



Assessing and Monitoring Long-Term Opioid Use for People With Chronic and Disabling Arthritis Pain

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Each day in the United States, 46 people die from overdoses involving prescription opioids—signifying a dramatic increase over the last two decades.¹ The rapid growth in opioid overdoses has put a spotlight on opioid prescribing patterns, with increased pressure on clinicians to reduce opioid prescribing, especially for long-term management of chronic, noncancer pain. Increased oversight and dissemination of opioid prescribing guidelines have begun to curb overprescribing. However, advocates fear the increased scrutiny prevents people who use prescription opioids as prescribed for chronic pain control from accessing these medications that improve their quality of life.

Musculoskeletal conditions such as arthritis are the leading cause of disability and chronic pain in the United States.^{2,3,4,5} Historically, clinicians have prescribed opioids to people experiencing severe and chronic arthritis pain with the goal of improving physical function, participation in daily activities, and quality of life. Although opioids can control acute pain effectively, the evidence is insufficient about the effectiveness of long-term use of opioids to control chronic pain among people with and without disabilities, and whether the potential risks outweigh the benefits.⁶ Additionally, most research broadly reports on people with chronic, noncancer pain rather than specific subgroups and conditions such as people with arthritis pain.

This literature review summarizes the existing research on opioid use disorder (OUD)⁷ and long-term opioid use by people who experience chronic noncancer pain. The literature review is the first phase of a 3-year National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR) project. The purpose of this project is to develop resources for clinicians and people with chronic and disabling arthritis so they can work together to assess OUD risk and more safely manage long-term use of opioids.

Arthritis: A Leading Cause of Chronic Pain and Disability

Musculoskeletal conditions—most commonly osteoarthritis but also rheumatoid arthritis—are the leading cause of disability and chronic pain in adults 18 years and older living in the United States.^{8,9,10,11} Almost half of all Americans 65 and older and nearly one in three people aged 45 to 64 years have some form of arthritis.¹² Many, but not all, people with arthritis develop chronic and disabling pain (Exhibit 1). Our research focuses in on two common types of arthritis: (1) osteoarthritis and rheumatoid arthritis and (2) spinal stenosis, which is a spinal condition that can result from osteoarthritis.

- **Osteoarthritis.** Commonly known as “wear-and-tear arthritis,” osteoarthritis is the most common chronic condition of the joints. It occurs when the cartilage or cushion between joints breaks down, leading to pain,

stiffness, and swelling. The most common symptoms of osteoarthritis are stiffness, particularly first thing in the morning or after resting, and pain. Affected joints may swell after extended activity.¹³

- **Rheumatoid arthritis.** This type of arthritis is an autoimmune disease in which the body's immune system mistakenly attacks the joints and other organs. The most common symptoms include joint inflammation and pain, fatigue, loss of appetite, and a low-grade fever.¹⁴
- **Spinal stenosis.** Spinal stenosis results from osteoarthritis. It causes the spinal column to narrow and leads to bony overgrowth of vertebrae and ligament thickening. If a significant overgrowth occurs, nerves in the spine may be compressed. The most common symptoms are pain in the neck or back; numbness, weakness, cramping, or pain in the arms or legs; pain going down the legs; and foot problems.¹⁵

Exhibit 1. Prevalence of Arthritis, Arthritis-Related Disability, and Pain

Data show that arthritis is common, does not just affect older adults, and often leads to pain and disability.

- Almost one in four U.S. adults lives with arthritis, or about 54.4 million people, with 8.4 million reporting the disease is disabling.^{16,17}
- Among people with osteoarthritis and rheumatoid arthritis, up to half report that arthritis limits their participation in physical activities, whereas up to 30 percent of people with arthritis report severe joint pain.^{18,19,20}
- Of the people who qualified for fee-for-service Medicare because of a disability and were Medicaid eligible, 28.2 percent had rheumatoid or osteoarthritis.²¹
- Arthritis also occurs in children. Of the children who are dually eligible for Medicare and Medicaid, 7.4 percent were diagnosed with rheumatoid arthritis.²²

Opioids Frequently Prescribed to Manage Chronic Arthritis Pain

Pain is the chief reason people with arthritis seek medical care.²³ To improve function and quality of life, people experiencing severe and chronic arthritis pain often are prescribed opioids for pain relief, and this practice has increased dramatically. In 1980, 2 percent of people experiencing chronic musculoskeletal pain, including pain from arthritis, left their doctor's office with an opioid prescription, compared with 9 percent in 2000.²⁴ In 2013, nearly one in three adults filling an opioid prescription had arthritis.²⁵ **People with arthritis represent half of all individuals receiving at least one opioid prescription in the United States.**²⁶

Estimates vary for opioid use and depend on the specific condition. In the case of osteoarthritis, between 15 and 48 percent of people take opioids regularly. Those reporting more pain or arthritis in the spine take opioids more regularly.^{27,28,29} For rheumatoid arthritis, approximately one in three people take opioids regularly.³⁰ In a study of spinal stenosis or spondylolisthesis, patients took opioids continuously after surgery for 1 year.³¹

