. *BMJ*. 2015;351:h2730.

67. 66. Upp J, Kent M, Tighe PJ. The evolution and practice of acute pain medicine. *Pain Med Malden Mass*. 2013;14(1):124-144. doi:10.1111/pme.12015

68. 67. Wardhan R, Chelly J. Recent advances in acute pain management: understanding the mechanisms of acute pain, the prescription of opioids, and the role of multimodal pain therapy. *F1000Research*. 2017;6:2065. doi:10.12688/f1000research.12286.1
69. 68. Brummett CM, Waljee JF, Goesling J, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. *JAMA Surg*. 2017;152(6):e170504. doi:10.1001/jamasurg.2017.0504
70. 69. American Society of Anesthesiologists. Patients Benefit From Enhanced Recovery Programs: Are Better Prepared for Surgery, Have Less Pain, Studies Show. <https://www.asahq.org/about-asahq/newsroom/news-releases/2016/10/patients-benefit-from-enhanced-recovery-programs>. Published 2016. Accessed April 24, 2019.
71. 70. American Society of Anesthesiologists. The Perioperative Surgical Home. 2014. <https://www.asahq.org/about-asahq/newsroom/news-releases/2016/10/patients-benefit-from-enhanced-recovery-programs>.
72. 71. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain*. 2016;17(2):131-157. doi:10.1016/j.jpain.2015.12.008
73. 72. Coluzzi F, Bifulco F, Cuomo A, et al. The challenge of perioperative pain management in opioid-tolerant patients. *Ther Clin Risk Manag*. 2017;13:1163-1173. doi:10.2147/TCRM.S141332
74. 73. Darnall BD, Sturgeon JA, Kao M-C, Hah JM, Mackey SC. From Catastrophizing to Recovery: a pilot study of a single-session treatment for pain catastrophizing. *J Pain Res*. 2014;7:219-226. doi:10.2147/JPR.S62329
75. 74. Dindo L, Zimmerman MB, Hadlandsmayth K, et al. Acceptance and Commitment Therapy for Prevention of Chronic Postsurgical Pain and Opioid

Use in At-Risk Veterans: A Pilot Randomized Controlled Study. *J Pain Off J Am Pain Soc*. May 2018. doi:10.1016/j.jpain.2018.04.016

76. Doering LV, McGuire A, Eastwood J-A, et al. Cognitive behavioral therapy for depression improves pain and perceived control in cardiac surgery patients. *Eur J Cardiovasc Nurs J Work Group Cardiovasc Nurs Eur Soc Cardiol*. 2016;15(6):417-424. doi:10.1177/1474515115592292
77. Riddle DL, Keefe FJ, Nay WT, McKee D, Attarian DE, Jensen MP. Pain coping skills training for patients with elevated pain catastrophizing who are scheduled for knee arthroplasty: a quasi-experimental study. *Arch Phys Med Rehabil*. 2011;92(6):859-865. doi:10.1016/j.apmr.2011.01.003
78. Khan TW, Manion S. Perioperative Surgical Home for the Patient with Chronic Pain. *Anesthesiol Clin*. 2018;36(2):281-294. doi:10.1016/j.anclin.2018.01.011
79. Reuben DB, Alvanzo AAH, Ashikaga T, et al. National Institutes of Health Pathways to Prevention Workshop: the role of opioids in the treatment of chronic pain. *Ann Intern Med*. 2015;162(4):295-300. doi:10.7326/M14-2775
80. Sutherland AM, Nicholls J, Bao J, Clarke H. Overlaps in pharmacology for the treatment of chronic pain and mental health disorders. *Prog Neuropsychopharmacol Biol Psychiatry*. 2018;87(Pt B):290-297. doi:10.1016/j.pnpbp.2018.07.017
81. Todd KH. A Review of Current and Emerging Approaches to Pain Management in the Emergency Department. *Pain Ther*. 2017;6(2):193-202. doi:10.1007/s40122-017-0090-5
82. Kaye AD, Cornett EM, Hart B, et al. Novel Pharmacological Nonopioid Therapies in Chronic Pain. *Curr Pain Headache Rep*. 2018;22(4):31. doi:10.1007/s11916-018-0674-8
83. Knezevic NN, Yekkirala A, Yaksh TL. Basic/ Translational Development of Forthcoming Opioid-and Nonopioid-Targeted Pain Therapeutics. *Anesth Analg*. 2017;125(5):1714-1732. doi:10.1213/ANE.0000000000002442

84. Nicol AL, Hurley RW, Benzon HT. Alternatives to Opioids in the Pharmacologic Management of Chronic Pain Syndromes: A Narrative Review of Randomized, Controlled, and Blinded Clinical Trials. *Anesth Analg*. 2017;125(5):1682-1703. doi:10.1213/ ANE.0000000000002426
85. Hooten W, Timming R, Belgrade M, et al. Assessment and Management of Chronic Pain. *Inst Clin Syst Improv*. November 2013:106.
86. Kapur BM, Lala PK, Shaw JLV. Pharmacogenetics of chronic pain management. *Clin Biochem*. 2014;47(13- 14):1169-1187. doi:10.1016/j.clinbiochem.2014.05.065
87. Staats P, Wallace M. *Just the Facts: Pain Medicine*. 2nd ed. New York, NY: McGraw-Hill; 2015.
88. Major JM, Zhou EH, Wong H-L, et al. Trends in rates of acetaminophen-related adverse events in the United States. *Pharmacoepidemiol Drug Saf*. 2016;25(5):590-598. doi:10.1002/pds.3906
89. Beal BR, Wallace MS. An Overview of Pharmacologic Management of Chronic Pain. *Med Clin North Am*. 2016;100(1):65-79. doi:10.1016/j.mcna.2015.08.006
90. Wiffen PJ, Derry S, Moore RA, et al. Antiepileptic drugs for neuropathic pain and fibromyalgia - an overview of Cochrane reviews. *Cochrane Database Syst Rev*. 2013;(11):CD010567. doi:10.1002/14651858. CD010567.pub2
91. Evoy KE, Morrison MD, Saklad SR. Abuse and Misuse of Pregabalin and Gabapentin. *Drugs*. 2017;77(4):403-426. doi:10.1007/s40265-017-0700-x
92. Lunn MPT, Hughes RAC, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. *Cochrane Database Syst Rev*. 2014;(1):CD007115. doi:10.1002/14651858.CD007115.pub3
93. Fava GA, Benasi G, Lucente M, Offidani E, Cosci F, Guidi J. Withdrawal Symptoms after Serotonin-Noradrenaline Reuptake Inhibitor Discontinuation: Systematic Review. *Psychother Psychosom*. 2018;87(4):195-203. doi:10.1159/000491524

94. Sun C, Hollenbach KA, Cantrell FL. Trends in carisoprodol abuse and misuse after regulatory scheduling: a retrospective review of California poison control calls from 2008 to 2015. *Clin Toxicol Phila Pa*. 2018;56(7):653-655.
doi:10.1080/15563650.2017.1414950
95. Von Korff M, Crane P, Lane M, et al. Chronic spinal pain and physical-mental comorbidity in the United States: results from the national comorbidity survey replication. *Pain*. 2005;113(3):331-339. doi:10.1016/j.pain.2004.11.010
96. Demyttenaere K, Bruffaerts R, Lee S, et al. Mental disorders among persons with chronic back or neck pain: results from the World Mental Health Surveys. *Pain*. 2007;129(3):332-342. doi:10.1016/j.pain.2007.01.022
97. Reddy S, Patt RB. The benzodiazepines as adjuvant analgesics. *J Pain Symptom Manage*. 1994;9(8):510-514.
98. Sun E, Dixit A, Humphreys K, Darnall B, Baker L, Mackey S. Association between concurrent use of prescription opioids and benzodiazepines and overdose: retrospective analysis. *BMJ*. 2017;356:j760.
99. Jann M, Kennedy WK, Lopez G. Benzodiazepines: a major component in unintentional prescription drug overdoses with opioid analgesics. *J Pharm Pract*. 2014;27(1):5-16. doi:10.1177/0897190013515001
100. Jones JD, Mogali S, Comer SD. Polydrug abuse: a review of opioid and benzodiazepine combination use. *Drug Alcohol Depend*. 2012;125(1-2):8-18.
doi:10.1016/j.drugalcdep.2012.07.004
101. National Institute on Drug Abuse. Benzodiazepines and Opioids. Drugs of Abuse. <https://www.drugabuse.gov/drugs-abuse/opioids/benzodiazepines-opioids>. Published March 2018. Accessed November 30, 2018.
102. Bandelow B, Michaelis S, Wedekind D. Treatment of anxiety disorders. *Dialogues Clin Neurosci*. 2017;19(2):93-107.

103. Kaczurkin AN, Foa EB. Cognitive-behavioral therapy for anxiety disorders: an update on the empirical evidence. *Dialogues Clin Neurosci*. 2015;17(3):337-346.
104. Patel R, Dickenson AH. Mechanisms of the gabapentinoids and $\alpha 2 \delta$ - calcium channel subunit in neuropathic pain. *Pharmacol Res Perspect*. 2016;4(2). doi:10.1002/prp2.205
105. Reed K, Day E, Keen J, Strang J. Pharmacological treatments for drug misuse and dependence. *Expert Opin Pharmacother*. 2015;16(3):325-333. doi:10.1517/14656566.2015.983472
106. Ahn JS, Lin J, Ogawa S, et al. Transdermal buprenorphine and fentanyl patches in cancer pain: a network systematic review. *J Pain Res*. 2017;10:1963- 1972. doi:10.2147/JPR.S140320
107. Fields HL, Margolis EB. Understanding opioid reward. *Trends Neurosci*. 2015;38(4):217-225. doi:10.1016/j.tins.2015.01.002
108. Schmid CL, Kennedy NM, Ross NC, et al. Bias Factor and Therapeutic Window Correlate to Predict Safer Opioid Analgesics. *Cell*. 2017;171(5):1165-1175.e13. doi:10.1016/j.cell.2017.10.035
109. Jalal H, Buchanich JM, Roberts MS, Balmert LC, Zhang K, Burke DS. Changing dynamics of the drug overdose epidemic in the United States from 1979 through 2016. *Science*. 2018;361(6408). doi:10.1126/science.aau1184
110. Warner M, Trinidad JP, Bastian BA, Minino AM, Hedegaard H. Drugs Most Frequently Involved in Drug Overdose Deaths: United States, 2010-2014. *Natl Vital Stat Rep Cent Dis Control Prev Natl Cent Health Stat Natl Vital Stat Syst*. 2016;65(10):1-15.
111. Kuczyńska K, Grzonkowski P, Kacprzak Ł, Zawilska JB. Abuse of fentanyl: An emerging problem to face. *Forensic Sci Int*. 2018;289:207-214. doi:10.1016/j.forsciint.2018.05.042
112. Centers for Disease Control and Prevention. Fentanyl. Opioid Overdose. <https://www.cdc.gov/drugoverdose/opioids/fentanyl.html>. Published 2017. Accessed October 29, 2018.

113. Soin A, Cheng J, Brown L, Moufawad S, Mekhail N. Functional outcomes in patients with chronic nonmalignant pain on long-term opioid therapy. *Pain Pract Off J World Inst Pain*. 2008;8(5):379-384. doi:10.1111/j.1533-2500.2008.00233.x
114. Krebs EE, Gravelly A, Nugent S, et al. Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE Randomized Clinical Trial. *JAMA*. 2018;319(9):872-882. doi:10.1001/jama.2018.0899
115. Tayeb BO, Barreiro AE, Bradshaw YS, Chui KKH, Carr DB. Durations of Opioid, Nonopioid Drug, and Behavioral Clinical Trials for Chronic Pain: Adequate or Inadequate? *Pain Med Malden Mass*. 2016;17(11):2036- 2046. doi:10.1093/pm/pnw245
116. Arthur J, Hui D. Safe Opioid Use: Management of Opioid-Related Adverse Effects and Aberrant Behaviors. *Hematol Oncol Clin North Am*. 2018;32(3):387-403. doi:10.1016/j.hoc.2018.01.003
117. Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. *Pain Physician*. 2008;11(2 Suppl):S105-120.
118. Harned M, Sloan P. Safety concerns with long-term opioid use. *Expert Opin Drug Saf*. 2016;15(7):955-962. doi:10.1080/14740338.2016.1177509
119. Brady KT, McCauley JL, Back SE. Prescription Opioid Misuse, Abuse, and Treatment in the United States: An Update. *Am J Psychiatry*. 2016;173(1):18-26. doi:10.1176/appi.ajp.2015.15020262
120. Simeone R. Doctor Shopping Behavior and the Diversion of Prescription Opioids. *Subst Abuse Res Treat*. 2017;11:1178221817696077. doi:10.1177/1178221817696077
121. Fishman MA, Kim PS. Buprenorphine for Chronic Pain: a Systemic Review. *Curr Pain Headache Rep*. 2018;22(12):83. doi:10.1007/s11916-018-0732-2
122. Oldfield BJ, Edens EL, Agnoli A, et al. Multimodal Treatment Options, Including Rotating to Buprenorphine, Within a Multidisciplinary Pain Clinic for Patients on Risky

Opioid Regimens: A Quality Improvement Study. *Pain Med Malden Mass*. 2018;19(suppl_1):S38-S45. doi:10.1093/pm/pny086

123. Biondi D, Xiang J, Benson C, Etropolski M, Moskovitz B, Rauschkolb C. Tapentadol immediate release versus oxycodone immediate release for treatment of acute low back pain. *Pain Physician*. 2013;16(3):E237-246.

