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Hassan R Mir

Anna N Miller

William T Obremskey

A Alex Jahangir

Joseph R Hsu

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Confronting the Opioid Crisis: Practical Pain Management and Strategies

AOA 2018 Critical Issues Symposium

Hassan R. Mir, MD, MBA, FACS, FAOA, Anna N. Miller, MD, FACS, FAOA, William T. Obrebsky, MD, MPH, MMHC, FAOA, A. Alex Jahangir, MD, MMHC, FAOA, and Joseph R. Hsu, MD, FAOA

Abstract: The United States is in the midst of an opioid crisis. Clinicians have been part of the problem because of overprescribing of narcotics for perioperative pain management. Clinicians need to understand the pathophysiology and science of addiction to improve perioperative management of pain for their patients. Multiple modalities for pain management exist that decrease the use of narcotics. Physical strategies, cognitive strategies, and multimodal medication can all provide improved pain relief and decrease the use of narcotics. National medical societies are developing clinical practice guidelines for pain management that incorporate multimodal strategies and multimodal medication. Changes to policy that improve provider education, access to naloxone, and treatment for addiction can decrease narcotic misuse and the risk of addiction.

Epidemiology

The United States finds itself in the midst of the current opioid crisis because of the alarming rise in the number of prescriptions for opioids and the number of pills that have been diverted for nonmedical use over the past few decades¹⁻³. The number of opioid-related deaths has more than quadrupled since 1999, and is now higher than deaths from illicit drugs such as heroin and cocaine combined, and even higher than deaths from motor-vehicle collisions⁴. The Surgeon General highlighted this crisis in 2016 in the report “Facing Addiction in America.”⁵ In addition to the rising death toll, opioids have had a major impact on public health because of related issues. For every 1 prescription opioid death, there are 20 specialty substance-abuse treatment admissions, 45 emergency department visits for nonmedical use and adverse events, 156 people

with substance use disorder and dependence, and 533 people using the drugs nonmedically overall^{5,6}.

The opioid crisis has been largely fueled by the oversupply of prescription opioids in circulation, which leads to diversion from friends and families to illicit use⁴. The Surgeon General’s report also confirmed that there has been a concomitant resurgence in the number of deaths related to heroin, and an even greater rise in the number of deaths related to illicit fentanyl². Therefore, the opioid crisis in the U.S. may be even worse than reported when considering the additional effects from related illicit drugs on death rates and the aforementioned other health and societal issues.

The opioid crisis in the U.S. has been referred to as an *epidemic*, a term that is typically reserved for widespread phenomena. When looking at international data, there has been a

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global increase in the amount of opioids utilized in terms of morphine milligram equivalents per capita over the past few decades that mimics the data seen in the U.S.; therefore, the opioid crisis could be considered an international epidemic or even a pandemic¹. However, when one looks more closely at the data, it can be argued that there are actually 2 facets to the global opioid situation. In much of the developed world (U.S., Canada, Europe, and Australia), the rates of opioid use per capita are extremely high, while in much of the developing world (Central Asia, Central and South America, and Africa) the rates of opioid use per capita are extremely low; in many of these developing nations, there are not enough medications to manage acute severe pain or more chronic cancer-related pain¹.

There are approximately 1 million physicians in the U.S., and nearly 2% (~20,000) are practicing orthopaedic surgeons⁷. Although small in number, orthopaedic surgeons (7.7%) are the fourth highest prescribers of opioids, behind primary care physicians (28.8%), internists (14.6%), and dentists (8.0%), for the percentage of prescriptions dispensed by U.S. retail pharmacies⁸. There are substantially more members of each of those specialties, with approximately 109,000 primary care physicians, 111,000 internists, and 195,000 dentists^{8,9}. Orthopaedic surgeons prescribe more narcotic medication per clinician when compared with any other specialty^{8,9}. Musculoskeletal conditions (surgical and nonsurgical) can be associated with substantial acute and chronic pain. Many patients who are treated by primary care physicians, internists, and emergency room physicians have musculoskeletal pain. Over the past few decades, the use of opioids for musculoskeletal pain diagnoses in ambulatory settings, including primary care clinics and emergency departments, has doubled^{10,11}. Therefore, the impact of orthopaedic surgeons on the management of musculoskeletal pain can have an effect within the specialty and an even greater potential impact outside of the specialty by decreasing the utilization of opioids as first-line treatment and monotherapy for acute and chronic musculoskeletal conditions.