Risks of OUD

Relief from pain can help people function better at home and work. However, regular use of opioid painkillers can increase risk of the development of OUD (see Exhibit 2 for more about OUD). **Approximately 1 out of 10 or 11**

individuals with chronic pain who take opioids on a long-term basis will be diagnosed with OUD.³² Opioid use poses serious risks—in 2017, almost 47,600 people died in the United States from overdoses related to opioids.³³ Over 17,000 of those deaths were related to prescription opioids, and the remaining deaths occurred from heroin and synthetic narcotics, primarily fentanyl. Studies on prevalence of OUD in individuals with a disability due to arthritis or arthritis stemming from a disability could not be found. Major risk factors for OUD are younger age, genetic markers for OUD, self or family history of substance use disorder, and presence or history of a mental health condition.^{34,35,36} Because OUD poses serious threats to the full inclusion and integration of people with disabilities into society, their health and their economic and social self-sufficiency, identifying strategies to systematically diagnose and treat OUD in people with chronic disabling arthritis pain and develop nondrug pain management strategies is a priority.

Exhibit 2. Opioid Use Disorder

What is it? OUD is a chronic condition defined by the symptoms and behaviors surrounding the use of opioids leading to impairment and/or distress. Examples of opioids include prescribed drugs such as hydrocodone (Vicodin®), tramadol (Ultram®, ConZip®), oxycodone (OxyContin®), fentanyl, methadone, and morphine, as well as illegal opioids like heroin.

What are the symptoms of OUD? Symptoms include some combination of the following feelings and behaviors negatively impacting quality of life and safety from harm³⁷:

- Craving or strong desire to use opioids
- A sense of loss of control over one's opioid use
- Opioids are taken in larger amounts or over a longer period of time than intended
- Persistent desire or unsuccessful efforts to cut down or control opioid use
- Recurrent opioid use in physically hazardous situations
- A great deal of time is spent in activities to obtain opioids, use an opioid or recover from its effects
- Failure to fulfill major role obligations at work, school, or home
- Reducing social, work, or recreation activities because of opioid use
- Use despite recognizing opioids are causing or exacerbating physical or psychological problems

Withdrawal symptoms (flu-like illness for a period of time after stopping opioids) and tolerance (needing more medication to achieve the same effect over time) to opioids occur with long-term, regular use of opioids. While individuals taking opioids as prescribed under the care of a medical professional may exhibit both withdrawal and tolerance, if they have no other symptoms of OUD then they are not considered to have OUD.

Mixed Support for Long-Term Use of Opioids

The effectiveness of opioids for managing chronic pain, defined as pain lasting longer than 3 months, in people with and without disabilities is unclear. Although numerous studies have attempted to determine whether the benefits of opioids for managing chronic noncancer pain outweigh the harms, many studies are observational, and as many as half of the participants discontinue opioid use because of side effects.³⁸ Opioid studies using a randomized controlled trial design, the gold standard for evaluating the effectiveness of a treatment, follow

different study protocols and vary widely in how they measure outcomes, making it difficult to compare studies and reach conclusions.³⁹ In the absence of strong evidence, government and professional society clinical guidelines for opioid use rely on available research and expert consensus to provide guidance to clinicians.

Because chronic use of opioid analgesics results in significantly increased risk of overdose death, and that higher doses are associated with markedly increased risk, most national guidelines suggest opioids be prescribed only in specific circumstances and after exhausting other methods of managing chronic noncancer pain. The Centers for Disease Control and Prevention (CDC) and the Department of Veterans Affairs and Department of Defense guidelines on opioid use for chronic pain state that the preferred approach is to begin with nonopioid treatments and, if ineffective, move to opioids at the lowest dose.^{40,41} The American Pain Society guideline released in 2009 states that long-term use of opioids for chronic noncancer pain can be effective for “carefully selected and monitored patients” based on an evidence review showing short-term (<12 weeks) and moderate improvements in pain and function compared with placebo in people with chronic noncancer pain.^{42,43} The American College of Rheumatology’s guidelines support opioid prescribing for people with knee and hip osteoarthritis who fail to respond to other treatments and who do not undergo joint arthroplasty, by choice or because of ineligibility.⁴⁴ In contrast, North American Spine Society guidelines do not address the use of opioids for degenerative spinal stenosis.^{45,46}

Perspectives of People Using Opioids for Chronic Pain

The growing pressure on medical providers to avoid prescribing opioids can contrast markedly with the experiences of some groups of people taking opioids to manage chronic pain. Working and work disabled people,⁴⁷ veterans,⁴⁸ and people within a health system⁴⁹ who were using opioids for chronic noncancer pain found prescription opioids beneficial, enabling them to function and have an improved quality of life. These groups reported benefits that were not detected through improvement in clinical measures of pain or functionality.

