Pain: Healthcare's Persistent Challenge (190)

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Contact hours: 14.5

Course price: $39

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Course Summary

Outlines efforts to improve pain management policies, procedures, and healthcare professional education in the United States. Covers both pharmacologic and non-pharmacologic treatment of pain and discusses the reasons for the startling increase in use, misuse, and abuse of prescription opioids. Describes pain management in special populations and offers effective tools for assessing and documenting pain. Describes common rehabilitation therapy treatments for pain, including manual therapy, therapeutic exercise, and ultrasound, among others as well as their effectiveness. Describes common complementary and alternative pain management techniques, including mediation, acupuncture, and yoga, among others. Describes barriers to effective pain management policies and procedures in healthcare organizations.

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Criteria for Successful Completions

80% or higher on the post test, a completed evaluation form, and payment where required. No partial credit will be awarded.

Course Objectives

When you finish this course you will be able to:

1. Explain when morphine and heroin were first developed.
2. Name three patient populations that experience undertreatment of pain.
3. Define government's two major responsibilities under the Central Principle of
4. Balance. Discuss the purpose of a prescription drug monitoring program.
5. Explain three physiologic effects of unrelieved pain.
6. Define acute pain, chronic pain, and complex regional pain syndrome.
7. Compare and contrast two overall approaches to pain management.
8. List five common pain conditions.
9. Explain one over-reaching issue encountered in the treatment of pain in special populations.
10. State three practices that all healthcare professionals are encouraged to use in the assessment of pain.

11. Explain how depression and anxiety are related to chronic pain.
12. Identify three commonly used pharmacologic components of non-opioid analgesic pain management.
13. Define prescription drug abuse, tolerance, dependence, and addiction.
14. List three patient populations that have experienced large increases in prescription opioid overdose deaths in recent years.
15. Summarize three approaches to curbing prescription opioid abuse.
16. Identify three non-pharmacologic treatments that have been shown to be effective in the treatment of pain.
17. Describe three complementary or integrative approaches that have been shown to be effective in the treatment of pain.
18. Discuss three barriers to the effective management of pain in the healthcare system.

Early Pain Theories and Remedies

Since ancient times, humans have sought to conquer pain using a variety of treatments ranging from the sublime to the bizarre. Although the Greeks and Romans first advanced a theory of sensation—the idea that the brain and nervous system have a role in producing the perception of pain—it was not until the Middle Ages and well into the Renaissance that evidence began to accumulate in support of these theories.

Illustration of Pain Pathway by René Descartes

Illustration of the pain pathway in René Descartes' *Traite de l'homme* (Treatise of Man), 1664. The long fiber running from the foot to the cavity in the head is pulled by the heat and releases a fluid that makes the muscles contract. Source: Public Domain.

In 1664 the French philosopher René Descartes described what, to this day, is still called a *pain pathway*. Descartes illustrated how particles of fire in contact with the foot travel to the brain and compared pain sensation to the ringing of a bell.

In the nineteenth century the application of new chemical and scientific techniques led to the development of morphine, codeine, and heroin—potent pain medications derived from opium. In the early 1800s morphine was marketed as a pain medication as well as treatment for opium and alcohol addiction. During this era, another potent pain medication and appetite suppressant—cocaine—was successfully isolated from coca leaves by a German chemist. In the late 1800s and early 1900s, heroin was marketed

by Bayer Pharmaceutical Products as a non-addictive morphine substitute and cough suppressant.

Left: Bayer Heroin bottle, originally containing 5 grams of Heroin substance. Right: A 100-ml bottle of laudanum. Note the dosages on the label for infants, children, and adults. Source for both images: Wikimedia Commons.

Laudanum, a popular tincture containing opium and alcohol and other ingredients such as honey, saffron, or cinnamon, was widely used—and completely legal—until the late 1800s. It was commonly used for pain, menstrual cramps, sleep aid, and a wide variety of other ailments both in children and adults.