124. Manchikanti L, Kaye AM, Knezevic NN, et al. Responsible, Safe, and Effective Prescription of Opioids for Chronic Non-Cancer Pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines. *Pain Physician*. 2017;20(2S):S3-S92.

125. Rosenberg JM, Bilka BM, Wilson SM, Spevak C. Opioid Therapy for Chronic Pain: Overview of the 2017 U.S. Department of Veterans Affairs and U.S. Department of Defense Clinical Practice Guideline. *Pain Med Malden Mass*. 2018;19(5):928-941. doi:10.1093/pm/pnx203

126. Smith HS, Peppin JF. Toward a systematic approach to opioid rotation. *J Pain Res*. 2014;7:589-608. doi:10.2147/ JPR.S55782

127. Bertilsson L, Dahl M-L, Dalén P, Al-Shurbaji A. Molecular genetics of CYP2D6: clinical relevance with focus on psychotropic drugs. *Br J Clin Pharmacol*. 2002;53(2):111-122.

128. Trescot AM, Datta S, Lee M, Hansen H. Opioid pharmacology. *Pain Physician*. 2008;11(2 Suppl):S133-153.

129. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016. *MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep*. 2016;65(1):1-49. doi:10.15585/mmwr. rr6501e1

130. 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 Malden Mass*. 2016;17(1):85-98. doi:10.1111/ pme.12907

131. Food and Drug Administration. Safe Disposal of Medicines - Disposal of Unused Medicines: What You Should Know. [https:// www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/](https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/)

[Ensuring Safe Use of Medicine/Safe Disposal of Medicines/ ucm186187.htm](http://www.cdc.gov/ensuring-safe-use-of-medicine/safe-disposal-of-medicines/ucm186187.htm). Published 2019. Accessed April 13, 2019.

132. Centers for Disease Control and Prevention. Medication Safety. Centers for Disease Control and Prevention. <http://www.cdc.gov/features/medicationstorage/index.html>. Published June 13, 2016. Accessed April 29, 2019.

133. Fairbairn N, Coffin PO, Walley AY. Naloxone for heroin, prescription opioid, and illicitly made fentanyl overdoses: Challenges and innovations responding to a dynamic epidemic. *Int J Drug Policy*. 2017;46:172-179. doi:10.1016/j.drugpo.2017.06.005

134. Moore PQ, Weber J, Cina S, Aks S. Syndrome surveillance of fentanyl-laced heroin outbreaks: Utilization of EMS, Medical Examiner and Poison Center databases. *Am J Emerg Med*. 2017;35(11):1706-1708. doi:10.1016/j.ajem.2017.05.003

135. LoVecchio F, Curry S, Waszolek K, Klemens J, Hovseth K, Glogan D. Poison control centers decrease emergency healthcare utilization costs. *J Med Toxicol Off J Am Coll Med Toxicol*. 2008;4(4):221-224.

136. Tak CR, Malheiro MC, Bennett HKW, Crouch BI. The value of a poison control center in preventing unnecessary ED visits and hospital charges: A multi-year analysis. *Am J Emerg Med*. 2017;35(3):438-443. doi:10.1016/j.ajem.2016.11.049

137. American Association of Poison Control Centers. *Final Report on the Value of the Poison Center System*.; 2012.

https://aapcc.s3.amazonaws.com/files/library/Value_of_the_Poison_Center_System_FINAL_9_26_2012_-_FINAL_FINAL_FINAL.pdf.

138. Food and Drug Administration. *Abuse-Deterrent Opioids - Evaluation and Labeling Guidance for Industry*. Silver Spring, MD: US Department of Health and Human Services; 2015.

139. Salwan AJ, Hagemeyer NE, Harirforoosh S. Abuse- Deterrent Opioid Formulations: A Key Ingredient in the Recipe to Prevent Opioid Disasters? *Clin Drug Investig*. 2018;38(7):573-577. doi:10.1007/s40261-018-0651-3

140. Haddox JD. Opioids with abuse-deterrent properties: A regulatory and technological overview. *J Opioid Manag.* 2017;13(6):397-413.
doi:10.5055/jom.2017.0417
141. Moorman-Li R, Motycka CA, Inge LD, Congdon JM, Hobson S, Pokropski B. A Review of Abuse-Deterrent Opioids For Chronic Nonmalignant Pain. *Pharm Ther.* 2012;37(7):412-418.
142. Food and Drug Administration. Key Facts about “Abuse- Deterrent” Opioids. <https://blogs.fda.gov/fdavoices/index.php/2016/10/key-facts-about-abuse-deterrent-opioids/>. Published 2016. Accessed December 29, 2017.
143. Davis MP, Pasternak G, Behm B. Treating Chronic Pain: An Overview of Clinical Studies Centered on the Buprenorphine Option. *Drugs.* July 2018. doi:10.1007/s40265-018-0953-z
144. Lewis CR, Vo HT, Fishman M. Intranasal naloxone and related strategies for opioid overdose intervention by nonmedical personnel: a review. *Subst Abuse Rehabil.* 2017;8:79-95. doi:10.2147/SAR.S101700
145. Substance Abuse and Mental Health Services Administration. *Opioid Overdose Prevention Toolkit*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016. <https://store.samhsa.gov/shin/content/SMA16-4742/SMA16-4742.pdf>. Accessed December 1, 2017.
146. Kerensky T, Walley AY. Opioid overdose prevention and naloxone rescue kits: what we know and what we don’t know. *Addict Sci Clin Pract.* 2017;12(1):4.
doi:10.1186/s13722-016-0068-3
147. Lim JK, Bratberg JP, Davis CS, Green TC, Walley AY. Prescribe to Prevent: Overdose Prevention and Naloxone Rescue Kits for Prescribers and Pharmacists. *J Addict Med.* 2016;10(5):300-308. doi:10.1097/ADM.0000000000000223
148. US Surgeon General. Surgeon General’s Advisory on Naloxone and Opioid Overdose | SurgeonGeneral.gov. <https://www.surgeongeneral.gov/priorities/opioid-overdose-prevention/naloxone-advisory.html>. Published 2019. Accessed April 13, 2019.

149. Wiesel SW, Cuckler JM, Deluca F, Jones F, Zeide MS, Rothman RH. Acute low-back pain. An objective analysis of conservative therapy. *Spine*. 1980;5(4):324-330.
150. Pedersen BK, Saltin B. Exercise as medicine - evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scand J Med Sci Sports*. 2015;25 Suppl 3:1-72. doi:10.1111/sms.12581
151. Vance CG, Rakel BA, Dailey DL, Sluka KA. Skin impedance is not a factor in transcutaneous electrical nerve stimulation effectiveness. *J Pain Res*. 2015;8:571- 580. doi:10.2147/JPR.S86577
152. McIntosh G, Hall H. Low back pain (acute). *BMJ Clin Evid*. 2011;2011. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3217769/>. Accessed August 29, 2018.
153. Kayman-Kose S, Ario DT, Toktas H, et al. Transcutaneous electrical nerve stimulation (TENS) for pain control after vaginal delivery and cesarean section. *J Matern Fetal Neonatal Med*. 2014;27(15):1572-1575. doi:10.3109/14767058.2013.870549
154. Johnson MI, Mulvey MR, Bagnall A-M. Transcutaneous electrical nerve stimulation (TENS) for phantom pain and stump pain following amputation in adults. *Cochrane Database Syst Rev*. 2015;8:CD007264. doi:10.1002/14651858.CD007264.pub3
155. Vance CGT, Rakel BA, Blodgett NP, et al. Effects of transcutaneous electrical nerve stimulation on pain, pain sensitivity, and function in people with knee osteoarthritis: a randomized controlled trial. *Phys Ther*. 2012;92(7):898-910. doi:10.2522/ptj.20110183
156. Vance CGT, Dailey DL, Rakel BA, Sluka KA. Using TENS for pain control: the state of the evidence. *Pain Manag*. 2014;4(3):197-209. doi:10.2217/pmt.14.13
157. Crawford C, Boyd C, Paat CF, et al. The Impact of Massage Therapy on Function in Pain Populations-A Systematic Review and Meta-Analysis of Randomized Controlled Trials: Part I, Patients Experiencing Pain in the General Population. *Pain Med Malden Mass*. 2016;17(7):1353-1375. doi:10.1093/pm/pnw099

158. Field T. Massage therapy research review. *Complement Ther Clin Pract*. 2014;20(4):224-229. doi:10.1016/j.ctcp.2014.07.002
159. Nelson NL, Churilla JR. Massage Therapy for Pain and Function in Patients With Arthritis: A Systematic Review of Randomized Controlled Trials. *Am J Phys Med Rehabil*. 2017;96(9):665-672. doi:10.1097/ PHM.0000000000000712
160. Clarke J, van Tulder M, Blomberg S, de Vet H, van der Heijden G, Bronfort G. Traction for low back pain with or without sciatica: an updated systematic review within the framework of the Cochrane collaboration. *Spine*. 2006;31(14):1591-1599. doi:10.1097/01.brs.00002222043.09835.72
161. Graham N, Gross A, Goldsmith CH, et al. Mechanical traction for neck pain with or without radiculopathy. *Cochrane Database Syst Rev*. 2008;(3):CD006408. doi:10.1002/14651858.CD006408.pub2
162. Ni S-H, Jiang W-T, Guo L, et al. Cryotherapy on postoperative rehabilitation of joint arthroplasty. *Knee Surg Sports Traumatol Arthrosc Off J ESSKA*. 2015;23(11):3354-3361. doi:10.1007/s00167-014-3135-x
163. Chou R, Huffman LH, American Pain Society, American College of Physicians. Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. *Ann Intern Med*. 2007;147(7):492-504.
164. Xia P, Wang X, Lin Q, Cheng K, Li X. Effectiveness of ultrasound therapy for myofascial pain syndrome: a systematic review and meta-analysis. *J Pain Res*. 2017;10:545-555. doi:10.2147/JPR.S131482
165. Zhang C, Xie Y, Luo X, et al. Effects of therapeutic ultrasound on pain, physical functions and safety outcomes in patients with knee osteoarthritis: a systematic review and meta-analysis. *Clin Rehabil*. 2016;30(10):960-971. doi:10.1177/0269215515609415
166. Robertson VJ, Baker KG. A review of therapeutic ultrasound: effectiveness studies. *Phys Ther*. 2001;81(7):1339-1350.