In large surveys of health plan enrollees⁵⁰ and a general health system population⁵¹ who took opioids for chronic noncancer pain, more than 60 percent found long-term use of opioids helpful in relieving their pain. In a survey of 54 working and work-disabled people, participants believed their pain would be severe if they did not have access to opioids, and they reported negative experiences when they tried to taper or discontinue opioids.⁵² A qualitative study with people with chronic noncancer pain who were recruited from primary care clinics found that tapering opioids to reduce or discontinue use can be perceived negatively because people fear increased pain and withdrawal symptoms and believe other pain management approaches are less effective.⁵³ These fears cannot be taken lightly. The sense of hopelessness and desperation commonly occurring with severe and uncontrolled chronic pain can even cause people to end their suffering through suicide.⁵⁴

People with chronic, noncancer pain also reported feeling stigmatized by the news media and healthcare providers.^{55,56} For example, news reports highlighting only the addiction risk of opioids without any mention of potential benefits for pain relief can stigmatize people who use the medications as prescribed and have perceived benefits from the treatment. Individuals also reported they often feel stigmatized by clinicians who, for example, continuously ask the reason for the opioid use.⁵⁷

Clinicians Caught in the Crossfire

Primary care providers and other clinicians caring for people with severe chronic pain can feel caught in the crossfire between regulatory efforts to restrict opioid prescribing, their concerns about the epidemic of opioid

overdose deaths, and people who believe they benefit from opioids. While providers are receiving strong regulatory signals to curtail opioid prescribing, people with chronic pain who believe they benefit from opioids may not be amenable to reducing or stopping opioid use.

For example, the CDC's 2016 guidelines note that risk is dose dependent and risk increases substantially when taking a daily dose of opioids that exceeds 90 morphine milligram equivalents (MME).⁵⁸ Similarly, Medicare Part D overutilization policies for 2019 and new state regulations limit first-time opioid prescriptions to a 7 days or less supply, depending on the state, and the new Part D policies place additional restrictions on the dosage and type of opioid prescribed. The policies require alerts on filling a prescription to pharmacists and providers for beneficiaries who fill prescriptions over 90 MME per day or beneficiaries whose use pattern is indicative of fills from multiple pharmacies and prescriptions obtained from different providers.^{59,60}

In 2014, the Drug Enforcement Administration reclassified hydrocodone combination products as a Schedule II drug—a drug with a high potential for abuse and dependence. Reclassification limits prescribing of all hydrocodone drugs to a 30-day supply, and providers must now see a patient before writing a new prescription every month.⁶¹ These restrictions can be time intensive for providers and onerous for people with disabilities who are taking opioids as prescribed and without signs and symptoms of OUD. For example, people with mobility and transportation challenges with tight budgets may be burdened by additional office visits and added copays for those visits and copays for short-term prescriptions.

OUD Difficult to Diagnose in People With Chronic Pain

Clinicians managing the care of people with chronic pain need to carefully consider and monitor for signs and symptoms of OUD.⁶² A misdiagnosis of OUD in people with disabilities can have far-reaching consequences on their access to ongoing pain management, including access to opioids for pain control.⁶³ A missed OUD diagnosis is also detrimental, as it is a missed opportunity to help link an individual to substance use treatment, thereby reducing risk of negative consequences of OUD including overdose and death. An accurate clinical diagnosis is critical but elusive in this population.

The difficulty of diagnosing OUD in people with chronic pain can be compounded if clinicians do not understand how to apply diagnostic criteria for substance use disorders or how to distinguish behavioral signs of addiction from behaviors related to chronic pain. As defined using criteria in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5),⁶⁴ OUD can result from prescription and/or illicit opioid use and includes features of cravings, withdrawal, tolerance, use in dangerous situations and despite negative consequences, and interference with major obligations at work, school, or home.⁶⁵

People on long-term opioid therapy inevitably develop physical dependence and tolerance to the medication. Physical dependence leads to withdrawal symptoms when opioids are reduced too quickly or suddenly stopped, while tolerance leads to needing higher doses to achieve the same effect. Although dependence and tolerance are among the DSM-5 criteria for substance use disorders,⁶⁶ they are insufficient for making an OUD diagnosis in the absence of other diagnostic criteria among people who are taking opioids as prescribed under medical supervision. However, providers may interpret physical dependence to mean a person has an OUD.^{67,68,69} In addition, people with chronic pain may seek additional prescription opioids, either by requesting higher doses or more opioids from their current provider or seeking prescriptions from other providers, which is also often perceived as a sign of OUD.⁷⁰ Providers need to carefully consider such pseudo-addictive drug-seeking behaviors to avoid drawing inaccurate

conclusions and discontinuing opioid therapy when the benefits outweigh the risks of harm.⁷¹ Another factor for consideration is genetic differences in opiate metabolism where some people have reduced enzyme activity that make higher doses of opiates necessary to control pain.⁷²