Science of Addiction

Opioid analgesics are a class of medication that works on mu receptors in the brain and the spinal cord. Specifically, these mu receptors (also known as opioid receptors) inhibit gamma-aminobutyric acid (GABA), which is the chief inhibitory neurotransmitter in mammals. As the opioids activate these mu receptors and inhibit GABA, dopamine is released (since GABA normally inhibits dopamine). Increased dopamine, specifically in the nucleus accumbens, increases feelings of pleasure, leading to the positive associations that patients have with opioid ingestion that are specifically related to addiction.

Increasing opioid strength also can be related to addiction and death¹². Specifically, commonly used medications such as fentanyl and hydromorphone are substantially stronger than morphine. In addition, medications that are thousands of times stronger are now starting to be disseminated on the black market¹³.

Addiction is defined as a “chronic, relapsing brain disease that is characterized by compulsive drug seeking and use,

despite harmful consequences.”¹⁴ Addiction is now considered a disease of the brain due to actual changes seen in the brain that may or may not be permanent¹⁵. In contrast, physical dependence is related to regular use of a substance; specifically, when the patient adapts to that regular use, he or she may have physical symptoms when the substance is stopped¹⁴.

Substance use disorder is defined as a “problematic pattern of use of an intoxicating substance, leading to clinically significant impairment or distress,”¹⁶ as manifested by at least 2 of the characteristics that are listed in Table I occurring within a 12-month period¹⁶.

Addiction in the brain acts in a cycle, starting with bingeing or becoming intoxicated (stage 1), followed by withdrawal or feeling negative (stage 2), and then finally moving to “preoccupation/anticipation” (stage 3), which leads back to stage 1¹⁷. It is important to note that addiction is separate from, but may be related to, drug abuse. Abuse is the use of illegal drugs or the misuse of prescription or over-the-counter medications, which can lead to negative consequences in personal relationships, legal encounters, and physical risks¹⁴. The abuse of prescription opioids has increased substantially in recent years; overdose deaths alone increased fivefold from 1999 to 2016¹⁸.

Certain factors are strongly associated with the risk of opioid overdose or addiction, and clinicians should take care to evaluate their patients for these risks: age >65 years or

TABLE I Characteristics of Substance Use Disorder

The substance is often taken in larger amounts or over a longer period than it was intended
There is a persistent desire or unsuccessful effort to cut down or control use of the substance
A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects
Craving or a strong desire or urge to use the substance
Recurrent use of the substance, resulting in a failure to fulfill major role obligations at work, school, or home
Continued use of the substance despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of its use
Important social, occupational, or recreational activities are given up or reduced because of use of the substance
Recurrent use of the substance in situations in which it is physically hazardous
Use of the substance is continued despite having knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
Tolerance: a need for markedly increased amounts of the substance to achieve intoxication or desired effect OR a markedly diminished effect with continued use of the same amount of the substance
Withdrawal: characteristic withdrawal syndrome for that substance OR the substance (or a closely related substance) is taken to relieve or avoid withdrawal symptoms

adolescents, sleep apnea and breathing disorders, kidney or liver disease, depression, other substance use disorders, and a history of overdose¹⁹. In addition, we as clinicians can exacerbate risk factors via the medication itself, including use of morphine milliequivalent doses of >100 daily, long-acting or extended-release medications, and combining benzodiazepines with opioids¹⁹. Clinicians should particularly be on high alert for patients in the first couple of weeks after medication initiation and for those patients who are using opioids for >3 months since these patients are at particularly high risk of overdose and addiction, respectively¹⁹. Patients taking narcotics for an extended period of time may be considered for referral to a mental health provider or addiction treatment.

Prescribing Practices and Recommendations

Because of the frequency of opioid use in routine orthopaedic procedures and the high risk of abuse and addiction associated with opioids, the Orthopaedic Trauma Association (OTA) developed evidence-based guidelines for pain management²⁰. Hsu et al. reviewed these guidelines since the vast majority of orthopaedic injuries are cared for in community hospitals by orthopaedic surgeons who are not affiliated with the OTA. We hope that wider dissemination of this information improves patient care, decreases diversion of narcotics, and decreases abuse and addiction.