Advertisement for curing morphine addictions from Overland Monthly, January 1900.

Although coca leaves, opium, and other narcotics had been used for millennia to treat pain, the isolation of the narcotic compounds within these drugs and their subsequent availability in tablet and powder forms led to their widespread adoption as pain medications, as well as to their widespread abuse.

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At the turn of the nineteenth century, "pure" aspirin was isolated from salicylate-rich plants. This discovery represented a major breakthrough in the history of pain medications. To this day aspirin is the most commonly used pain reliever worldwide.

A 1923 advertisement for aspirin. Source Wikimedia Commons.

During the twentieth century many opioid and non-opioid medications continued to be developed. In the 1950s, a drug called Percodan was approved by the Food and Drug Administration. A combination of oxycodone and aspirin, the relative ease with which this powerful opioid medication could be obtained, along with the contention that a narcotic prescribed by a physician could not lead to addiction, exacerbated an ongoing opioid abuse problem that has ebbed and flowed for millennia.

The Experience of Pain

In our astoundingly complex healthcare system, providers are expected to be knowledgeable about pain management across an entire spectrum of diseases and injuries —from temporary discomfort to chronic problems. They are also expected to understand the complex psychological issues related to pain, and to be knowledgeable about diversion of prescription pain medications and drug-seeking behaviors.

Many factors contribute to this difficult picture. The general public may be surprised to learn that pain education and training is far from comprehensive and many clinicians may lack a thorough understanding of the causes and mechanisms of pain. Misinformation about addiction, unnecessarily restrictive drug control regulations and practices, fear of legal sanctions for legitimate medical practice, and the inflated cost of pain treatment complicate this picture. These barriers can be understood not only as a failure to provide essential medicines to relieve suffering but also as human rights abuses (Lohman et al., 2010).

The Institute of Medicine (IOM) estimates that treatment and management of pain costs about $635 billion annually in the United States in direct medical costs and lost productivity (IOM, 2011). Despite these costs—approaching two-thirds of a **trillion** dollars a year—our failure to enact policies on pain treatment, management, and palliative care, along with the failure to put in place functioning drug supply systems, has hampered the development of consistent pain policies throughout the United States.

Pain Often Undertreated

Despite the amount of money spent each year on the treatment and management of pain, it is nevertheless inadequately treated in vulnerable populations such as children, older adults, and ethnic minorities. Patients with cognitive impairments, cancer patients, and those with active addiction or a history of substance abuse are also undertreated.

Untreated pain has a profound impact on quality of life and can have physical, psychological, social, and economic consequences. Inappropriately managed acute pain can result in immunologic and neural changes, which can progress to chronic pain if untreated. Clinical outcomes of untreated postoperative pain include increased risk of atelectasis, respiratory infection, myocardial ischemia, infarct or cardiac failure, and thromboembolic disease. Common sequelae of untreated chronic pain include decreased mobility, impaired immunity, decreased concentration, anorexia, and sleep disturbances (King & Fraser, 2013).

Surprisingly, undertreatment of pain can be an issue for those with diseases and conditions known to cause pain, such as cancer, HIV, and trauma. Conservative estimates by the World Health Organization (WHO) suggest that 1 million terminal HIV/AIDS patients, 5.5 million cancer patients, and 800,000 trauma patients have little or no access to treatment for moderate to severe pain (King & Fraser, 2013).

Older adults and those of racial and ethnic minorities are at higher risk of being undertreated for pain. Studies have shown that minority patients with pain are more likely to report greater activity limitations, severe pain, and functional impairments compared with non-Hispanic whites. The sources of pain disparities among racial and ethnic minorities are complex and are related to lack of provider education, system-level lack of access to pain medications, and cultural beliefs about pain (Makris et al., 2015).

In the African American population, lower rates of clinician assessment and higher rates of undertreatment have been found in all settings and across all types of pain (IOM, 2011). Similar results have been found among Hispanics, Asian Americans, and Native Americans.