Current Practices for Monitoring Chronic Opioid Use

To reduce the likelihood of failing to diagnose or misdiagnosing OUD, clinicians and other providers should follow an evidence-based protocol to assess OUD risk in people on long-term opioid treatment regimens⁷³ Clinical guidelines for chronic pain encourage written informed consent before prescribing opioids, the use of opioid risk assessment tools, routine pain assessments, and urine toxicology testing to assess the presence or absence of the prescribed opioid and nonprescribed drugs, respectively.^{74,75}

Rather than consistently screening for OUD in all people on long-term opioid therapy, providers tend to focus on people at highest risk, such as those with a history of substance use disorders and who are perceived to request more opioids unnecessarily or opioids at higher doses.^{76,77,78,79} Providers also may rely on general impressions of risk based on their perceptions of trustworthiness and how well the person's disease state justifies the person's pain.^{80,81,82} Additionally, providers may be uncomfortable broaching the topic of OUD or using urine toxicology screening with people perceived to be unreceptive. Clinicians may also be concerned about alienating people or feel ill equipped to offer alternative pain management solutions.^{83,84} Alternative pain management solutions frequently are not covered by insurance, but this is beginning to change.⁸⁵ Moreover, providers can fail to follow opioid guidelines systematically because they lack sufficient knowledge and training, question the evidence base of the guidelines, and lack time to apply complex guidelines in real-world practice.

A Roadmap for Toolkit Development

Drawing on the literature review results, the next project step is to identify or adapt evidence-based resources to assist clinicians and people with chronic and disabling arthritis pain in overcoming barriers to underdiagnosing or overdiagnosing OUD. An analysis of the literature suggests the following approach for developing an effective toolkit for assessing OUD risks and monitoring for OUD when using opioids long term among people with disability from arthritis.

- **Clinicians and people with disabilities due to arthritis need to establish a collaborative relationship, including shared decision-making about opioid use and monitoring.** An effective partnership requires that clinicians and people with disabling chronic pain must have a shared understanding about the role of opioids in achieving pain management goals, the risk factors for overdose and developing OUD and side effects of opioid use, and their respective roles and responsibilities in managing the risks together.
- **Providers can partner effectively with people with disabilities due to arthritis when they are aware of biases they bring to the relationship.** They can best manage OUD risk with use of objective decision support tools and synthesized evidence-based guidelines rather than preconceived notions of risk. Their focus should be on objectively assessing risk for all people on opioids, not just those people they deem “risky.”
- **People with disabilities due to arthritis need access to evidence-based and relevant information to be partners in their care.** Information can help make the risks of opioid use more relevant to people with disabilities and explain why clinicians need to routinely assess their opioid use even when they have been on opioids for a long time. They need to be aware of the importance of taking the lowest opioid dose

possible and the steps to reducing overdose risk. Such steps include accepting a prescription for naloxone and making sure members are trained in how to use it because overdose death rises with higher doses even in the absence of OUD. Before initiating opioids, people with chronic pain should understand that even short-term opioid use can lead to physical dependence and that reducing or discontinuing opioids will require tapering the dose to prevent or lessen withdrawal symptoms.

- **People with disabilities due to arthritis need to understand the importance of not relying solely on opioids to manage chronic pain, and they should know how to proactively manage factors in their lives that affect their pain experience.** They need to be aware of the role stress management and mental health plays in pain control, the evidence for alternative therapies, and how to apply the evidence to developing a personal pain management program.

Endnotes

1. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and opioid-involved overdose deaths—United States, 2013-2017. *MMWR*. 2019;67(5152):1419-1142. https://www.cdc.gov/mmwr/volumes/67/wr/mm675152e1.htm?s_cid=mm675152e1_w. Accessed May 30, 2019.
2. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390(10100):1211-1259. [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(17\)32154-2/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)32154-2/fulltext). Accessed May 30, 2019.
3. Centers for Disease Control and Prevention. Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation—United States, 2010-2012. *MMWR*. 2013;62(44):869-873.
4. Brault MW, Hootman J, Helmick CG, Theis KA, Armour BS. Prevalence and most common causes of disability among adults—United States, 2005. *MMWR*. 2009;58(16):421-426.
5. Barbour KE, Helmick CG, Boring M, Brady TJ. Vital signs: prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation—United States, 2013-2015. *MMWR*. 2017;66(9):246-253.
6. Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113-130. <https://doi.org/10.1016/j.jpain.2008.10.008>. Accessed May 30, 2019.
7. Kennedy J, Burley M, Roll M. The prevalence and treatment of opioid misuse among working-age adults with disabilities, 2016. Technical report developed by Collaborative on Health Reform and Independent Living under a grant from the National Institute on Disability, Independent Living, and Rehabilitation Research (#90DP0075-01-00).
8. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390(10100):1211-1259. [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(17\)32154-2/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)32154-2/fulltext). Accessed May 30, 2019.
9. Centers for Disease Control and Prevention. Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation—United States, 2010-2012. *MMWR*. 2013;62(44):869-873.
10. Brault MW, Hootman J, Helmick CG, Theis KA, Armour BS. Prevalence and most common causes of disability among adults—United States, 2005. *MMWR*. 2009;58(16):421-426.
11. Barbour KE, Helmick CG, Boring M, Brady TJ. Vital signs: prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation—United States, 2013-2015. *MMWR*. 2017;66(9):246-253. <http://dx.doi.org/10.15585/mmwr.mm6609e1>. Accessed May 30, 2019.
12. Barbour KE, Helmick CG, Boring M, Brady TJ. Vital signs: prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation—United States, 2013-2015. *MMWR*. 2017;66:246-253. <http://dx.doi.org/10.15585/mmwr.mm6609e1>. Accessed May 30, 2019.
13. Arthritis Foundation. *Osteoarthritis*. <https://www.arthritis.org/about-arthritis/types/osteoarthritis/>. Accessed May 30, 2019.