Clinical Management

With our patients, balancing comfort and safety with pain alleviation means evolving beyond the opioid monotherapy strategies that have dominated the past 3 decades²¹. While opioids have some benefit in the acute setting, multimodal pain alleviation involves pharmaceutical, physical, and cognitive strategies. The recently published Clinical Practice Guidelines (CPGs) from the OTA detail the evidence behind practical solutions for a multimodal approach to acute injury or surgery²⁰.

One barrier to this balanced approach has been orthopaedic surgeons' fear of utilizing nonsteroidal anti-inflammatory drugs (NSAIDs) in the setting of bone healing²¹. More recent evidence-based reviews suggest that this fear was not well founded scientifically^{20,22}. NSAIDs have not been indicated in increasing the risk of nonunion or other complications, especially with perioperative use. Including other medications such as gabapentin²³ and acetaminophen can help to decrease the dose and duration of opioid use while providing appropriate pain relief. Adequate and precise opioid prescription allows the concomitant use of additional acetaminophen, as detailed in the medication taper method in the OTA CPGs²⁰. Adequate prescribing practices can be based on using medications that the patient has recently required postoperatively or historical use with similar injuries to guide the prescription of medication at hospital discharge²⁴.

Physical strategies alter pain receptors by blocking fibers or providing superficial alternative stimulation to blunt deep pain. Physical strategies for pain alleviation include nerve blocks²⁵ and field blocks^{26,27}. Cryotherapy, or ice therapy, has

demonstrated reasonable clinical benefits with pain relief²⁸⁻³⁰ that is consistent with basic science mechanisms³¹⁻³³. Cryotherapy can even be effective under splints or casts³⁴⁻³⁷. Transcutaneous electrical nerve stimulation (TENS) has been shown to improve pain relief while decreasing opioid consumption in a variety of settings³⁸⁻⁴⁰.

Cognitive strategies for pain alleviation target the well-established relationship between anxiety and pain⁴¹⁻⁴⁴. While cognitive strategies can be resource intensive, some, including music therapy and aromatherapy, are very scalable. Both music therapy and aromatherapy have been shown to decrease anxiety and pain in evidence-based reviews⁴⁵. Cognitive behavioral therapy can be effective⁴⁶, but it is difficult to scale unless web-based strategies are employed^{47,48}.

Perioperative analgesia in patients with chronic opioid use should be managed with a multimodal analgesia regimen. An acute pain service (APS) can assist with coordinating inpatient and outpatient medication. Having only 1 prescriber is optimal for patients who have been using illicit opioids or for patients who have been misusing prescription opioids.

Patients who have been consuming routine and scheduled oral opioids prior to surgery should continue baseline medication on the morning of surgery and throughout the postoperative period. Transdermal fentanyl patches should be converted to an intravenous morphine equivalent dose because of alterations in fentanyl release that are secondary to perioperative fluid shifts and body temperature changes. When oral medications cannot be consumed because of NPO (nothing by mouth) status or when patients are unable to receive medications by mouth, a 24-hour morphine equivalent dose should be calculated to provide the equivalent in intravenous medication or transdermal buprenorphine until oral medications can be resumed.

Regular assessment of pain for both inpatients and outpatients is suggested in order to evaluate the need for initiation or continuation of multimodal therapy. Nursing staff should conduct sedation assessment on all inpatients who are receiving pain medication. Naloxone also should be prescribed when factors that increase a risk of overdose are present.

A prescription drug monitoring program (PDMP) should be regularly queried before opioids are prescribed. Orthopaedic departments need to support opioid education efforts for patients and clinicians. Clinical decision support in the electronic medical record is beneficial for prescribers in order to minimize errors and provide information on multimodal medication and opioid dosing.

State Policy and the Opioid Epidemic

In the U.S., individual states have employed many ways to try to fight the opioid epidemic. These have included prescribing limits and guidelines, mandatory patient and provider-level prescription monitoring, standards of practice, prescriber education, expanded access to naloxone, and expanded access to treatment. As described below, these initiatives have had mixed results in fighting the epidemic.

Mandatory Prescription Monitoring

Every state except Missouri currently has a prescription monitoring program. In 32 states, the prescription monitoring program is mandatory. In 2012, Kentucky became the first state to establish such a program. In the first year of the program, Kentucky saw a 30% decrease in the concurrent prescribing of opioids and sedatives, as well as a 25% decrease in deaths from opioid abuse⁴⁹. Most of these databases are updated daily, although some are only updated weekly. Additionally, there is inconsistent sharing of information among states. For example, Tennessee has 8 border states, but it does not share data with 3 of the states that border it, resulting in incomplete information for clinicians as they make decisions regarding prescribing. We believe that a national prescription monitoring program would be ideal.