Gender plays a significant role in pain management. A large number of studies indicate that there is **gender bias** (an unintended and systematic neglect of one gender) in healthcare. Women are more often neglected than men and medically unjustified differences in the availability of examination and treatment of women have been demonstrated with a number of conditions, including coronary heart disease, neck pain, irritable bowel syndrome, tuberculosis, renal transplantation, and HIV treatment (Hammarström et al., 2015). In one study, HIV-infected women with pain were twice as likely to be undertreated as their male counterparts (Lohman et al., 2010).

A Swedish study aimed to understand whether gender plays a role in a patient's access to pain rehabilitation services. Researchers found that men more often than women were referred to physiotherapy and x-ray independent of self-reported pain intensity, pain activity, and pain localization. Higher scores on self-reported pain did not trigger referral to rehabilitation. In fact, a negative trend was found among women. The higher the scores of pain, the less likely that women were referred to rehabilitation (Hammarström et al., 2015).

Not surprisingly, nursing home residents report inadequate pain control. It is estimated that 45% to 80% of patients in nursing homes have substantial pain that is undertreated. This suggests that when nursing home residents have moderate to severe pain, they have only about a 50% chance of obtaining adequate pain relief.

People may be discouraged from seeking treatment because they lack health insurance or lack a "usual" source of care. Some may not seek out treatment due to distrust of clinicians, low expectations of treatment outcomes, language barriers, and communication difficulties (IOM, 2011).

Global Health and Pain

By any measure, pain is an enormous problem throughout the world. Globally, it has been estimated that 1 in 5 adults suffer from pain and that another 1 in 10 adults are diagnosed with chronic pain each year. The five greatest causes of pain are

1. Cancer
2. Osteoarthritis
3. Rheumatoid arthritis
4. Surgeries and injuries
5. Spinal problems (Goldberg & McGee, 2011)

Clearly, the etiology of pain is a complex, multidisciplinary issue with multiple serious consequences, including depression, inability to work, disrupted social relationships, and suicidal thoughts (Goldberg & McGee, 2011).

In developing countries, traffic collisions, lung cancer, and HIV/AIDS are among the leading causes of mortality. Each is likely to cause pain that is severe, debilitating, and untreated. Conservative estimates by WHO suggest that 800,000 trauma patients, 5.5 million cancer patients, and 1 million terminal HIV/AIDS patients have little or no access to treatment for moderate to severe pain (King & Fraser, 2013).

Worldwide, medications for the treatment of pain are distributed unevenly. Approximately 89% of the total world consumption of morphine occurs in North America and Europe. Low- and middle-income countries consume only 6% of the morphine used worldwide, even though they are home to about half of all cancer patients and more than 90% of HIV-infected patients. Despite the availability of medications, however, inadequate pain management is still prevalent in developed countries (Lohman et al., 2010).

Regulatory Issues re Pain Management

Patients, providers, communities, and health systems have struggled to achieve balance between access to opioid treatment for chronic pain and potential harmful consequences of long-term opioid therapy—especially misuse, addiction, and overdose. Regulatory agencies and expert groups have published prescriber guidelines aimed at improving evidence-based practices, including:

1. Use of opioid treatment agreements
2. Regular monitoring for efficacy, safety, and misuse using tools such urine drug testing and querying prescription monitoring databases
3. Provision of, or referral to, addiction treatment if recurrent misuse or opioid use disorder is identified.

These practices are becoming the standard of care for individuals on long-term opioid therapy (Becker et al., 2016).

In 2016 the U.S. Centers for Disease Control and Prevention (CDC) issued *Guideline for Prescribing Opioids for Chronic Pain*. The guideline calls for a drastic reduction in the use of opioids for the treatment of chronic, noncancer pain. Dosage recommendations for exercising caution are lower than older opioid prescribing guidelines and recognize that even relatively low doses (20–50 morphine milligram equivalents per day) increase risk (CDC, 2016a).