14. Arthritis Foundation. *Rheumatoid arthritis*. <https://www.arthritis.org/about-arthritis/types/rheumatoid-arthritis/>. Accessed May 30, 2019.
15. Arthritis Foundation. *Spinal stenosis*. <https://www.arthritis.org/about-arthritis/types/spinal-stenosis/>. Accessed May 30, 2019.
16. Barbour KE, Helmick CG, Theis KA, et al. Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation—United States, 2010-2012. *MMWR*. 2013;62:869-873.
17. Barbour KE, Moss S, Croft JB, et al. Geographic variations in arthritis prevalence, health-related characteristics, and management—United States, 2015. *MMWR Surveill Summ*. 2018;67(No. SS-4):1-28. <http://dx.doi.org/10.15585/mmwr.ss6704a1>. Accessed May 30, 2019.
18. Barbour KE, Moss S, Croft JB, et al. Geographic variations in arthritis prevalence, health-related characteristics, and management—United States, 2015. *MMWR Surveill Summ*. 2018;67(No. SS-4):1-28. <http://dx.doi.org/10.15585/mmwr.ss6704a1>. Accessed May 30, 2019.
19. Barbour KE, Boring M, Helmick CG, Murphy LB, Qin J. Prevalence of severe joint pain among adults with doctor-diagnosed arthritis—United States, 2002-2014. *MMWR*. 2016;65:1052-1056. <http://dx.doi.org/10.15585/mmwr.mm6539a2>. Accessed May 30, 2019.
20. Barbour KE, Helmick CG, Boring M, Brady TJ. Vital signs: prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation—United States, 2013-2015. *MMWR*. 2017;66:246-253. <http://dx.doi.org/10.15585/mmwr.mm6609e1>. Accessed May 30, 2019.
21. Centers for Medicare & Medicaid Services. *Physical and Mental Health Condition Prevalence and Comorbidity Among Fee-for-Service Medicare-Medicaid Enrollees*. Baltimore, MD: Centers for Medicare & Medicaid Services; 2014. https://www.cms.gov/medicare-medicare-coordination/medicare-and-medicare-coordination/medicare-medicare-coordination-office/downloads/dual_condition_prevalence_comorbidity_2014.pdf. Accessed May 30, 2019.
22. Centers for Medicare & Medicaid Services. *Physical and Mental Health Condition Prevalence and Comorbidity Among Fee-for-Service Medicare-Medicaid Enrollees*. Baltimore, MD: Centers for Medicare & Medicaid Services; 2014. https://www.cms.gov/medicare-medicare-coordination/medicare-and-medicare-coordination/medicare-medicare-coordination-office/downloads/dual_condition_prevalence_comorbidity_2014.pdf. Accessed May 30, 2019.
23. Barbour KE, Moss S, Croft JB, et al. Geographic variations in arthritis prevalence, health-related characteristics, and management—United States, 2015. *MMWR Surveill Summ*. 2018;67(No. SS-4):1-28. <http://dx.doi.org/10.15585/mmwr.ss6704a1>. Accessed May 30, 2019.
24. Caudill-Slosberg MA, Schwartz LM, Woloshin S. Office visits and analgesic prescriptions for musculoskeletal pain in US: 1980 vs. 2000. *Pain*. 2004;109(3):514-519. <https://doi.org/10.1016/J.PAIN.2004.03.006>. Accessed May 30, 2019.
25. Hootman JE, Cisternas M, Murphy L, Losby J. Prevalence and trends in prescribed opioid use among US adults with arthritis, 2008-2013, Medical Expenditure Panel Survey [abstract]. *Arthritis Rheumatol*. 2016;68 (suppl 10). <https://acrabstracts.org/abstract/prevalence-and-trends-in-prescribed-opioid-use-among-us-adults-with-arthritis-2008-2013-medical-expenditure-panel-survey/>. Accessed May 30, 2019.
26. Hootman JE, Cisternas M, Murphy L, Losby J. Prevalence and trends in prescribed opioid use in among U.S. adults with arthritis, 2008–2013, Medical Expenditure Panel Survey. Paper presented at: 2016 ACR/ARHP Annual Meeting; November 11-16, 2016; Washington, DC. Abstract 2185. <https://acrabstracts.org/abstract/prevalence-and-trends-in-prescribed-opioid-use-among-us-adults-with-arthritis-2008-2013-medical-expenditure-panel-survey/>. Accessed May 30, 2019.
27. Power JD, Perruccio AV, Gandhi R, et al. Factors associated with opioid use in end-stage knee, hip and spine osteoarthritis. Paper presented at: 2017 ACR/ARHP Annual Meeting; November 3-8, 2017; San Diego, CA. Abstract 2235. <https://acrabstracts.org/abstract/factors-associated-with-opioid-use-in-end-stage-knee-hip-and-spine-osteoarthritis/>. Accessed May 30, 2019.
28. Landsman-Blumberg PB, Katz N, Gajria K, et al. Health care resource use and cost differences by opioid therapy type among chronic noncancer pain patients. *J Pain Res*. 2017;10:1713-1722. <https://doi.org/10.2147/JPR.S130913>. Accessed May 30, 2019.
29. Wright EA, Katz JN, Abrams S, Solomon DH, Losina E. Trends in prescription of opioids from 2003-2009 in persons with knee osteoarthritis. *Arthritis Care Res*. 2014;66(10):1489-1495. <https://doi.org/10.1002/acr.22360>. Accessed May 30, 2019.