Standards of Practice

Some states have passed legislation to create standards around prescribing practices. One example is in the state of Rhode Island. In 2017, Rhode Island passed legislation that created the nation's first comprehensive statewide standards for treating overdose and opioid use in hospitals and emergency departments⁵⁰. A 3-level system of categorization that defines each hospital and emergency department's current capacity to treat opioid-use disorder was established. The expectation was that every hospital-based or freestanding emergency department will meet the requirements for a level-3 designation, which represents a common foundation for all facilities that demonstrate a solid commitment to this health-care problem by creating the required infrastructure and subject-matter expertise to appropriately treat these patients. Some of the requirements for the level-3 designation include the following:

- Dispense the opioid antidote naloxone to all patients at risk.
- Educate all patients who are prescribed opioids on safe storage and disposal.
- Provide comprehensive discharge planning to people who have overdosed.
- Screen all patients for substance use disorder.
- Report all overdoses to the state health department within 48 hours.
- Offer patients peer recovery support services.

Prescriber Education

Twenty-three states and the District of Columbia have requirements for practitioners to obtain a certain number of continuing education hours in ≥1 of the following topics: prescribing controlled substances, pain management, and identifying substance use disorders, among others⁵⁰.

Expanded Access to Naloxone

Currently, all 50 states allow medical clinicians to prescribe naloxone to patients who are at risk for opioid overdose⁵¹. The concern, however, is that sometimes those at the highest

risk for overdose do not have access to or contact with a medical provider to receive a prescription. Increasing ease of access to naloxone has been shown to be an effective way to prevent opioid deaths. Forty-five states allow a third party who is not at personal risk of an opioid overdose to be prescribed naloxone that can be administered to another person⁵¹. A final manner in which to expand access to naloxone is non-patient-specific prescriptions. This practice is allowed in 49 states. Non-patient-specific prescriptions authorize naloxone distribution to individuals and organizations that meet specific criteria without needing to interact with a prescriber beforehand. An example of this is allowing pharmacies to dispense naloxone to individuals who request it without their own prescription, a practice that is currently allowed in 41 states⁵¹.

Expanded Access to Addiction Treatment

Expanded access to treatment also has been shown to be an important tool in the fight against opioid addiction. Unfortunately, universal access to addiction treatment has been hampered because of the fight regarding the expansion of Medicaid. Specifically, states that have expanded access to Medicaid provide more of the lifesaving treatments, including medication-assisted therapy, which has been shown to be effective in treating patients with opioid addiction, compared with states that have not expanded Medicaid⁵². Of the Medicaid-enrolled individuals in opioid addiction treatment, those who use opioid antagonist therapy include 45% of individuals in states with coverage for methadone maintenance and 30% of individuals in states with block grant coverage only. In comparison, only 17% of individuals in states with no coverage get medication-assisted therapy⁵².

The United States is in the midst of an opioid crisis. Clinicians have been part of the problem because of overprescribing of narcotics for perioperative pain management. Clinicians need to understand the pathophysiology and science of addiction to improve perioperative management of pain for their patients. Multiple modalities for pain management exist that decrease the use of narcotics. Physical strategies, cognitive strategies, and multimodal medication can all provide improved pain relief and decrease the use of narcotics. National medical societies are developing CPGs for pain management that incorporate multimodal strategies and multimodal medication. Changes to policy that improve provider education, access to naloxone, and treatment for addiction can decrease narcotic misuse and the risk of addiction. ■

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Hassan R. Mir, MD, MBA, FACS, FAOA¹

Anna N. Miller, MD, FACS, FAOA²

William T. Obremsky, MD, MPH, MMHC, FAOA³

A. Alex Jahangir, MD, MMHC, FAOA³

Joseph R. Hsu, MD, FAOA⁴¹Department of Orthopaedic Surgery, University of South Florida, Florida Orthopedic Institute, Tampa, Florida²Department of Orthopaedic Surgery, Washington University School of Medicine, St. Louis, Missouri³Department of Orthopaedic Surgery, Vanderbilt University Medical Center, Nashville, Tennessee⁴Atrium Health Musculoskeletal Institute, Carolinas Medical Center, Charlotte, North CarolinaEmail address for W.T. Obremskey: william.obremskey@Vanderbilt.eduORCID iD for H.R. Mir: [0000-0002-0260-3468](https://orcid.org/0000-0002-0260-3468)ORCID iD for A.N. Miller: [0000-0002-7056-8502](https://orcid.org/0000-0002-7056-8502)ORCID iD for W.T. Obremskey: [0000-0002-8942-1842](https://orcid.org/0000-0002-8942-1842)ORCID iD for A.A. Jahangir: [0000-0001-7514-6846](https://orcid.org/0000-0001-7514-6846)ORCID iD for J.R. Hsu: [0000-0002-7050-6504](https://orcid.org/0000-0002-7050-6504)