167. Ebadi S, Henschke N, Nakhostin Ansari N, Fallah E, van Tulder MW. Therapeutic ultrasound for chronic low-back pain. *Cochrane Database Syst Rev*. 2014;(3):CD009169. doi:10.1002/14651858.CD009169.pub2
168. Rutjes AW, Nüesch E, Sterchi R, Jüni P. Therapeutic ultrasound for osteoarthritis of the knee or hip. *Cochrane Database Syst Rev*. 2010;(1):CD003132. doi:10.1002/14651858.CD003132.pub2
169. Azadinia F, Ebrahimi E, Kamyab M, Parnianpour M, Cholewicki J, Maroufi N. Can lumbosacral orthoses cause trunk muscle weakness? A systematic review of literature. *Spine J Off J North Am Spine Soc*. 2017;17(4):589-602. doi:10.1016/j.spinee.2016.12.005
170. Manchikanti L, Falco FJE, Singh V, et al. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part I: introduction and general considerations. *Pain Physician*. 2013;16(2 Suppl):S1-48.
171. Manchikanti L, Helm S, Singh V, et al. An algorithmic approach for clinical management of chronic spinal pain. *Pain Physician*. 2009;12(4):E225-264.
172. Perrine DC, Votta-Velis G, Borgeat A. Ultrasound indications for chronic pain management: an update on the most recent evidence. *Curr Opin Anaesthesiol*. 2016;29(5):600-605. doi:10.1097/ACO.0000000000000369
173. Shah RD, Cappiello D, Suresh S. Interventional Procedures for Chronic Pain in Children and Adolescents: A Review of the Current Evidence. *Pain Pract Off J World Inst Pain*. 2016;16(3):359-369. doi:10.1111/papr.12285
174. Lee JH, Kim DH, Kim DH, et al. Comparison of Clinical Efficacy of Epidural Injection With or Without Steroid in Lumbosacral Disc Herniation: A Systematic Review and Meta-analysis. *Pain Physician*. 2018;21(5):449-468.
175. Bicket MC, Chakravarthy K, Chang D, Cohen SP. Epidural steroid injections: an updated review on recent trends in safety and complications. *Pain Manag*. 2015;5(2):129-146. doi:10.2217/pmt.14.53

176. Kozlov N, Benzon HT, Malik K. Epidural steroid injections: update on efficacy, safety, and newer medications for injection. *Minerva Anesthesiol.* 2015;81(8):901-909.
177. Park CJ, Shin YD, Lim SW, Bae YM. The effect of facet joint injection on lumbar spinal stenosis with radiculopathy. *Pak J Med Sci.* 2018;34(4):968-973.
doi:10.12669/pjms.344.15010
178. Peh W. Image-guided facet joint injection. *Biomed Imaging Interv J.* 2011;7(1).
doi:10.2349/bij.7.1.e4
179. Wolter T, Deininger M, Hubbe U, Mohadjer M, Knoeller S. Cryoneurolysis for zygapophyseal joint pain: a retrospective analysis of 117 interventions. *Acta Neurochir (Wien).* 2011;153(5):1011-1019. doi:10.1007/s00701-011-0966-9
180. Hwang SY, Lee JW, Lee GY, Kang HS. Lumbar facet joint injection: feasibility as an alternative method in high-risk patients. *Eur Radiol.* 2013;23(11):3153-3160.
doi:10.1007/s00330-013-2921-z
181. Sehgal N, Shah RV, McKenzie-Brown AM, Everett CR. Diagnostic utility of facet (zygapophysial) joint injections in chronic spinal pain: a systematic review of evidence. *Pain Physician.* 2005;8(2):211-224.
182. Shim E, Lee JW, Lee E, et al. Facet joint injection versus epidural steroid injection for lumbar spinal stenosis: intra-individual study. *Clin Radiol.* 2017;72(1):96.e7-96. e14. doi:10.1016/j.crad.2016.08.006
183. Wong M, Vijayanathan S, Kirkham B. Sacroiliitis presenting as sciatica. *Rheumatol Oxf Engl.* 2005;44(10):1323-1324. doi:10.1093/rheumatology/keh704
184. Roberts SL, Burnham RS, Ravichandiran K, Agur AM, Loh EY. Cadaveric study of sacroiliac joint innervation: implications for diagnostic blocks and radiofrequency ablation. *Reg Anesth Pain Med.* 2014;39(6):456-464.
doi:10.1097/AAP.0000000000000156
185. Cheng J. Cryoanalgesia for refractory neuralgia. *J Perioper Sci.* 2015;2(2):1-7.
186. Trescot AM. Cryoanalgesia in interventional pain management. *Pain Physician.* 2003;6(3):345-360.

187. Yoon JHE, Grechushkin V, Chaudhry A, Bhattacharji P, Durkin B, Moore W. Cryoneurolysis in Patients with Refractory Chronic Peripheral Neuropathic Pain. *J Vasc Interv Radiol JVIR*. 2016;27(2):239-243. doi:10.1016/j.jvir.2015.11.027
188. Moesker AA, Karl HW, Trescot AM. Treatment of phantom limb pain by cryoneurolysis of the amputated nerve. *Pain Pract Off J World Inst Pain*. 2014;14(1):52-56. doi:10.1111/papr.12020
189. Radnovich R, Scott D, Patel AT, et al. Cryoneurolysis to treat the pain and symptoms of knee osteoarthritis: a multicenter, randomized, double-blind, sham-controlled trial. *Osteoarthritis Cartilage*. 2017;25(8):1247-1256. doi:10.1016/j.joca.2017.03.006
190. Law L, Derian A. Cryoanalgesia. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2018. <http://www.ncbi.nlm.nih.gov/books/NBK482123/>. Accessed October 11, 2018.
191. Cahana A, Van Zundert J, Macrea L, Van Kleef M, Sluijter M. Pulsed Radiofrequency: Current Clinical and Biological Literature Available. *Pain Med*. 2006;7(5):411- 423. doi:10.1111/j.1526-4637.2006.00148.x
192. Byrd D, Mackey S. Pulsed Radiofrequency for Chronic Pain. *Curr Pain Headache Rep*. 2008;12(1):37-41.
193. Pain Interventional Center. Pulsed Radiofrequency Lesioning: What to Expect. 2010. https://mydoctor.kaiserpermanente.org/ncal/Images/Pulsed%20Radiofrequency%20Lesioning%20-%20What%20to%20Expect_tcm75-698675.pdf. Accessed October 11, 2018.
194. Chua NHL, Vissers KC, Sluijter ME. Pulsed radiofrequency treatment in interventional pain management: mechanisms and potential indications—a review. *Acta Neurochir (Wien)*. 2011;153(4):763-771. doi:10.1007/s00701-010-0881-5
195. Nicolaou A, Wilkinson P. Information sheet for adult patients undergoing: Peripheral Nerve Injections: General Information for the Treatment of Pain. February

2017. [https://www.rcoa.ac.uk/sites/default/files/images/FPM-](https://www.rcoa.ac.uk/sites/default/files/images/FPM-gen%20info%20periph%20nerve%20injection.pdf)

[gen%20info%20periph%20nerve%20injection.pdf](https://www.rcoa.ac.uk/sites/default/files/images/FPM-gen%20info%20periph%20nerve%20injection.pdf). Accessed October 12, 2018.

196. Curatolo M. Regional anesthesia in pain management. *Curr Opin Anaesthesiol*. 2016;29(5):614-619. doi:10.1097/ACO.0000000000000353

197. Joshi G, Gandhi K, Shah N, Gadsden J, Corman SL. Peripheral nerve blocks in the management of postoperative pain: challenges and opportunities. *J Clin Anesth*. 2016;35:524-529. doi:10.1016/j.jclinane.2016.08.041

198. Casati A, Baciarello M, Di Cianni S, et al. Effects of ultrasound guidance on the minimum effective anaesthetic volume required to block the femoral nerve. *Br J Anaesth*. 2007;98(6):823-827. doi:10.1093/bja/aem100

199. Marhofer P, Schrögender K, Koinig H, Kapral S, Weinstabl C, Mayer N. Ultrasonographic guidance improves sensory block and onset time of three-in-one blocks. *Anesth Analg*. 1997;85(4):854-857.

200. Peer S, Kovacs P, Harpf C, Bodner G. High-resolution sonography of lower extremity peripheral nerves: anatomic correlation and spectrum of disease. *J Ultrasound Med Off J Am Inst Ultrasound Med*. 2002;21(3):315-322.

201. Walker FO, Cartwright MS, Wiesler ER, Caress J. Ultrasound of nerve and muscle. *Clin Neurophysiol Off J Int Fed Clin Neurophysiol*. 2004;115(3):495-507. doi:10.1016/j.clinph.2003.10.022

202. Peng PWH, Narouze S. Ultrasound-guided interventional procedures in pain medicine: a review of anatomy, sonoanatomy, and procedures: part I: nonaxial structures. *Reg Anesth Pain Med*. 2009;34(5):458-474. doi:10.1097/AAP.0b013e3181aea16f

203. Valdivieso R. Chapter 67 - Peripheral Nerve Blocks. In: Duke J, ed. *Anesthesia Secrets (Fourth Edition)*. Philadelphia: Mosby; 2011:466-471. doi:10.1016/B978-0-323-06524-5.00068-4

204. Kara M, Yalcin S, Malas FU, Tiftik T, Ozcakar L. Ultrasound imaging for the upper limb nerves in CRPS: a patient with electrical injury. *Pain Physician*. 2014;17(4):E556-557.
205. Anthony M. Headache and the greater occipital nerve. *Clin Neurol Neurosurg*. 1992;94(4):297-301.
206. Peng PWH, Tumber PS. Ultrasound-guided interventional procedures for patients with chronic pelvic pain - a description of techniques and review of literature. *Pain Physician*. 2008;11(2):215-224.
207. Konno T, Aota Y, Kuniya H, et al. Anatomical etiology of "pseudo-sciatica" from superior cluneal nerve entrapment: a laboratory investigation. *J Pain Res*. 2017;10:2539-2545. doi:10.2147/JPR.S142115
208. Moe J, Moloney Johns A. Sympathetic Nerve Blocks for Pain. Health Encyclopedia. [https:// www.urmc.rochester.edu/encyclopedia/content.aspx?contenttypeid=135&contentid=54](https://www.urmc.rochester.edu/encyclopedia/content.aspx?contenttypeid=135&contentid=54). Published 2018. Accessed October 12, 2018.
209. Elmoftly DH, Anitescu M, Buvanendran A. Best practices in the treatment of neuropathic pain. *Pain Manag*. 2013;3(6):475-483. doi:10.2217/pmt.13.50
210. Rigaud J, Delavierre D, Sibert L, Labat J-J. Sympathetic nerve block in the management of chronic pelvic and perineal pain. *Progres En Urol J Assoc Francaise Urol Soc Francaise Urol*. 2010;20(12):1124-1131. doi:10.1016/j. purol.2010.08.047
211. Straube S, Derry S, Moore RA, McQuay HJ. Cervico-thoracic or lumbar sympathectomy for neuropathic pain and complex regional pain syndrome. *Cochrane Database Syst Rev*. 2010;(7):CD002918. doi:10.1002/14651858.CD002918.pub2
212. Slavin KV. Spinal stimulation for pain: future applications. *Neurother J Am Soc Exp Neurother*. 2014;11(3):535-542. doi:10.1007/s13311-014-0273-2
213. Verrills P, Sinclair C, Barnard A. A review of spinal cord stimulation systems for chronic pain. *J Pain Res*. 2016;9:481-492. doi:10.2147/JPR.S108884

214. Deer TR, Levy RM, Kramer J, et al. Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain syndrome and causalgia at 3 and 12 months: a randomized comparative trial. *Pain*. 2017;158(4):669-681. doi:10.1097/j. pain.0000000000000814
215. Deer T, Slavin KV, Amirdelfan K, et al. Success Using Neuromodulation With BURST (SUNBURST) Study: Results From a Prospective, Randomized Controlled Trial Using a Novel Burst Waveform. *Neuromodulation J Int Neuromodulation Soc*. 2018;21(1):56-66. doi:10.1111/ ner.12698
216. Kapural L, Yu C, Doust MW, et al. Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial. *Anesthesiology*. 2015;123(4):851-860. doi:10.1097/ ALN.0000000000000774
217. Kumar K, Taylor RS, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain*. 2007;132(1-2):179-188. doi:10.1016/j. pain.2007.07.028
218. North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. *Neurosurgery*. 2005;56(1):98-106; discussion 106-107.
219. Goadsby PJ, de Coo IF, Silver N, et al. Non-invasive vagus nerve stimulation for the acute treatment of episodic and chronic cluster headache: A randomized, double-blind, sham-controlled ACT2 study. *Cephalalgia Int J Headache*. 2018;38(5):959-969. doi:10.1177/0333102417744362
220. Lipton RB, Goadsby PJ. Comment: Noninvasive neurostimulation for migraine should be part of the general neurologist's therapeutic armamentarium. *Neurology*. 2018;91(4):167. doi:10.1212/ WNL.0000000000005870
221. Silberstein SD, Mechtler LL, Kudrow DB, et al. Non- Invasive Vagus Nerve Stimulation for the ACute Treatment of Cluster Headache: Findings From the

Randomized, Double-Blind, Sham-Controlled ACT1 Study. *Headache*. 2016;56(8):1317-1332. doi:10.1111/head.12896

222. Hayek SM, Deer TR, Pope JE, Panchal SJ, Patel VB. Intrathecal therapy for cancer and non-cancer pain. *Pain Physician*. 2011;14(3):219-248.