30. Landsman-Blumberg PB, Katz N, Gajria K, et al. Health care resource use and cost differences by opioid therapy type among chronic noncancer pain patients. *J Pain Res.* 2017;10:1713-1722. <https://doi.org/10.2147/JPR.S130913>. Accessed May 30, 2019.
31. Adogwa O, Davison MA, Vuong V, et al. Gender differences in opioid use in patients with symptomatic lumbar stenosis or spondylolisthesis undergoing lumbar decompression and fusion [published online ahead of print December 19, 2018]. *Spine.* <https://www.ncbi.nlm.nih.gov/pubmed/30601354>. Accessed May 30, 2019.
32. Vowles KE, McEntee ML, Julnes PS, Frohe T, Neve JP, van der Goes DN. Rates of opioid misuse, abuse and addiction in chronic pain: a systemic review and data synthesis. *Pain.* 2015;156(4):596-576.
33. National Institute on Drug Abuse. *Overdose death rates.* <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>. Accessed May 30, 2019.
34. Ciesielski T, Iyengar R, Bothra A, Tomala D, Cislo G, Gage BF. A tool to assess risk of de novo opioid abuse or dependence. *Am J Med.* 2016;129(7):699-705.
35. Peacock A, Degenhardt L, McRim GC, et al. A typology of predictive risk factors for non-adherent medication-related behaviors among chronic non-cancer pain patients prescribed opioids: a cohort study. *Pain Physician.* 2016;19(3):E421-E434.
36. Donaldson K, Demers L, Taylor K, Lopez J, Chang, S. Multi-variant genetic panel for genetic risk of opioid addiction. *Ann Clin Lab Sci.* 2017;47(4):452-456.
37. American Society of Addiction Medicine. *DSM-5 criteria for diagnosis of opioid use disorder.* Chevy Chase, MD: American Society of Addiction Medicine. https://www.asam.org/docs/default-source/education-docs/dsm-5-dx-oud-8-28-2017.pdf?sfvrsn=70540c2_2. Accessed May 30, 2019.
38. American Pain Society in conjunction with American Academy of Pain Medicine. *Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain: An Evidence Review.* Glenview, IL: American Pain Society; 2009. <http://americanpainsociety.org/uploads/education/guidelines/chronic-opioid-therapy-cnpc.pdf>. Accessed May 30, 2019.
39. Tayeb BO, Barreiro AE, Bradshaw YS, et al. Duration of opioid, nonopioid drug and behavioral clinical trials for chronic pain: adequate or inadequate? *Pain Med.* 2016;17:2036-2046.
40. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *MMWR Recomm Rep.* 2016;65(No. RR-1):1–49. <http://dx.doi.org/10.15585/mmwr.rr6501e1>. Accessed May 30, 2019.
41. Department of Veterans Affairs and Department of Defense. *VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain.* Washington, DC: Department of Veterans Affairs and Department of Defense; 2017 (version 3.0). <https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPGProviderSummary022817.pdf>. Accessed May 30, 2019.
42. Chou R, Fanciullo GJ, Fine PG, et al; for The American Pain Society–American Academy of Pain Medicine Opioids Guidelines Panel. Opioid treatment guidelines: clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain.* 2009;10(2):113-130.
43. American Pain Society in conjunction with American Academy of Pain Medicine. *Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain: An Evidence Review.* Glenview, IL: American Pain Society; 2009. <http://americanpainsociety.org/uploads/education/guidelines/chronic-opioid-therapy-cnpc.pdf>. Accessed May 30, 2019.
44. Hochberg MC, Altman RD, Toupin AK, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the knee, hip and knee. *Arthritis Care Res.* 2012 Apr;64(4):465-474.
45. NASS Evidence-Based Clinical Guidelines Committee. *Evidence-Based Clinical Guidelines for Multidisciplinary Spine Care: Diagnosis and Treatment of Degenerative Lumbar Spinal Stenosis.* Burr Ridge, IL: North American Spine Society; 2011. <https://www.spine.org/Documents/ResearchClinicalCare/Guidelines/LumbarStenosis.pdf>. Accessed May 30, 2019.
46. Tayeb BO, Barreiro AE, Bradshaw YS, et al. Duration of opioid, nonopioid drug and behavioral clinical trials for chronic pain: adequate or inadequate? *Pain Med.* 2016;17:2036-2046.
47. Robinson JP, Dansie EJ, Wilson HD, Rapp S, Turk DC. Attitudes and beliefs of working and work-disabled people with chronic pain prescribed long-term opioids. *Pain Med.* 2015;16(7):1311-1324.
48. Simmonds MJ, Finley EP, Vale S, Pugh MJ, Turner BJ. A qualitative study of veterans on long-term opioid analgesics: barriers and facilitators to multimodality pain management. *Pain Med.* 2015;16(4):726-732.