References

- United Nations Office on Drugs and Crime. International Narcotics Control Board Report 2015. United Nations Publications; 2016.
- Volkow ND. America's addiction to opioids: heroin and prescription drug abuse. 2014. <https://archives.drugabuse.gov/testimonies/2014/Americas-addiction-to-opioids-heroin-prescription-drug-abuse>. Accessed 2019 Jun 19.
- Manchikanti L, Singh A. Therapeutic opioids: a ten-year perspective on the complexities and complications of the escalating use, abuse, and nonmedical use of opioids. *Pain Physician*. 2008 Mar;11(2)(Suppl):S63-88.
- Centers for Disease Control and Prevention. Multiple cause of death data. <https://wonder.cdc.gov/mcd.html>. 2018. Accessed 2019 Jun 19.
- U.S. Department of Health and Human Services, Office of the Surgeon General. Facing addiction in America. The Surgeon General's report on alcohol, drugs, and health. <https://addiction.surgeongeneral.gov/sites/default/files/surgeon-generals-report.pdf>. Accessed 2019 Jun 19.
- U.S. Department of Health and Human Services. Drug Abuse Warning Network, 2011: national estimates of drug-related emergency department visits. 2013. <https://www.samhsa.gov/data/sites/default/files/DAWN2k11ED/DAWN2k11ED/DAWN2k11ED.pdf>. Accessed 2019 Jun 19.
- American Association of Medical Colleges. 2014 Physician specialty data book. 2014. <https://www.aamc.org/data/workforce/reports/439208/specialtydataandreports.html>. Accessed 2019 Jun 19.
- Volkow ND, McLellan TA, Cotto JH, Karithanom M, Weiss SRB. Characteristics of opioid prescriptions in 2009. *JAMA*. 2011 Apr 6;305(13):1299-301.
- American Dental Association. Supply and profile of dentists. <https://www.ada.org/en/science-research/health-policy-institute/data-center/supply-and-profile-of-dentists>. Accessed 2019 Jun 19.
- Daubresse M, Chang HY, Yu Y, Viswanathan S, Shah ND, Stafford RS, Kruszewski SP, Alexander GC. Ambulatory diagnosis and treatment of nonmalignant pain in the United States, 2000-2010. *Med Care*. 2013 Oct;51(10):870-8.
- Mazer-Amirshahi M, Mullins PM, Rasooly I, Van Den Anker J, Pines JM. Rising opioid prescribing in adult U.S. emergency department visits: 2001-2010. In: *Academic Emergency Medicine*; 2014.
- Centers for Medicare & Medicaid Services. Opioid oral morphine milligram equivalent (MME) conversion factors. <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-April-2017.pdf>. Published 2017 Apr.
- Keating D, Granados S. See how deadly street opioids like 'elephant tranquilizer' have become. *The Washington Post*. https://www.washingtonpost.com/graphics/2017/health/opioids-scale/?noredirect=on&utm_term=.8229179d9f9b. Published 2017 Oct 25.
- National Institute on Drug Abuse. The science of drug use and addiction: the basics. 2018. <https://www.drugabuse.gov/publications/media-guide/science-drug-use-addiction-basics>. Accessed 2019 Jun 19.
- National Institute on Drug Abuse. Drugs, brains, and behavior: the science of addiction. 2018. <https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction>. Accessed 2019 Jun 19.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Fifth edition. 2014.
- Munro M. The hijacked brain. *Nature*. 2015 Jun 25;522(7557):S46-7.
- Seth P, Rudd RA, Noonan RK, Haegerich TM. Quantifying the epidemic of prescription opioid overdose deaths. *Am J Public Health*. 2018 Apr;108(4):500-2.
- Volkow ND, McLellan AT. Opioid abuse in chronic pain—misconceptions and mitigation strategies. *N Engl J Med*. 2016 Mar 31;374(13):1253-63.
- Hsu JR, Mir H, Wally MK, Seymour RB. Orthopaedic trauma association musculoskeletal pain task force. Clinical practice guidelines for pain management in acute musculoskeletal injury. *J Orthop Trauma*. 2019 May;33(5):e158-82.
- Seymour RB, Ring D, Higgins T, Hsu JR. Leading the way to solutions to the opioid epidemic: AOA Critical Issues. *J Bone Joint Surg Am*. 2017 Nov 1;99(21):e113. doi: .