223. Smith TJ, Staats PS, Deer T, et al. Randomized clinical trial of an implantable drug delivery system compared with comprehensive medical management for refractory cancer pain: impact on pain, drug-related toxicity, and survival. *J Clin Oncol Off J Am Soc Clin Oncol*. 2002;20(19):4040-4049. doi:10.1200/JCO.2002.02.118

224. Raffaelli W, Marconi G, Fanelli G, Taddei S, Borghi GB, Casati A. Opioid-related side-effects after intrathecal morphine: a prospective, randomized, double-blind dose-response study. *Eur J Anaesthesiol*. 2006;23(7):605-610. doi:10.1017/S026502150600038X

225. Sebaaly A, Nabhane L, Issa El Khoury F, Kreichati G, El Rachkidi R. Vertebral Augmentation: State of the Art. *Asian Spine J*. 2016;10(2):370-376. doi:10.4184/asj.2016.10.2.370

226. Genev IK, Tobin MK, Zaidi SP, Khan SR, Amirouche FML, Mehta AI. Spinal Compression Fracture Management: A Review of Current Treatment Strategies and Possible Future Avenues. *Glob Spine J*. 2017;7(1):71-82. doi:10.1055/s-0036-1583288

227. Shi-Ming G, Wen-Juan L, Yun-Mei H, Yin-Sheng W, Mei-Ya H, Yan-Ping L. Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for osteoporotic vertebral compression fracture: A metaanalysis. *Indian J Orthop*. 2015;49(4):377-387. doi:10.4103/0019-5413.154892

228. Kam NM, Maingard J, Kok HK, et al. Combined Vertebral Augmentation and Radiofrequency Ablation in the Management of Spinal Metastases: an Update. *Curr Treat Options Oncol*. 2017;18(12):74. doi:10.1007/s11864-017-0516-7

229. Wong CSM, Wong SHS. A New Look at Trigger Point Injections. *Anesthesiol Res Pract*. 2012;2012. doi:10.1155/2012/492452

230. Hong CZ. Lidocaine injection versus dry needling to myofascial trigger point. The importance of the local twitch response. *Am J Phys Med Rehabil*. 1994;73(4):256-263.
231. Borg-Stein J, Iaccarino MA. Myofascial pain syndrome treatments. *Phys Med Rehabil Clin N Am*. 2014;25(2):357-374. doi:10.1016/j.pmr.2014.01.012
232. Garvey TA, Marks MR, Wiesel SW. A prospective, randomized, double-blind evaluation of trigger-point injection therapy for low-back pain. *Spine*. 1989;14(9):962-964.
233. Robbins MS, Kuruvilla D, Blumenfeld A, et al. Trigger point injections for headache disorders: expert consensus methodology and narrative review. *Headache*. 2014;54(9):1441-1459. doi:10.1111/head.12442
234. Cunningham J, Marshall N, Hide G, et al. A randomized, double-blind, controlled study of ultrasound-guided corticosteroid injection into the joint of patients with inflammatory arthritis. *Arthritis Rheum*. 2010;62(7):1862- 1869. doi:10.1002/art.27448
235. Hazani R, Engineer NJ, Elston J, Wilhelmi BJ. Anatomic Landmarks for Basal Joint Injections. *Eplasty*. 2012;12. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3261775/>. Accessed October 12, 2018.
236. National Spine & Pain Centers. Joint Injections Facts & Information. National Spine & Pain Centers. [https:// treatingpain.com/treatment/joint-injections](https://treatingpain.com/treatment/joint-injections). Published 2018. Accessed October 12, 2018.
237. Nunley PD, Deer TR, Benyamin RM, Staats PS, Block JE. Interspinous process decompression is associated with a reduction in opioid analgesia in patients with lumbar spinal stenosis. *J Pain Res*. 2018;Volume 11:2943-2948. doi:10.2147/JPR.S182322
238. Nunley PD, Patel VV, Orndorff DG, Lavelle WF, Block JE, Geisler FH. Five-year durability of stand-alone interspinous process decompression for lumbar spinal stenosis. *Clin Interv Aging*. 2017;12:1409-1417. doi:10.2147/CIA.S143503
239. De la Rosa MB, Kozik EM, Sakaguchi DS. Adult Stem Cell-Based Strategies for Peripheral Nerve Regeneration. *Adv Exp Med Biol*. August 2018. doi:10.1007/5584_2018_254

240. Gu X, Yu X, Zhao C, et al. Efficacy and Safety of Autologous Bone Marrow Mesenchymal Stem Cell Transplantation in Patients with Diabetic Retinopathy. *Cell Physiol Biochem Int J Exp Cell Physiol Biochem Pharmacol*. 2018;49(1):40-52. doi:10.1159/000492838
241. Kishk NA, Gabr H, Hamdy S, et al. Case control series of intrathecal autologous bone marrow mesenchymal stem cell therapy for chronic spinal cord injury. *Neurorehabil Neural Repair*. 2010;24(8):702-708. doi:10.1177/1545968310369801
242. Kerns RD, Sellinger J, Goodin BR. Psychological treatment of chronic pain. *Annu Rev Clin Psychol*. 2011;7:411-434. doi:10.1146/annurev-clinpsy-090310-120430
243. Manchikanti L, Fellows B, Singh V. Understanding psychological aspects of chronic pain in interventional pain management. *Pain Physician*. 2002;5(1):57-82.
244. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med*. 2007;147(7):478-491.
245. Bushnell MC, Ceko M, Low LA. Cognitive and emotional control of pain and its disruption in chronic pain. *Nat Rev Neurosci*. 2013;14(7):502-511. doi:10.1038/nrn3516
246. Kligler B, Bair MJ, Banerjea R, et al. Clinical Policy Recommendations from the VHA State-of-the-Art Conference on Non-Pharmacological Approaches to Chronic Musculoskeletal Pain. *J Gen Intern Med*. 2018;33(Suppl 1):16-23. doi:10.1007/s11606-018-4323-z
247. Kellezi B, Coupland C, Morriss R, et al. The impact of psychological factors on recovery from injury: a multicentre cohort study. *Soc Psychiatry Psychiatr Epidemiol*. 2017;52(7):855-866. doi:10.1007/s00127-016-1299-z
248. Lerman SF, Rudich Z, Brill S, Shalev H, Shahar G. Longitudinal associations between depression, anxiety, pain, and pain-related disability in chronic pain patients. *Psychosom Med*. 2015;77(3):333-341. doi:10.1097/PSY.0000000000000158

249. Vranceanu A-M, Bachoura A, Weening A, Vrahas M, Smith RM, Ring D. Psychological factors predict disability and pain intensity after skeletal trauma. *J Bone Joint Surg Am*. 2014;96(3):e20. doi:10.2106/ JBJS.L.00479
250. Pitcher MH, Von Korff M, Bushnell MC, Porter L. Prevalence and Profile of High-Impact Chronic Pain in the United States. *J Pain Off J Am Pain Soc*. August 2018. doi:10.1016/j.jpain.2018.07.006
251. Darnall B. Applying Psychological Science for Pain Relief and Opioid Reduction. Keynote Speaker presented at the: American Psychological Association 2018 Annual National Convention; 2018; San Francisco, CA.
252. Roditi D, Robinson ME. The role of psychological interventions in the management of patients with chronic pain. *Psychol Res Behav Manag*. 2011;4:41-49. doi:10.2147/PRBM.S15375
253. Gatzounis R, Schrooten MGS, Crombez G, Vlaeyen JWS. Operant learning theory in pain and chronic pain rehabilitation. *Curr Pain Headache Rep*. 2012;16(2):117-126. doi:10.1007/s11916-012-0247-1
254. McCracken LM, Turk DC. Behavioral and cognitive-behavioral treatment for chronic pain: outcome, predictors of outcome, and treatment process. *Spine*. 2002;27(22):2564-2573. doi:10.1097/01. BRS.0000032130.45175.66
255. Smeets RJ, Severens JL, Beelen S, Vlaeyen JW, Knottnerus JA. More is not always better: cost-effectiveness analysis of combined, single behavioral and single physical rehabilitation programs for chronic low back pain. *Eur J Pain Lond Engl*. 2009;13(1):71-81. doi:10.1016/j.ejpain.2008.02.008
256. Kaiser RS, Mooreville M, Kannan K. Psychological Interventions for the Management of Chronic Pain: a Review of Current Evidence. *Curr Pain Headache Rep*. 2015;19(9):43. doi:10.1007/s11916-015-0517-9
257. Eccleston C, Morley S, Williams A, Yorke L, Mastroiannopoulou K. Systematic review of randomised controlled trials of psychological therapy for chronic pain in

children and adolescents, with a subset meta-analysis of pain relief. *Pain*. 2002;99(1-2):157-165.

258. Jensen MP, Turner JA, Romano JM. Changes in beliefs, catastrophizing, and coping are associated with improvement in multidisciplinary pain treatment. *J Consult Clin Psychol*. 2001;69(4):655-662.

259. Turner J, Jensen M, Romano J. Do beliefs, coping, and catastrophizing independently predict functioning in patients with chronic pain? *Pain*. 2000;85(1-2):115-125.

260. Skelly AC, Chou R, Dettori JR, et al. *Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2018. [http:// www.ncbi.nlm.nih.gov/books/NBK519953/](http://www.ncbi.nlm.nih.gov/books/NBK519953/). Accessed November 28, 2018.

261. McCracken LM, Vowles K. Acceptance and Commitment Therapy and Mindfulness for Chronic Pain: Model, Process, and Progress. *Am Psychol*. 2014.

262. Vowles KE, McCracken LM. Acceptance and values-based action in chronic pain: a study of treatment effectiveness and process. *J Consult Clin Psychol*. 2008;76(3):397-407. doi:10.1037/0022-006X.76.3.397

263. Cherkin DC, Sherman KJ, Balderson BH, et al. Effect of Mindfulness-Based Stress Reduction vs Cognitive Behavioral Therapy or Usual Care on Back Pain and Functional Limitations in Adults With Chronic Low Back Pain: A Randomized Clinical Trial. *JAMA*. 2016;315(12):1240-1249. doi:10.1001/jama.2016.2323

264. Zeidan F, Vago DR. Mindfulness meditation-based pain relief: a mechanistic account. *Ann N Y Acad Sci*. 2016;1373(1):114-127. doi:10.1111/nyas.13153

265. Hilton L, Hempel S, Ewing BA, et al. Mindfulness Meditation for Chronic Pain: Systematic Review and Meta-analysis. *Ann Behav Med Publ Soc Behav Med*. 2017;51(2):199-213. doi:10.1007/s12160-016-9844-2

266. Pradhan EK, Baumgarten M, Langenberg P, et al. Effect of Mindfulness-Based Stress Reduction in rheumatoid arthritis patients. *Arthritis Rheum*. 2007;57(7):1134-1142. doi:10.1002/art.23010
267. Anheyer D, Haller H, Barth J, Lauche R, Dobos G, Cramer H. Mindfulness-Based Stress Reduction for Treating Low Back Pain: A Systematic Review and Meta-analysis. *Ann Intern Med*. 2017;166(11):799-807. doi:10.7326/M16-1997
268. Carlson LE, Garland SN. Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients. *Int J Behav Med*. 2005;12(4):278-285. doi:10.1207/s15327558ijbm1204_9
269. Grossman P, Niemann L, Schmidt S, Walach H. Mindfulness-based stress reduction and health benefits. A meta-analysis. *J Psychosom Res*. 2004;57(1):35-43. doi:10.1016/S0022-3999(03)00573-7
270. Omidi A, Zargar F. Effects of mindfulness-based stress reduction on perceived stress and psychological health in patients with tension headache. *J Res Med Sci Off J Isfahan Univ Med Sci*. 2015;20(11):1058-1063. doi:10.4103/1735-1995.172816
271. Lumley MA, Schubiner H, Lockhart NA, et al. Emotional awareness and expression therapy, cognitive behavioral therapy, and education for fibromyalgia: a cluster-randomized controlled trial. *Pain*. 2017;158(12):2354- 2363. doi:10.1097/j.pain.0000000000001036
272. Burger AJ, Lumley MA, Carty JN, et al. The effects of a novel psychological attribution and emotional awareness and expression therapy for chronic musculoskeletal pain: A preliminary, uncontrolled trial. *J Psychosom Res*. 2016;81:1-8. doi:10.1016/j.jpsychores.2015.12.003
273. Neblett R. Surface Electromyographic (SEMG) Biofeedback for Chronic Low Back Pain. *Healthcare*. 2016;4(2). doi:10.3390/healthcare4020027
274. Nestoriuc Y, Martin A, Rief W, Andrasik F. Biofeedback treatment for headache disorders: a comprehensive efficacy review. *Appl Psychophysiol Biofeedback*. 2008;33(3):125-140. doi:10.1007/s10484-008-9060-3

275. Elkins G, Jensen MP, Patterson DR. Hypnotherapy for the management of chronic pain. *Int J Clin Exp Hypn*. 2007;55(3):275-287.
doi:10.1080/00207140701338621
276. Kaushik R, Kaushik RM, Mahajan SK, Rajesh V. Biofeedback assisted diaphragmatic breathing and systematic relaxation versus propranolol in long term prophylaxis of migraine. *Complement Ther Med*. 2005;13(3):165-174.
doi:10.1016/j.ctim.2005.04.004
277. Turner JA, Anderson ML, Balderson BH, Cook AJ, Sherman KJ, Cherkin DC. Mindfulness-based stress reduction and cognitive behavioral therapy for chronic low back pain: similar effects on mindfulness, catastrophizing, self-efficacy, and acceptance in a randomized controlled trial. *Pain*. 2016;157(11):2434- 2444.
doi:10.1097/j.pain.0000000000000635
278. Turk DC, Melzack R. *Handbook of Pain Assessment*. Third. New York, NY: Guilford Press; 2011.
279. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. *J Addict Med*. 2015;9(5):358-367. doi:10.1097/ADM.0000000000000166
280. Heyward J, Jones C, Compton W. Coverage of Nonpharmacologic Treatments for Low Back Pain Among US Public and Private Insurers. *JAMA Netw Open*. 2018;1(6). <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2705853>.
281. Kerns RD, Krebs EE, Atkins D. Making Integrated Multimodal Pain Care a Reality: A Path Forward. *J Gen Intern Med*. 2018;33(Suppl 1):1-3. doi:10.1007/s11606-018-4361-6
282. Heapy AA, Higgins DM, Goulet JL, et al. Interactive Voice Response–Based Self-management for Chronic Back Pain. *JAMA Intern Med*. 2017;177(6):765-773.
doi:10.1001/jamainternmed.2017.0223
283. Wahass SH. The Role of Psychologists in Health Care Delivery. *J Fam Community Med*. 2005;12(2):63-70.