49. Thakral M, Walker RL, Saunders K, et al. Comparing pain and depressive symptoms of chronic opioid therapy patients receiving dose reduction and risk mitigation initiatives with usual care. *J Pain*. 2018;19(1):111-120.
50. Sullivan MD, Von Korff M, Banta-Green C, et al. Problems and concerns of patients receiving chronic opioid therapy for chronic non-cancer pain. *Pain*. 2010;149:345-353.
51. Thielke SM, Turner JA, Shortreed SM, et al. Do patient-perceived pros and cons of opioids predict sustained higher-dose use? *Clin J Pain*. 2014;30(2):93-101.
52. Robinson JP, Dansie EJ, Wilson HD, Rapp S, Turk DC. Attitudes and beliefs of working and work-disabled people with chronic pain prescribed long-term opioids. *Pain Med*. 2015;16(7):1311-1324.
53. Frank JW, Levy C, Matlock DD, et al. Patients' perspectives on tapering of chronic opioid therapy: a qualitative study. *Pain Med*. 2016;17(10):1838-1847. <https://doi.org/10.1093/pm/pnw078>. Accessed May 30, 2019.
54. Cheatle MD. Depression, chronic pain, and suicide by overdose: on the edge. *Pain Med*. 2011;12(suppl_2):S43-S48.
55. Brooks EA, Unruh A, Lynch ME. Exploring the lived experience of adults using prescription opioids to manage chronic noncancer pain. *Pain Res Manag*. 2015;20(1):15-22.
56. Penney LS, Ritenbaugh C, DeBar LL, Elder C, Deyo RA. Provider and patient perspectives on opioids and alternative treatments for managing chronic pain: a qualitative study. *BMC Fam Pract*. 2016;17(1):164.
57. Brooks EA, Unruh A, Lynch ME. Exploring the lived experience of adults using prescription opioids to manage chronic noncancer pain. *Pain Res Manag*. 2015;20(1):15-22.
58. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States. *MMWR Recomm Rep*; 2016;65(No.RR-1):1-49. <https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm>. Accessed May 30, 2019.
59. Davis C, The Network for Public Health Law, Southeastern Region Office & the National Health Law Program. *Appendix B: State-By-State Summary of Opioid Prescribing Regulations and Guidelines* (Page 2.2). N.D. <https://www.azdhs.gov/documents/prevention/womens-childrens-health/injury-prevention/opioid-prevention/appendix-b-state-by-state-summary.pdf>. Accessed May 30, 2019.
60. Medicare Learning Network. A prescriber's guide to the new Medicare Part D opioid overutilization policies for 2019. *MLM Matters*; 2018:E18016. <https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/SE18016.pdf>. Accessed May 30, 2019.
61. U.S. Department of Justice, Drug Enforcement Administration. Schedules of controlled substances: rescheduling of hydrocodone combination products from schedule III to schedule II. 21 CFR 1308. https://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0822.htm. Effective October 6, 2014. Accessed May 30, 2019.
62. Jamison RN, Dorado K, Mei A, Edwards RR, Martel MO. Influence of opioid-related side effects on disability, mood, and opioid misuse risk among patients with chronic pain in primary care. *Pain Rep*. 2017;2(2):e589.
63. Dineen KK. *The Good, the Deviant, and the Human: Exploring Select Provider and Systems Barriers to Appropriate Treatment and Prescribing Practices for Patients in Pain* [dissertation]. St. Louis, MO: Saint Louis University; 2016. <https://search.proquest.com/openview/a953ca9980f21de2b6bdc1b1933615be/1?pq-origsite=gscholar&cbl=18750&diss=y>. Accessed May 30, 2019.
64. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association; 2013.
65. American Society of Addiction Medicine. *DSM-5 Criteria for Diagnosis of Opioid Use Disorder*. Chevy Chase, MD: American Society of Addiction Medicine. https://www.asam.org/docs/default-source/education-docs/dsm-5-dx-oud-8-28-2017.pdf?sfvrsn=70540c2_2. Accessed May 30, 2019.
66. Hasin DS, O'Brien CP, Auricombe M, et al. DSM-5 criteria for substance use disorder: recommendations and rationale. *Am J Psychiatry*. 2013;170(8):834-851.
67. Sehgal N, Manchikanti L, Smith H. Prescription opioid abuse in chronic pain: a review of opioid abuse predictors and strategies to curb opioid abuse. *Pain Physician*. 2012;15(3 Suppl):ES67-ES92. http://www.thblack.com/links/RSD/PainPhys2012_15_ES67_RxOpioidAbuseInChronPain-26p.pdf. Accessed May 30, 2019.
68. Volkow ND, McLellan AT. Opioid abuse in chronic pain—misconceptions and mitigation strategies. *N Engl J Med*. 2016;374(13):1253-1263.