- Dodwell ER, Latorre JG, Parisini E, Zwettler E, Chandra D, Mulpuri K, Snyder B. NSAID exposure and risk of nonunion: a meta-analysis of case-control and cohort studies. *Calcif Tissue Int*. 2010 Sep;87(3):193-202. Epub 2010 Jun 15.
- Ho KY, Gan TJ, Habib AS. Gabapentin and postoperative pain—a systematic review of randomized controlled trials. *Pain*. 2006 Dec 15;126(1-3):91-101. Epub 2006 Jul 18.
- Chen EY, Marcantonio A, Tornetta P 3rd. Correlation between 24-hour predischARGE opioid use and amount of opioids prescribed at hospital discharge. *JAMA Surg*. 2018 Feb 21;153(2):e174859-174859. Epub 2018 Feb 21.
- Yang L, Li M, Chen C, Shen J, Bu X. Fascia iliaca compartment block versus no block for pain control after lower limb surgery: a meta-analysis. *J Pain Res*. 2017 Dec 14;10:2833-41.
- Hamilton TW, Athanassoglou V, Mellon S, Strickland LH, Trivella M, Murray D, Pandit HG. Liposomal bupivacaine infiltration at the surgical site for the management of postoperative pain. *Cochrane Database Syst Rev*. 2017 Feb 1;2:CD011419.
- Koehler D, Marsh JL, Karam M, Fruehling C, Willey M. Efficacy of surgical-site, multimodal drug injection following operative management of femoral fractures: A randomized controlled trial. *J Bone Joint Surg Am*. 2017 Mar 15;99(6):512-9.
- Thienpont E. Does advanced cryotherapy reduce pain and narcotic consumption after knee arthroplasty? *Clin Orthop Relat Res*. 2014 Nov;472(11):3417-23. Epub 2014 Jul 25.
- Cohn BT, Draeger RI, Jackson DW. The effects of cold therapy in the postoperative management of pain in patients undergoing anterior cruciate ligament reconstruction. *Am J Sports Med*. 1989 May-Jun;17(3):344-9.
- Adie S, Kwan A, Naylor JM, Harris IA, Mittal R. Cryotherapy following total knee replacement. *Cochrane Database Syst Rev*. 2012 Sep 12;(9):CD007911.
- Ho SSW, Illgen RL, Meyer RW, Torok PJ, Cooper MD, Reider B. Comparison of various icing times in decreasing bone metabolism and blood flow in the knee. *Am J Sports Med*. 1995 Jan-Feb;23(1):74-6.
- Deal DN, Tipton J, Rosencrance E, Curl WW, Smith TL. Ice reduces edema. A study of microvascular permeability in rats. *J Bone Joint Surg Am*. 2002 Sep;84(9):1573-8.
- Stålman A, Berglund L, Dungen E, Arner P, Felländer-Tsai L. Temperature-sensitive release of prostaglandin E₂ and diminished energy requirements in synovial tissue with postoperative cryotherapy: a prospective randomized study after knee arthroscopy. *J Bone Joint Surg Am*. 2011 Nov 2;93(21):1961-8.
- Okcu G, Yercan HS. Is it possible to decrease skin temperature with ice packs under casts and bandages? A cross-sectional, randomized trial on normal and swollen ankles. *Arch Orthop Trauma Surg*. 2006 Dec;126(10):668-73. Epub 2006 Jul 11.
- Metzman L, Gamble JG, Rinsky LA. Effectiveness of ice packs in reducing skin temperature under casts. *Clin Orthop Relat Res*. 1996 Sep;(330):217-21.
- Weresh MJ, Bennett GL, Njus G. Analysis of cryotherapy penetration: a comparison of the plaster cast, synthetic cast, Ace wrap dressing, and Robert-Jones dressing. *Foot Ankle Int*. 1996 Jan;17(1):37-40.
- Ibrahim T, Ong SM, Saint Clair Taylor GJ. The effects of different dressings on the skin temperature of the knee during cryotherapy. *Knee*. 2005 Jan;12(1):21-3.
- Björdal JM, Johnson MI, Ljunggreen AE. Transcutaneous electrical nerve stimulation (TENS) can reduce postoperative analgesic consumption. A meta-analysis with assessment of optimal treatment parameters for postoperative pain. *Eur J Pain*. 2003;7(2):181-8.
- Mahure SA, Rokito AS, Kwon YW. Transcutaneous electrical nerve stimulation for postoperative pain relief after arthroscopic rotator cuff repair: a prospective double-blinded randomized trial. *J Shoulder Elbow Surg*. 2017 Sep;26(9):1508-13. Epub 2017 Jul 20.
- Tedesco D, Gori D, Desai KR, Asch S, Carroll IR, Curtin C, McDonald KM, Fantini MP, Hernandez-Boussard T. Drug-free interventions to reduce pain or opioid consumption after total knee arthroplasty: a systematic review and meta-analysis. *JAMA Surg*. 2017 Oct 18;152(10):e172872. Epub 2017 Oct 18.