284. Darnall BD, Scheman J, Davin S, et al. Pain Psychology: A Global Needs Assessment and National Call to Action. *Pain Med Malden Mass*. 2016;17(2):250-263. doi:10.1093/pm/pnv095
285. Wandner LD, Prasad R, Ramezani A, Malcore SA, Kerns RD. Core competencies for the emerging specialty of pain psychology. *Am Psychol*. August 2018. doi:10.1037/amp0000330
286. Becker WC, DeBar LL, Heapy AA, et al. A Research Agenda for Advancing Non-pharmacological Management of Chronic Musculoskeletal Pain: Findings from a VHA State-of-the-art Conference. *J Gen Intern Med*. 2018;33(Suppl 1):11-15. doi:10.1007/s11606-018-4345-6
287. American Academy of Pain Medicine. *Minimum Insurance Benefits for Patients with Chronic Pain*. Chicago, IL: Author; 2014. <http://www.painmed.org/files/minimum-insurance-benefits-for-patients-with-chronic-pain.pdf>.
288. Pennsylvania Department of Drug and Alcohol Programs. *Pennsylvania Drug and Alcohol Annual Plan and Report*. Harrisburg, PA: Pennsylvania Department of Drug and Alcohol Programs; 2015.
289. Centers for Medicare & Medicaid Services. *Best Practices for Addressing Prescription Opioid Overdoses, Misuse and Addiction*. Baltimore, MD: US Department of Health and Human Services; 2016.
290. Darnall BD, Carr DB, Schatman ME. Pain Psychology and the Biopsychosocial Model of Pain Treatment: Ethical Imperatives and Social Responsibility. *Pain Med Off J Am Acad Pain Med*. 2017;18(8):1413-1415. doi:10.1093/pm/pnw166
291. National League of Cities and National Association of Counties. *A Prescription for Action: Local Leadership in Ending the Opioid Crisis*. Washington, DC; 2016. http://opioidaction.org/wp-content/uploads/2017/01/NACo-NLC-JointOpioidReport_FINAL_12.15.16.pdf. Accessed November 21, 2017.

292. National Governors Association. *Governor's Priorities for Addressing the Nation's Opioid Crisis*. Washington, DC: Author; 2016. <https://www.nga.org/cms/home/special/col2-content/governors-priorities-opioid.html>.
293. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. *Arch Intern Med*. 2003;163(20):2433-2445. doi:10.1001/archinte.163.20.2433
294. Beck JG, Clapp JD. A different kind of co-morbidity: Understanding posttraumatic stress disorder and chronic pain. *Psychol Trauma Theory Res Pract Policy*. 2011;3(2):101-108. doi:10.1037/a0021263
295. Burke ALJ, Mathias JL, Denson LA. Psychological functioning of people living with chronic pain: a meta-analytic review. *Br J Clin Psychol*. 2015;54(3):345-360. doi:10.1111/bjc.12078
296. Knaster P, Karlsson H, Estlander A-M, Kalso E. Psychiatric disorders as assessed with SCID in chronic pain patients: the anxiety disorders precede the onset of pain. *Gen Hosp Psychiatry*. 2012;34(1):46-52. doi:10.1016/j.genhosppsy.2011.09.004
297. Stayner RS, Ramezani A. Chronic pain and psychiatric illness: Managing comorbid conditions. MDedge Psychiatry. <https://www.mdedge.com/psychiatry/article/106106/somatic-disorders/chronic-pain-and-psychiatric-illness-managing-comorbid>. Published February 2016. Accessed November 15, 2018.
298. Webster LR. Risk Factors for Opioid-Use Disorder and Overdose. *Anesth Analg*. 2017;125(5):1741-1748. doi:10.1213/ANE.0000000000002496
299. Outcalt SD, Kroenke K, Krebs EE, et al. Chronic pain and comorbid mental health conditions: independent associations of posttraumatic stress disorder and depression with pain, disability, and quality of life. *J Behav Med*. 2015;38(3):535-543. doi:10.1007/s10865-015-9628-3
300. Turk DC, Wilson HD, Cahana A. Treatment of chronic non-cancer pain. *Lancet Lond Engl*. 2011;377(9784):2226-2235. doi:10.1016/S0140-6736(11)60402-9

301. Guarino H, Acosta M, Marsch LA, Xie H, Aponte- Melendez Y. A Mixed-methods Evaluation of the Feasibility, Acceptability and Preliminary Efficacy of a Mobile Intervention for Methadone Maintenance Clients. *Psychol Addict Behav J Soc Psychol Addict Behav*. 2016;30(1):1-11. doi:10.1037/adb0000128
302. American Society of Anesthesiologists, American Society of Regional Anesthesia and Pain Medicine. Practice guidelines for chronic pain management: an updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. *Anesthesiology*. 2010;112(4):810-833. doi:10.1097/ALN.0b013e3181c43103
303. Erie County Opiate Epidemic Task Force. *Erie County Community Wide Guidelines: Acute Pain Management*. Buffalo, NY: Erie County Department of Health; 2016. <http://www2.erie.gov/health/sites/www2.erie.gov.health/files/uploads/pdfs/ECAcutePainMgmtGuidelines12062016.pdf>. Accessed November 21, 2017.
304. Horgas AL. Pain Management in Older Adults. *Nurs Clin North Am*. 2017;52(4):e1-e7. doi:10.1016/j.cnur.2017.08.001
305. New Mexico Department of Health. *New Mexico Clinical Guidelines on Prescribing Opioids for Treatment of Pain*. Albuquerque, NM: New Mexico Department of Health; 2011. <https://nmhealth.org/publication/view/general/271/>. Accessed November 28, 2017.
306. Paice JA, Portenoy R, Lacchetti C, et al. Management of Chronic Pain in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol Off J Am Soc Clin Oncol*. 2016;34(27):3325- 3345. doi:10.1200/JCO.2016.68.5206
307. Qaseem A, Wilt TJ, McLean RM, Forciea MA, Clinical Guidelines Committee of the American College of Physicians. Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med*. 2017;166(7):514-530. doi:10.7326/M16-2367

308. Tick H, Nielsen A, Pelletier KR, et al. Evidence-Based Nonpharmacologic Strategies for Comprehensive Pain Care: The Consortium Pain Task Force White Paper. *Explore N Y N*. 2018;14(3):177-211. doi:10.1016/j.explore.2018.02.001
309. National Center for Complementary and Integrative Health. Complementary, Alternative, or Integrative Health: What's In a Name? NCCIH. <https://nccih.nih.gov/health/integrative-health>. Published 2017. Accessed December 26, 2017.
310. Barnes PM, Bloom B, Nahin RL. Complementary and alternative medicine use among adults and children: United States, 2007. *Natl Health Stat Rep*. 2008;(12):1-23.
311. Hempel S, Taylor SL, Solloway MR, et al. *Evidence Map of Acupuncture*. Washington (DC): Department of Veterans Affairs; 2014. <http://www.ncbi.nlm.nih.gov/books/NBK185072/>. Accessed August 9, 2018.
312. MacPherson H, Vertosick EA, Foster NE, et al. The persistence of the effects of acupuncture after a course of treatment: a meta-analysis of patients with chronic pain. *Pain*. 2017;158(5):784-793. doi:10.1097/j.pain.0000000000000747
313. Trinh K, Graham N, Irnich D, Cameron ID, Forget M. Acupuncture for neck disorders. *Cochrane Database Syst Rev*. 2016;(5):CD004870. doi:10.1002/14651858.CD004870.pub4
314. Vickers AJ, Cronin AM, Maschino AC, et al. Acupuncture for chronic pain: individual patient data meta-analysis. *Arch Intern Med*. 2012;172(19):1444-1453. doi:10.1001/archinternmed.2012.3654
315. Vickers AJ, Vertosick EA, Lewith G, et al. Acupuncture for Chronic Pain: Update of an Individual Patient Data Meta-Analysis. *J Pain Off J Am Pain Soc*. 2018;19(5):455-474. doi:10.1016/j.jpain.2017.11.005
316. Cho H-W, Hwang E-H, Lim B, et al. How current Clinical Practice Guidelines for low back pain reflect Traditional Medicine in East Asian Countries: a systematic review of Clinical Practice Guidelines and systematic reviews. *PloS One*. 2014;9(2):e88027. doi:10.1371/journal.pone.0088027

317. Nahin RL, Boineau R, Khalsa PS, Stussman BJ, Weber WJ. Evidence-Based Evaluation of Complementary Health Approaches for Pain Management in the United States. *Mayo Clin Proc.* 2016;91(9):1292-1306. doi:10.1016/j.mayocp.2016.06.007
318. Witt CM, Vertosick EA, Foster NE, et al. The Effect of Patient Characteristics on Acupuncture Treatment Outcomes: An Individual Patient Data Meta-Analysis of 20,827 Chronic Pain Patients in Randomized Controlled Trials. *Clin J Pain.* March 2019. doi:10.1097/ AJP.0000000000000691
319. North Carolina Medical Board. *Policy for the Use of Opiates for the Treatment of Pain.* Raleigh, NC: Author; 2014. [https://www.ncmedboard.org/images/uploads/other_pdfs/Policy for the Use of Opiates for the Treatment of Pain June 4 2014.pdf](https://www.ncmedboard.org/images/uploads/other_pdfs/Policy_for_the_Use_of_Opiates_for_the_Treatment_of_Pain_June_4_2014.pdf). Accessed November 27, 2017.
320. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res.* 2012;64(4):465-474.
321. Cornelius R, Herr KA, Gordon DB, Kretzer K, Butcher HK. Evidence-Based Practice Guideline : Acute Pain Management in Older Adults. *J Gerontol Nurs.* 2017;43(2):18-27. doi:10.3928/00989134-20170111-08
322. Cooney MF. Postoperative Pain Management: Clinical Practice Guidelines. *J Perianesth Nurs.* 2016;31(5):445- 451. doi:10.1016/j.jopan.2016.08.001
323. Blanchette M-A, Stochkendahl MJ, Borges Da Silva R, Boruff J, Harrison P, Bussi res A. Effectiveness and Economic Evaluation of Chiropractic Care for the Treatment of Low Back Pain: A Systematic Review of Pragmatic Studies. *PloS One.* 2016;11(8):e0160037. doi:10.1371/journal.pone.0160037
324. Cuenca-Mart nez F, Cort s-Amador S, Esp -L pez GV. Effectiveness of classic physical therapy proposals for chronic non-specific low back pain: a literature review. *Phys Ther Res.* 2018;21(1):16-22. doi:10.1298/ptr.E9937

325. Miake-Lye I, Lee J, Lugar T, et al. *Massage for Pain: An Evidence Map*. Washington (DC): Department of Veterans Affairs (US); 2016.
<http://www.ncbi.nlm.nih.gov/books/NBK424144/>. Accessed October 4, 2018.
326. Kukimoto Y, Ooe N, Ideguchi N. The Effects of Massage Therapy on Pain and Anxiety after Surgery: A Systematic Review and Meta-Analysis. *Pain Manag Nurs Off J Am Soc Pain Manag Nurses*. 2017;18(6):378- 390. doi:10.1016/j.pmn.2017.09.001
327. Lin Y-C, Wan L, Jamison RN. Using Integrative Medicine in Pain Management: An Evaluation of Current Evidence. *Anesth Analg*. 2017;125(6):2081-2093.
doi:10.1213/ANE.0000000000002579
328. Millstine D, Chen CY, Bauer B. Complementary and integrative medicine in the management of headache. *BMJ*. 2017;357:j1805.
329. Wong JJ, Shearer HM, Mior S, et al. Are manual therapies, passive physical modalities, or acupuncture effective for the management of patients with whiplash-associated disorders or neck pain and associated disorders? An update of the Bone and Joint Decade Task Force on Neck Pain and Its Associated Disorders by the OPTIMa collaboration. *Spine J Off J North Am Spine Soc*. 2016;16(12):1598-1630.
doi:10.1016/j.spinee.2015.08.024
330. Cherkin DC, Sherman KJ, Balderson BH. Effects of mindfulness-based stress reduction vs cognitive-behavioral therapy and usual care on back pain and functional limitations among adults with chronic low back pain: a randomized clinical trial. *JAMA*. 2017;314(12):1240-1249.
331. Herman PM, Kommareddi M, Sorbero ME, et al. Characteristics of Chiropractic Patients Being Treated for Chronic Low Back and Neck Pain. *J Manipulative Physiol Ther*. 2018;41(6):445-455. doi:10.1016/j.jmpt.2018.02.001
332. Gu Q, Hou J-C, Fang X-M. Mindfulness Meditation for Primary Headache Pain: A Meta-Analysis. *Chin Med J (Engl)*. 2018;131(7):829-838. doi:10.4103/0366-6999.228242