69. Podichetty VK, Mazanec DJ, Biscup RS. Chronic non-malignant musculoskeletal pain in older adults: clinical issues and opioid intervention. *Postgrad Med J*. 2003;79(937):627-633.
70. Robinson R, Gatchel R, Polatin P, Deschner M, Noe C, Gajraj N. Screening for problematic prescription opioid use. *Clin J Pain*. 2001;17(3):220-228. https://journals.lww.com/clinicalpain/Abstract/2001/09000/Screening_for_Problematic_Prescription_Opioid_Use.6.aspx. Accessed May 30, 2019.
71. Podichetty VK, Mazanec DJ, Biscup RS. Chronic non-malignant musculoskeletal pain in older adults: clinical issues and opioid intervention. *Postgrad Med J*. 2003;79(937):627-623.
72. Agarwal D, Udoji MA, Trescot A. Genetic testing for opioid pain management: a primer. *Pain Ther*. 2017;691:93-105. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5447546/>. Accessed May 30, 2019.
73. Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113-130. <https://doi.org/10.1016/j.jpain.2008.10.008>. Accessed May 30, 2019.
74. Nuckols TK, Anderson L, Popescu I, et al. Opioid prescribing: a systematic review and critical appraisal of guidelines for chronic pain. *Ann Intern Med*. 2014;160(1):38-47.
75. Tournebize JT, Gibaja V, Muszczak A, Kahn JP. Are physicians safely prescribing opioids for chronic noncancer pain? A systematic review of current evidence. *Pain Pract*. 2016;16:3:370-383.
76. Venner KL, Sanchez V, Garcia J, Williams RL, Sussman AL. Moving away from the tip of the pyramid: screening and brief intervention for risky alcohol and opioid use in underserved patients. *J Am Board Fam Med*. 2018;31:243-251.
77. Morse JS, Stockbridge H, Egan KE, Mai J, Wickizer T, Franklin GM. Primary care survey of the value and effectiveness of the Washington state opioid dosing guideline. *J Opioid Manag*. 2011;7(6):427-433.
78. Krebs EE, Bergman AA, Coffing JM, Campbell SR, Frankel RM, Matthias MS. Barriers to guideline concordant opioid management in primary care—a qualitative study. *J Pain*. 2014;15(11):1148-1155.
79. Nuckols TK, Anderson L, Popescu I, et al. Opioid prescribing: a systematic review and critical appraisal of guidelines for chronic pain. *Ann Intern Med*. 2014;160(1):38-47.
80. Harle CA, Bauer SE, Hoang HQ, Cook RL, Hurley RW, Fillingim RB. Decision support for chronic pain care: how do primary care physicians decide when to prescribe opioids? A qualitative study. *BMC Fam Pract*. 2015;16(1):48.
81. Elder NC, Simmons T, Regan S, Gerrety E. Care for patients with chronic nonmalignant pain with and without chronic opioid prescriptions: a report from the Cincinnati area Research Group (CARinG) Network. *J Am Board Fam Med*. 2012;25:652-660.
82. Krebs EE, Bergman AA, Coffing JM, Campbell SR, Frankel RM, Matthias MS. Barriers to guideline concordant opioid management in primary care—a qualitative study. *J Pain*. 2014;15(11):1148-1155.
83. Harle CA, Bauer SE, Hoang HQ, Cook RL, Hurley RW, Fillingim RB. Decision support for chronic pain care: how do primary care physicians decide when to prescribe opioids? A qualitative study. *BMC Fam Pract*. 2015;16(1):48.
84. Penney LS, Ritenbaugh C, DeBar LL, Elder C, Deyo RA. Provider and patient perspectives on opioids and alternative treatments for managing chronic pain: a qualitative study. *BMC Fam Pract*. 2016;17(1):164.
85. Dorr H, Townley C. *Chronic Pain Management Therapies in Medicaid: Policy Considerations for Nonpharmacological Alternative to Opioids*. Portland, ME: National Academy for State Health Policy; 2016. <https://nashp.org/wp-content/uploads/2016/09/Pain-Brief.pdf>. Accessed May 30, 2019.