- 41.** Riddle DL, Golladay GJ, Hayes A, Ghomrawi HMK. Poor expectations of knee replacement benefit are associated with modifiable psychological factors and influence the decision to have surgery: a cross-sectional and longitudinal study of a community-based sample. *Knee*. 2017 Mar;24(2):354-61. Epub 2016 Dec 1.
- 42.** Morgounovski J, Vuistiner P, Léger B, Luthi F. The fear-avoidance model to predict return to work after an orthopedic trauma. *Ann Phys Rehabil Med*. 2016;59:e110-1.
- 43.** Vranceanu AM, Hageman M, Strooker J, ter Meulen D, Vrahas M, Ring D. A preliminary RCT of a mind body skills based intervention addressing mood and coping strategies in patients with acute orthopaedic trauma. *Injury*. 2015 Apr;46(4):552-7. Epub 2014 Nov 10.
- 44.** Helmerhorst GTT, Vranceanu AM, Vrahas M, Smith M, Ring D. Risk factors for continued opioid use one to two months after surgery for musculoskeletal trauma. *J Bone Joint Surg Am*. 2014 Mar 19;96(6):495-9.
- 45.** Lakhan SE, Sheaffer H, Tepper D. The effectiveness of aromatherapy in reducing pain: a systematic review and meta-analysis. *Pain Res Treat*. 2016;2016:8158693. Epub 2016 Dec 14.
- 46.** Ehde DM, Dillworth TM, Turner JA. Cognitive-behavioral therapy for individuals with chronic pain: efficacy, innovations, and directions for research. *Am Psychol*. 2014 Feb-Mar;69(2):153-66.
- 47.** Macea DD, Gajos K, Daglia Calil YA, Fregni F. The efficacy of Web-based cognitive behavioral interventions for chronic pain: a systematic review and meta-analysis. *J Pain*. 2010 Oct;11(10):917-29. Epub 2010 Jul 22.
- 48.** Palermo TM, Eccleston C, Lewandowski AS, Williams AC de C, Morley S. Randomized controlled trials of psychological therapies for management of chronic pain in children and adolescents: an updated meta-analytic review. *Pain*. 2010 Mar;148(3):387-97. Epub 2009 Nov 11.
- 49.** Kentucky Cabinet for Health and Family Services. Kentucky House Bill 1 impact evaluation: executive summary. 2015. <https://chfs.ky.gov/agencies/os/oig/dai/deppb/Documents/KentuckyHB1ImpactStudyExecutiveSummary03262015.pdf>. Accessed 2019 Jun 19.
- 50.** National Alliance for Model State Drug Laws. Overview of state pain management and prescribing policies. <https://namsdl.org/wp-content/uploads/Overview-of-State-Pain-Management-and-Prescribing-Policies-1.pdf>.
- 51.** SAMHSA. Expansion of naloxone in the prevention of opioid overdose FAQs. https://www.samhsa.gov/sites/default/files/programs_campaigns/medication_assisted/expansion-of-naloxone-faq.pdf.
- 52.** Saloner B, Stoller KB, Barry CL. Medicaid coverage for methadone maintenance and use of opioid agonist therapy in specialty addiction treatment. *Psychiatr Serv*. 2016 Jun 1;67(6):676-9. Epub 2016 Feb 29.