333. Chang DG, Holt JA, Sklar M, Groessl EJ. Yoga as a treatment for chronic low back pain: A systematic review of the literature. *J Orthop Rheumatol*. 2016;3(1):1-8.
334. Cramer H, Lauche R, Haller H, Dobos G. A systematic review and meta-analysis of yoga for low back pain. *Clin J Pain*. 2013;29(5):450-460. doi:10.1097/AJP.0b013e31825e1492
335. Groessl EJ, Liu L, Chang DG, et al. Yoga for Military Veterans with Chronic Low Back Pain: A Randomized Clinical Trial. *Am J Prev Med*. 2017;53(5):599-608. doi:10.1016/j.amepre.2017.05.019
336. Saper RB, Lemaster C, Delitto A, et al. Yoga, Physical Therapy, or Education for Chronic Low Back Pain: A Randomized Noninferiority Trial. *Ann Intern Med*. 2017;167(2):85-94. doi:10.7326/M16-2579
337. Wieland LS, Skoetz N, Pilkington K, Vempati R, D'Adamo CR, Berman BM. Yoga treatment for chronic non-specific low back pain. *Cochrane Database Syst Rev*. 2017;1:CD010671. doi:10.1002/14651858.CD010671.pub2
338. Cramer H, Ward L, Saper R, Fishbein D, Dobos G, Lauche R. The Safety of Yoga: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Am J Epidemiol*. 2015;182(4):281-293. doi:10.1093/aje/kwv071
339. Kong LJ, Lauche R, Klose P, et al. Tai Chi for Chronic Pain Conditions: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Sci Rep*. 2016;6:25325. doi:10.1038/srep25325
340. Lee MS, Pittler MH, Ernst E. Tai chi for osteoarthritis: a systematic review. *Clin Rheumatol*. 2008;27(2):211-218. doi:10.1007/s10067-007-0700-4
341. Siddall PJ, Lovell M, MacLeod R. Spirituality: what is its role in pain medicine? *Pain Med Malden Mass*. 2015;16(1):51-60. doi:10.1111/pme.12511
342. Huguet A, Miró J. The severity of chronic pediatric pain: an epidemiological study. *J Pain Off J Am Pain Soc*. 2008;9(3):226-236. doi:10.1016/j.jpain.2007.10.015

343. King S, Chambers CT, Huguet A, et al. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. *Pain*. 2011;152(12):2729-2738. doi:10.1016/j.pain.2011.07.016
344. Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JA, et al. Pain in children and adolescents: a common experience. *Pain*. 2000;87(1):51-58.
345. Schwaller F, Fitzgerald M. The consequences of pain in early life: injury-induced plasticity in developing pain pathways. *Eur J Neurosci*. 2014;39(3):344-352. doi:10.1111/ejn.12414
346. Hermann C, Hohmeister J, Demirakça S, Zohsel K, Flor H. Long-term alteration of pain sensitivity in school-aged children with early pain experiences. *Pain*. 2006;125(3):278-285. doi:10.1016/j.pain.2006.08.026
347. Dooley JM, Augustine HF, Brna PM, Digby AM. The prognosis of pediatric headaches--a 30-year follow-up study. *Pediatr Neurol*. 2014;51(1):85-87. doi:10.1016/j.pediatrneurol.2014.02.022
348. Walker LS, Dengler-Crish CM, Rippel S, Bruehl S. Functional abdominal pain in childhood and adolescence increases risk for chronic pain in adulthood. *Pain*. 2010;150(3):568-572. doi:10.1016/j.pain.2010.06.018
349. Zernikow B, Ruhe A-K, Stahlschmidt L, et al. Clinical and Economic Long-Term Treatment Outcome of Children and Adolescents with Disabling Chronic Pain. *Pain Med Malden Mass*. 2018;19(1):16-28. doi:10.1093/pm/pnx067
350. Simon LS. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. *J Pain Palliat Care Pharmacother*. 2012;26(2):197-198. doi:10.3109/15360288.2012.678473
351. Bicket MC, Mao J. Chronic Pain in Older Adults. *Geriatr Anesth*. 2015;33(3):577-590. doi:10.1016/j.anclin.2015.05.011
352. Tracy B, Morrison RS. Pain Management in Older Adults. *Clin Ther*. 2013;35(11):1659-1668. doi:10.1016/j.clinthera.2013.09.026

353. Weiner DK, Fang M, Gentili A, et al. Deconstructing chronic low back pain in the older adult--step by step evidence and expert-based recommendations for evaluation and treatment: part I: Hip osteoarthritis. *Pain Med Malden Mass*. 2015;16(5):886-897. doi:10.1111/pme.12757
354. van den Beuken-van Everdingen MHJ, Hochstenbach LMJ, Joosten EAJ, Tjan-Heijnen VCG, Janssen DJA. Update on Prevalence of Pain in Patients With Cancer: Systematic Review and Meta-Analysis. *J Pain Symptom Manage*. 2016;51(6):1070-1090.e9. doi:10.1016/j.jpainsymman.2015.12.340
355. Finucane TE, Nirmalasari O, Graham A. Palliative care in the ambulatory geriatric practice. *Clin Geriatr Med*. 2015;31(2):193-206. doi:10.1016/j.cger.2015.01.008
356. Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL. Sex, gender, and pain: a review of recent clinical and experimental findings. *J Pain Off J Am Pain Soc*. 2009;10(5):447-485. doi:10.1016/j.jpain.2008.12.001
357. Madsen T, McGregor A. Sex Differences in Pain. Sex Differences in Pain. <http://sgwhc.org/resources/professional-education/case-studies/sex-differences-in-pain/>. Published April 25, 2013. Accessed October 10, 2018.
358. Ruau D, Liu LY, Clark JD, Angst MS, Butte AJ. Sex Differences in Reported Pain Across 11,000 Patients Captured in Electronic Medical Records. *J Pain*. 2012;13(3):228-234. doi:10.1016/j.jpain.2011.11.002
359. Back SE, Payne RL, Simpson AN, Brady KT. Gender and Prescription Opioids: Findings from the National Survey on Drug Use and Health. *Addict Behav*. 2010;35(11):1001-1007. doi:10.1016/j.addbeh.2010.06.018
360. Glerum K, Choo E. Gender and Prescription Opioid Abuse. American Medical Women's Association. <https://www.amwa-doc.org/sghc/sghc-case-studies/gender-and-prescription-opioid-abuse/>. Published 2015. Accessed October 10, 2018.
361. Green TC, Black R, Grimes Serrano JM, Budman SH, Butler SF. Typologies of prescription opioid use in a large sample of adults assessed for substance abuse treatment. *PLoS One*. 2011;6(11):e27244. doi:10.1371/journal.pone.0027244

362. Centers for Disease Control and Prevention. Vital Signs: Overdoses of Prescription Opioid Pain Relievers and Other Drugs Among Women — United States, 1999– 2010. Morbidity and Mortality Weekly Report. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6226a3.htm>. Published July 5, 2013. Accessed October 10, 2018.
363. Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain Off J Am Pain Soc*. 2009;10(2):113-130. doi:10.1016/j.jpain.2008.10.008
364. Shah S, Banh ET, Koury K, Bhatia G, Nandi R, Gulur P. Pain Management in Pregnancy: Multimodal Approaches. *Pain Res Treat*. 2015;2015. doi:10.1155/2015/987483
365. Hadi I, da Silva O, Natale R, Boyd D, Morley-Forster PK. Opioids in the parturient with chronic nonmalignant pain: a retrospective review. *J Opioid Manag*. 2006;2(1):31-34.
366. Ray-Griffith SL, Wendel MP, Stowe ZN, Magann EF. Chronic pain during pregnancy: a review of the literature. *Int J Womens Health*. 2018;10:153-164. doi:10.2147/IJWH.S151845
367. Kato GJ, Piel FB, Reid CD, et al. Sickle cell disease. *Nat Rev Dis Primer*. 2018;4:18010. doi:10.1038/nrdp.2018.10
368. Brousseau DC, Panepinto JA, Nimmer M, Hoffmann RG. The number of people with sickle-cell disease in the United States: national and state estimates. *Am J Hematol*. 2010;85(1):77-78. doi:10.1002/ajh.21570
369. Brousseau DC, Owens PL, Mosso AL, Panepinto JA, Steiner CA. Acute care utilization and rehospitalizations for sickle cell disease. *JAMA*. 2010;303(13):1288-1294. doi:10.1001/jama.2010.378
370. Lanzkron S, Carroll CP, Haywood CJ. The burden of emergency department use for sickle-cell disease: an analysis of the national emergency department sample database. *Am J Hematol*. 2010;85(10):797-799. doi:10.1002/ajh.21807

371. Dampier C, Palermo TM, Darbari DS, Hassell K, Smith W, Zempsky W. AAPT Diagnostic Criteria for Chronic Sickle Cell Disease Pain. *J Pain Off J Am Pain Soc*. 2017;18(5):490-498. doi:10.1016/j.jpain.2016.12.016
372. Sil S, Cohen LL, Dampier C. Psychosocial and Functional Outcomes in Youth With Chronic Sickle Cell Pain. *Clin J Pain*. 2016;32(6):527-533. doi:10.1097/AJP.0000000000000289
373. Smith WR, Penberthy LT, Bovbjerg VE, et al. Daily assessment of pain in adults with sickle cell disease. *Ann Intern Med*. 2008;148(2):94-101.
374. Brandow AM, Zappia KJ, Stucky CL. Sickle cell disease: a natural model of acute and chronic pain. *Pain*. 2017;158 Suppl 1:S79-S84. doi:10.1097/j.pain.0000000000000824
375. Darbari DS, Ballas SK, Clauw DJ. Thinking beyond sickling to better understand pain in sickle cell disease. *Eur J Haematol*. 2014;93(2):89-95. doi:10.1111/ejh.12340
376. Miller AC, Gladwin MT. Pulmonary complications of sickle cell disease. *Am J Respir Crit Care Med*. 2012;185(11):1154-1165. doi:10.1164/rccm.201111-2082CI
377. Vanderhave KL, Perkins CA, Scannell B, Brighton BK. Orthopaedic Manifestations of Sickle Cell Disease. *J Am Acad Orthop Surg*. 2018;26(3):94-101. doi:10.5435/JAAOS-D-16-00255
378. Brandow AM, DeBaun MR. Key Components of Pain Management for Children and Adults with Sickle Cell Disease. *Hematol Oncol Clin North Am*. 2018;32(3):535-550. doi:10.1016/j.hoc.2018.01.014
379. Bulgin D, Tanabe P, Jenerette C. Stigma of Sickle Cell Disease: A Systematic Review. *Issues Ment Health Nurs*. 2018;39(8):675-686. doi:10.1080/01612840.2018.1443530
380. Wakefield EO, Pantaleao A, Popp JM, et al. Describing Perceived Racial Bias Among Youth With Sickle Cell Disease. *J Pediatr Psychol*. 2018;43(7):779-788. doi:10.1093/jpepsy/jsy015

381. Mathur VA, Kiley KB, Haywood C, et al. Multiple Levels of Suffering: Discrimination in Health-Care Settings is Associated With Enhanced Laboratory Pain Sensitivity in Sickle Cell Disease. *Clin J Pain*. 2016;32(12):1076-1085. doi:10.1097/AJP.0000000000000361
382. Haywood C, Diener-West M, Strouse J, et al. Perceived discrimination in health care is associated with a greater burden of pain in sickle cell disease. *J Pain Symptom Manage*. 2014;48(5):934-943. doi:10.1016/j.jpainsymman.2014.02.002
383. Mathur VA, Richeson JA, Paice JA, Muzyka M, Chiao JY. Racial bias in pain perception and response: experimental examination of automatic and deliberate processes. *J Pain Off J Am Pain Soc*. 2014;15(5):476- 484. doi:10.1016/j.jpain.2014.01.488
384. Martin SR, Cohen LL, Mougianis I, Griffin A, Sil S, Dampier C. Stigma and Pain in Adolescents Hospitalized for Sickle Cell Vasoocclusive Pain Episodes. *Clin J Pain*. 2018;34(5):438-444. doi:10.1097/ AJP.0000000000000553
385. Glassberg JA, Tanabe P, Chow A, et al. Emergency provider analgesic practices and attitudes toward patients with sickle cell disease. *Ann Emerg Med*. 2013;62(4):293-302.e10. doi:10.1016/j.annemergmed.2013.02.004
386. Campbell CM, Edwards RR. Ethnic differences in pain and pain management. *Pain Manag*. 2012;2(3):219-230. doi:10.2217/pmt.12.7
387. Fiscella K, Sanders MR. Racial and Ethnic Disparities in the Quality of Health Care. *Annu Rev Public Health*. 2016;37:375-394. doi:10.1146/annurev-publhealth-032315-021439
388. Vallerand AH, Cosler P, Henningfield JE, Galassini P. Pain management strategies and lessons from the military: A narrative review. *Pain Res Manag*. 2015;20(5):261-268.
389. Bosco MA, Murphy JL, Clark ME. Chronic pain and traumatic brain injury in OEF/OIF service members and Veterans. *Headache*. 2013;53(9):1518-1522. doi:10.1111/ head.12172

390. Vacchiano CA, Wofford KA, Titch JF. Chapter 1 posttraumatic stress disorder: a view from the operating theater. *Annu Rev Nurs Res*. 2014;32:1-23. doi:10.1891/0739-6686.32.1
391. US Department of Veterans Affairs. Mental health: Veteran suicide data. https://www.mentalhealth.va.gov/mentalhealth/suicide_prevention/data.asp. Published 2018.
392. Ilgen MA, Kleinberg F, Ignacio RV, et al. Noncancer pain conditions and risk of suicide. *JAMA Psychiatry*. 2013;70(7):692-697. doi:10.1001/jamapsychiatry.2013.908
393. Bao Y, Pan Y, Taylor A, et al. Prescription Drug Monitoring Programs Are Associated With Sustained Reductions In Opioid Prescribing By Physicians. *Health Aff Proj Hope*. 2016;35(6):1045-1051. doi:10.1377/hlthaff.2015.1673
394. Brandeis. *Guidance on PDMP Best Practices: Options for Unsolicited Reporting*. Brandeis University Prescription Drug Monitoring Program Center of Excellence; 2018. http://www.pdmpassist.org/pdf/Mandatory_Query_20180615.pdf.
395. National Alliance for Model State Drug Laws. *Prescription Drug Monitoring Programs*.; 2018. <http://www.namsdl.org/prescription-monitoring-programs.cfm>.
396. Green TC, Mann MR, Bowman SE, et al. How does use of a prescription monitoring program change medical practice? *Pain Med Malden Mass*. 2012;13(10):1314-1323. doi:10.1111/j.1526-4637.2012.01452.x
397. Irvine JM, Hallvik SE, Hildebran C, Marino M, Beran T, Deyo RA. Who uses a prescription drug monitoring program and how? Insights from a statewide survey of Oregon clinicians. *J Pain Off J Am Pain Soc*. 2014;15(7):747-755. doi:10.1016/j.jpain.2014.04.003
398. McAllister MW, Aaronson P, Spillane J, et al. Impact of prescription drug-monitoring program on controlled substance prescribing in the ED. *Am J Emerg Med*. 2015;33(6):781-785. doi:10.1016/j.ajem.2015.03.036
399. Dowell D, Zhang K, Noonan RK, Hockenberry JM. Mandatory Provider Review And Pain Clinic Laws Reduce The Amounts Of Opioids Prescribed And Overdose

Death Rates. *Health Aff Proj Hope*. 2016;35(10):1876-1883.
doi:10.1377/hlthaff.2016.0448

400. Johnson H, Paulozzi L, Porucznik C, Mack K, Herter B, Hal Johnson Consulting and Division of Disease Control and Health Promotion, Florida Department of Health. Decline in drug overdose deaths after state policy changes - Florida, 2010-2012. *MMWR Morb Mortal Wkly Rep*. 2014;63(26):569-574.

401. Buchmueller T, Carey C. The Effect of Prescription Drug Monitoring Programs on Opioid Utilization in Medicare. *Am Econ J Econ Policy*. 2018;10(1):77-112.

402. 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.e1-3. doi:10.1016/j.annemergmed.2009.12.011

403. American Medical Association. *Combating the Opioid Abuse Epidemic: Professional and Academic Perspectives*. Chicago, IL: American Medical Association; 2015.

404. Carrizosa N, Latham K. *Prescription Opioids: Prescriber Education and the Maryland Prescription Drug Monitoring Program*. Office of Legislative Oversight; 2017. <https://www.montgomerycountymd.gov/OLO/Resources/Files/2017%20Reports/OLO%20Report%20 2017%20-11%20Prescription%20Opioids.pdf>. Accessed November 30, 2017.

405. Massachusetts Department of Public Health. *Recommendations of the Governor's Opioid Working Group*. Boston, MA; 2015. <https://www.mass.gov/files/2017-08/recommendations-of-the-governors-opioid-working-group.pdf>.

406. South Dakota Department of Health. *South Dakota's Statewide Targeted Response to the Opioid Crisis*. Pierre, SD: South Dakota Department of Health; 2017.

407. Colorado Chapter of the American College of Emergency Physicians. *2017 Opioid Prescribing & Treatment Guidelines: Confronting the Opioid Epidemic in Colorado's Emergency Departments*. Northglenn, CO: Author; 2017.

http://coacep.org/docs/COACEP_Opioid_Guidelines-Final.pdf. Accessed November 21, 2017.

408. Barnett ML, Gray J, Zink A, Jena AB. Coupling Policymaking with Evaluation — The Case of the Opioid Crisis. *N Engl J Med*. 2017;377(24):2306-2309. doi:10.1056/NEJMp1710014
409. Radomski TR, Bixler FR, Zickmund SL, et al. Physicians' Perspectives Regarding Prescription Drug Monitoring Program Use Within the Department of Veterans Affairs: a Multi-State Qualitative Study. *J Gen Intern Med*. 2018;33(8):1253-1259. doi:10.1007/s11606-018-4374-1
410. Indian Health Services. Chapter 32: State Prescription Drug Monitoring Programs. In: *The Indian Health Manual*. Rockville, MD: United States Department of Health and Human Services Indian Health Services; 2016. <https://www.ihs.gov/ihtm/pc/part-3/p3c32/>.
411. Pergolizzi J, Pappagallo M, Stauffer J, et al. The role of urine drug testing for patients on opioid therapy. *Pain Pract Off J World Inst Pain*. 2010;10(6):497-507. doi:10.1111/j.1533-2500.2010.00375.x
412. Kaye AD, Jones MR, Kaye AM, et al. Prescription Opioid Abuse in Chronic Pain: An Updated Review of Opioid Abuse Predictors and Strategies to Curb Opioid Abuse (Part 2). *Pain Physician*. 2017;20(2S):S111-S133.
413. 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
414. Yudko E, Lozhkina O, Fouts A. A comprehensive review of the psychometric properties of the Drug Abuse Screening Test. *J Subst Abuse Treat*. 2007;32(2):189-198. doi:10.1016/j.jsat.2006.08.002
415. Reinert DF, Allen JP. The alcohol use disorders identification test: an update of research findings. *Alcohol Clin Exp Res*. 2007;31(2):185-199. doi:10.1111/j.1530-0277.2006.00295.x

416. Chou R, Deyo R, Devine B, et al. *The Effectiveness and Risks of Long-Term Opioid Treatment of Chronic Pain*. Agency for Healthcare Research and Quality (US); 2014.
417. Chou R, Turner JA, Devine EB, et al. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. *Ann Intern Med*. 2015;162(4):276-286. doi:10.7326/M14-2559
418. Starrels JL, Wu B, Peyser D, et al. It made my life a little easier: primary care providers' beliefs and attitudes about using opioid treatment agreements. *J Opioid Manag*. 2014;10(2):95-102. doi:10.5055/jom.2014.0198
419. Bair MJ, Krebs EE. Why is urine drug testing not used more often in practice? *Pain Pract Off J World Inst Pain*. 2010;10(6):493-496. doi:10.1111/j.1533-2500.2010.00425.x
420. Tobin DG, Andrews R, Becker WC. Prescribing opioids in primary care: Safely starting, monitoring, and stopping. *Cleve Clin J Med*. 2016;83(3):207-215. doi:10.3949/ccjm.83a.15034
421. Krebs EE, Lorenz KA, Bair MJ, et al. Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. *J Gen Intern Med*. 2009;24(6):733-738. doi:10.1007/s11606-009-0981-1
422. Polomano RC, Galloway KT, Kent ML, et al. Psychometric Testing of the Defense and Veterans Pain Rating Scale (DVPRS): A New Pain Scale for Military Population. *Pain Med Malden Mass*. 2016;17(8):1505-1519. doi:10.1093/pm/pnw105
423. Vallerand A, Nowak L. Chronic opioid therapy for nonmalignant pain: the patient's perspective. Part II-- Barriers to chronic opioid therapy. *Pain Manag Nurs Off J Am Soc Pain Manag Nurses*. 2010;11(2):126-131. doi:10.1016/j.pmn.2009.03.006
424. McAllister MJ. How to End the Stigma of Pain. <http://www.instituteforchronicpain.org/understanding-chronic-pain/healthcare-system-failings/how-to-end-the-stigma-of-pain>. Published 2017. Accessed August 31, 2018.

425. Larance B, Campbell G, Moore T, et al. Concerns and Help-Seeking Among Patients Using Opioids for Management of Chronic Noncancer Pain. *Pain Med Malden Mass*. 2018. doi:10.1093/pm/pny078
426. Slade SC, Molloy E, Keating JL. Stigma experienced by people with nonspecific chronic low back pain: a qualitative study. *Pain Med Malden Mass*. 2009;10(1):143-154. doi:10.1111/j.1526-4637.2008.00540.x
427. Stumbo SP, Yarborough BJH, McCarty D, Weisner C, Green CA. Patient-reported pathways to opioid use disorders and pain-related barriers to treatment engagement. *J Subst Abuse Treat*. 2017;73:47-54. doi:10.1016/j.jsat.2016.11.003
428. Alford DP, German JS, Samet JH, Cheng DM, Lloyd- Travaglini CA, Saitz R. Primary Care Patients with Drug Use Report Chronic Pain and Self-Medicate with Alcohol and Other Drugs. *J Gen Intern Med*. 2016;31(5):486-491. doi:10.1007/s11606-016-3586-5
429. Chou R, Korthuis PT, Weimer M, et al. *Medication- Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016.
<http://www.ncbi.nlm.nih.gov/books/NBK402352/>. Accessed January 14, 2018.
430. Salsitz E, Wiegand T. Pharmacotherapy of Opioid Addiction: "Putting a Real Face on a False Demon." *J Med Toxicol Off J Am Coll Med Toxicol*. 2016;12(1):58-63. doi:10.1007/s13181-015-0517-5
431. Winstanley EL, Clark A, Feinberg J, Wilder CM. Barriers to implementation of opioid overdose prevention programs in Ohio. *Subst Abuse*. 2016;37(1):42-46. doi:10.1080/08897077.2015.1132294
432. Substance Abuse and Mental Health Services Administration, Office of the Surgeon General. *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health*. Washington (DC): US Department of Health and Human Services; 2016. [http:// www.ncbi.nlm.nih.gov/books/NBK424857/](http://www.ncbi.nlm.nih.gov/books/NBK424857/). Accessed October 30, 2017.

433. President's Commission on Combating Drug Addiction and the Opioid Crisis. *Draft of Final Report*. Washington, DC: Author; 2017.
<https://www.whitehouse.gov/ondcp/presidents-commission/>. Accessed November 16, 2017.
434. Gross A, Miller J, D'Sylva J, et al. Manipulation or mobilisation for neck pain. *Cochrane Database Syst Rev*. 2010;(1):CD004249. doi:10.1002/14651858.CD004249.pub3
435. Suman A, Bostick GP, Schopflocher D, et al. Long-term evaluation of a Canadian back pain mass media campaign. *Eur Spine J*. 2017;26(9):2467-2474.
doi:10.1007/s00586-017-5249-6
436. Suman A, Bostick GP, Schaafsma FG, Anema JR, Gross DP. Associations between measures of socio-economic status, beliefs about back pain, and exposure to a mass media campaign to improve back beliefs. *BMC Public Health*. 2017;17(1):504.
doi:10.1186/s12889-017-4387-4
437. American Psychological Association. *Managing Chronic Pain: How Psychologists Help with Pain Management*. Washington, DC: American Psychological Association; 2012.
438. Clement I, Lorenz A, Ulm B, Plidschun A, Huber S. Implementing Systematically Collected User Feedback to Increase User Retention in a Mobile App for Self-Management of Low Back Pain: Retrospective Cohort Study. *JMIR MHealth UHealth*. 2018;6(6):e10422. doi:10.2196/10422
439. Palermo TM, de la Vega R, Dudeney J, Murray C, Law E. Mobile health intervention for self-management of adolescent chronic pain (WebMAP mobile): Protocol for a hybrid effectiveness-implementation cluster randomized controlled trial. *Contemp Clin Trials*. October 2018. doi:10.1016/j.cct.2018.10.003
440. Zhou C, Crawford A, Serhal E, Kurdyak P, Sockalingam S. The Impact of Project ECHO on Participant and Patient Outcomes: A Systematic Review. *Acad Med J Assoc Am Med Coll*. 2016;91(10):1439-1461. doi:10.1097/ACM.0000000000001328

441. Fishman SM, Carr DB, Hogans B, et al. Scope and Nature of Pain- and Analgesia-Related Content of the United States Medical Licensing Examination (USMLE). *Pain Med Malden Mass*. 2018;19(3):449-459. doi:10.1093/pm/pnx336
442. President's Commission on Combating Drug Addiction and the Opioid Crisis. Interim Report. <https://www.whitehouse.gov/sites/whitehouse.gov/files/ondcp/commission-interim-report.pdf>. Published July 31, 2017. Accessed December 1, 2017.
443. Davis D, Galbraith R, American College of Chest Physicians Health and Science Policy Committee. Continuing medical education effect on practice performance: effectiveness of continuing medical education: American College of Chest Physicians Evidence-Based Educational Guidelines. *Chest*. 2009;135(3 Suppl):42S-48S. doi:10.1378/chest.08-2517
444. Mazmanian PE, Davis DA, Galbraith R, American College of Chest Physicians Health and Science Policy Committee. Continuing medical education effect on clinical outcomes: effectiveness of continuing medical education: American College of Chest Physicians Evidence-Based Educational Guidelines. *Chest*. 2009;135(3 Suppl):49S-55S. doi:10.1378/chest.08-2518
445. O'Neil KM, Addrizzo-Harris DJ, American College of Chest Physicians Health and Science Policy Committee. Continuing medical education effect on physician knowledge application and psychomotor skills: effectiveness of continuing medical education: American College of Chest Physicians Evidence-Based Educational Guidelines. *Chest*. 2009;135(3 Suppl):37S- 41S. doi:10.1378/chest.08-2516
446. Frank JW, Carey EP, Fagan KM, et al. Evaluation of a telementoring intervention for pain management in the Veterans Health Administration. *Pain Med Malden Mass*. 2015;16(6):1090-1100. doi:10.1111/pme.12715
447. Rochfort A, Beirne S, Doran G, et al. Does patient self-management education of primary care professionals improve patient outcomes: a systematic review. *BMC Fam Pract*. 2018;19(1):163. doi:10.1186/s12875-018-0847-x

448. Shelley BM, Katzman JG, Comerici GD, et al. ECHO Pain Curriculum: Balancing Mandated Continuing Education With the Needs of Rural Health Care Practitioners. *J Contin Educ Health Prof*. 2017;37(3):190-194. doi:10.1097/ CEH.0000000000000165
449. World Health Organization. ICD-11 for Mortality and Morbidity Statistics. <https://icd.who.int/browse11/l-m/en#/http%3a%2f%2fid.who.int%2fid%2fentity%2f1581976053>. Published 2019.
450. International Association for the Study of Pain. Chronic Pain has arrived in the ICD-11. [https:// www.iasp-pain.org/PublicationsNews/NewsDetail.aspx?ItemNumber=8340&navItemNumber=643](https://www.iasp-pain.org/PublicationsNews/NewsDetail.aspx?ItemNumber=8340&navItemNumber=643). Published 2019. Accessed March 23, 2019.
451. Seers T, Derry S, Seers K, Moore RA. Professionals underestimate patients' pain: a comprehensive review. *Pain*. 2018;159(5):811-818. doi:10.1097/j.pain.0000000000001165
452. Bruera E. Parenteral Opioid Shortage - Treating Pain during the Opioid-Overdose Epidemic. *N Engl J Med*. 2018;379(7):601-603. doi:10.1056/NEJMp1807117
453. Sinatra R. Causes and consequences of inadequate management of acute pain. *Pain Med Malden Mass*. 2010;11(12):1859-1871. doi:10.1111/j.1526-4637.2010.00983.x
454. Baratta JL, Schwenk ES, Viscusi ER. Clinical consequences of inadequate pain relief: barriers to optimal pain management. *Plast Reconstr Surg*. 2014;134(4 Suppl 2):15S-21S. doi:10.1097/ PRS.0000000000000681
455. Muhuri P, Gfroerer J, Davies C. Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States. *SAMHSA CBHSQ Data Rev*. August 2013. <https://www.samhsa.gov/data/sites/default/files/DR006/DR006/nonmedical-pain-reliever-use-2013.htm>.
456. Nelson LS, Juurlink DN, Perrone J. Addressing the Opioid Epidemic. *JAMA*. 2015;314(14):1453-1454. doi:10.1001/jama.2015.12397

457. Hollingsworth H, Herndon C. The parenteral opioid shortage: Causes and solutions. *J Opioid Manag*. 2018;14(2):81-82. doi:10.5055/jom.2018.0434
458. Food and Drug Administration. Report on Drug Shortages for Calendar Year 2017. 2017. <https://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM610662.pdf>. Accessed November 30, 2018.
459. Institute for Safe Medication Practices. Weathering the storm: Managing the drug shortage crisis. *ISMP Medicat Saf Alert*. 2010;15(20):1-4.
460. Caulder CR, Mehta B, Bookstaver PB, Sims LD, Stevenson B. Impact of Drug Shortages on Health System Pharmacies in the Southeastern United States. *Hosp Pharm*. 2015;50(4):279-286. doi:10.1310/hpj5004-279
461. Institute for Safe Medication Practices. A shortage of everything except errors: Harm associated with drug shortages. *ISMP Medicat Saf Alert*. 2012;17:1-3.
462. Hughes KM, Goswami ES, Morris JL. Impact of a Drug Shortage on Medication Errors and Clinical Outcomes in the Pediatric Intensive Care Unit. *J Pediatr Pharmacol Ther JPPT Off J PPAG*. 2015;20(6):453-461. doi:10.5863/1551-6776-20.6.453
463. Food and Drug Administration. Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions; Public Meeting; Request for Comments. *Fed Regist*. 2018;83(175):45640-45642.
464. Lin D, Jones C, Compton W. Prescription drug coverage for treatment of low back pain among US Medicaid, Medicare Advantage, and commercial insurers. *JAMA Netw Open*. 2018;1(2).
465. Rosenbaum S, Kamoie B, Mauery D, Walitt B. *Medical Necessity in Private Health Plans: Implications for Behavioral Health Care*. Rockville, MD: Center for Mental Health Services, Substance Abuse and Mental Health Services Administration; 2003.
466. American Board of Pain Medicine. American Board of Pain Medicine FAQs. <http://www.abpm.org/faq>. Published August 2018. Accessed October 10, 2018.

467. American Board of Medical Specialties. *ABMS Guide to Medical Specialties*. Chicago, IL: American Board of Medical Specialties; 2018. https://www.abms.org/media/114634/guide-to-medicalspecialties_04_2016.pdf.
468. American Society of Regional Anesthesia and Pain. The specialty of chronic pain management. <https://www.asra.com/page/44/the-specialty-of-chronic-pain-management>. Published 2018. Accessed October 10, 2018.
469. Serafini M. The Physicians' Quandary with Opioids: Chronic Pain vs. Addiction. NEJM Catalyst. <https://catalyst.nejm.org/quandary-opioids-chronic-pain-addiction/>. Published April 26, 2018. Accessed October 10, 2018.
470. Dubois MY, Gallagher RM, Lippe PM. Pain medicine position paper. *Pain Med Malden Mass*. 2009;10(6):972- 1000. doi:10.1111/j.1526-4637.2009.00696.x
471. National Institutes of Health. PA-16-187: Mechanisms, Models, Measurement, and Management in Pain Research (R21). <https://grants.nih.gov/grants/guide/pa-files/pa-16-187.html>. Published March 22, 2019. Accessed March 22, 2019.
472. Centers for Disease Control and Prevention. Drug Overdose Deaths. <https://www.cdc.gov/drugoverdose/data/statedeaths.html>. Published 2019.
473. Pitt AL, Humphreys K, Brandeau ML. Modeling Health Benefits and Harms of Public Policy Responses to the US Opioid Epidemic. *Am J Public Health*. 2018;108(10):1394-1400. doi:10.2105/AJPH.2018.304590
474. Chen Q, Laroche MR, Weaver DT, et al. Prevention of Prescription Opioid Misuse and Projected Overdose Deaths in the United States. *JAMA Netw Open*. 2019;2(2):e187621. doi:10.1001/jamanetworkopen.2018.7621
475. Busse JW, Juurlink D, Guyatt GH. Addressing the limitations of the CDC guideline for prescribing opioids for chronic noncancer pain. *CMAJ Can Med Assoc J J Assoc Medicale Can*. 2016;188(17-18):1210-1211. doi:10.1503/cmaj.161023
476. Gordon AL, Connolly SL. Treating Pain in an Established Patient: Sifting Through the Guidelines. *R I Med J*. 2017;100(10):41-44.

477. Anson P. AMA: 'Inappropriate Use' of CDC Guideline Should Stop. Pain News Network. <https://www.painnewsnetwork.org/stories/2018/11/14/ama-calls-for-misapplication-of-cdc-opioid-guideline-to-end>. Published November 14, 2018. Accessed November 30, 2018.
478. American Society of Hematology. CDC Issues Key Clarification on Guideline for Prescribing Opioids for Chronic Pain. /Newsroom/Press-Releases/2019/9537. aspx. Published April 9, 2019. Accessed April 13, 2019.
479. Michigan Department of Licensing and Regulatory Affairs, Michigan Department of Health and Human Services. Michigan Opioid Laws: Frequently Asked Questions (FAQs). 2018. https://www.msms.org/Portals/0/Documents/MSMS/Resources/For_Practices/Pain_Management/LARA_DHHS_Opioid_Laws_FAQ_REVISED_07-03-2018.pdf?ver=2018-07-05-104031-253.
480. National Conference of State Legislatures. Prescribing policies: States confront opioid overdose epidemic. <http://www.ncsl.org/research/health/prescribing-policies-states-confront-opioid-overdose-epidemic.aspx>. Published 2018.
481. Ohio Academy of Family Physicians. Opioid Prescribing Guidelines – Ohio Academy of Family Physicians. 2017. <https://www.ohioafp.org/public-policy/state-legislative-regulatory-issues/opioid-prescribing-guidelines/>. Accessed October 30, 2018.
482. State Volunteer Mutual Insurance Company. Summary of Tennessee Opioid Prescribing Laws. 2018. [https:// home.svmic.com/resources/2018-summary-of-tennessee-opioid-prescribing-laws](https://home.svmic.com/resources/2018-summary-of-tennessee-opioid-prescribing-laws).
483. Ciccone T, Kean N. Responses and criticisms over new CDC opioid prescribing guidelines. Pr Pain Manag. 2016;16. <https://www.practicalpainmanagement.com/resources/news-and-research/responses-criticisms-over-new-cdc-opioid-prescribing-guidelines>.
484. Hoffman J, Goodnough A. Good News: Opioid Prescribing Fell. The Bad? Pain Patients Suffer, Doctors Say. *New York Times*. <https://www.nytimes.com/2019/03/06/health/opioids-pain-cdc-guidelines.html>. Published March 6, 2019.

485. US Food and Drug Administration. FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering. <https://www.fda.gov/Drugs/DrugSafety/ucm635038.htm>. Published 2019.

486. Rathmell JP, Fields HL. Chapter 10: Pain: Pathophysiology and Management. In: *Harrison's Principles of Internal Medicine*. 20th ed. New York, NY: McGraw-Hill; 2018:65-73.

487. Centers for Medicare & Medicaid Services. 2019 Medicare Advantage and Part D Rate Announcement and Call Letter | CMS. <https://www.cms.gov/newsroom/fact-sheets/2019-medicare-advantage-and-part-d-rate-announcement-and-call-letter>. Published 2018. Accessed December 1, 2018.

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U.S. Department of Health and Human Services (2019, May). Pain Management Best Practices Inter-Agency Task Force Report: Updates, Gaps, Inconsistencies, and Recommendations. Retrieved from U. S. Department of Health and Human Services website: <https://www.hhs.gov/ash/advisory-committees/pain/reports/index.html>

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