Additionally, the CDC Guideline cautions that opioids pose risk to all patients, and currently available tools cannot rule out risk for abuse or other serious harm. It provides recommendations on providing safer care for all patients. The Guideline also encourages use of recent technological advances, such as state prescription drug monitoring programs. The Guideline provides more specific recommendations than previous guidelines on monitoring and discontinuing opioids when risks and harms outweigh benefits (CDC, 2016a).

The Joint Commission

In recent years, the Joint Commission's requirement for assessment and reassessment of pain has transformed how healthcare providers approach pain management. The Joint Commission, in collaboration with the University of Wisconsin, Madison, has developed pain management standards for accredited ambulatory care facilities, behavioral healthcare organizations, critical access hospitals, home care providers, hospitals, office-based surgery practices, and long-term care providers. The standards require organizations to:

- Recognize the right of patients to appropriate assessment and management of pain.
- Screen patients for pain during their initial assessment and, when clinically required, during ongoing periodic re-assessments.
- Educate patients suffering from pain and their families about pain management as a part of care. (The Joint Commission, 2013)

The Joint Commission's pain guidelines further state that:

- Clinicians must be competent in the assessment and management of pain.
- Pain should not interfere with optimal level of function or rehabilitation.
- Pain and symptom management must be included in discharge planning. (The Joint Commission, 2013)

Choice of a pain assessment tool is left to the discretion of an individual healthcare facility, but the Joint Commission encourages a simple 0 to 10 pain scale. Healthcare providers are required to address the needs of non-communicative patients—including those with dementia—by using an alternative means of assessment.

Despite widespread belief to the contrary, the Joint Commission does not require healthcare organizations to assess pain as a fifth vital sign (The Joint Commission, 2016), although the Commission does require that patients be screened for pain during the initial assessment. Some large organizations, including the Veteran's Administration (VA), in an effort to make pain a more visible part of patient assessment, decided to describe pain as the "fifth vital sign", to be assessed along with temperature, pulse, respiration, and blood pressure. Acknowledging that assessing pain as a fifth vital sign may have contributed to the overprescribing of opioids, in June 2016 the American Medical Association recommended that pain be removed as one of the vital signs for which patients are assessed.

Controlled Substances Act

The Controlled Substances Act (CSA) established in 1970 is a system that regulates the manufacture and distribution of certain substances with a potential for abuse. The CSA groups or classifies drugs into five "schedules," based on whether they have a currently accepted medical use in treatment in the United States, their relative abuse potential, and the likelihood of causing dependence when abused (DEA, 2016).

The Five Schedules of the Controlled Substances Act

- Substances in **Schedule I** have (1) no currently accepted medical use in the United States, (2) a lack of accepted safety for use under medical supervision, and (3) a high potential for abuse. Examples include heroin, marijuana, LSD, peyote, and ecstasy (DEA, 2016).
- Substances in **Schedule II** have a high potential for abuse, which may lead to severe psychological or physical dependence. Examples include Dilaudid, methadone, Demerol, oxycodone, and fentanyl (DEA, 2016).
- Substances in **Schedule III** have a potential for abuse less than substances in Schedules I or II. Abuse may lead to moderate or low physical dependence or high psychological dependence. Examples include Tylenol with codeine, Suboxone, substances containing not more than 90 mg of codeine per dosage, ketamine, and anabolic steroids (DEA, 2016).
- Substances in **Schedule IV** have a low potential for abuse relative to substances in Schedule III. They consist primarily of preparations containing limited quantities of certain narcotics such as Xanax, Soma, Klonopin, Tranxene, Valium, Ativan, Versed, Restoril, and Halcion (DEA, 2016).
- Substances in **Schedule V** include cough preparations containing not more than 200 milligrams of codeine per 100 milliliters or per 100 grams (Robitussin AC, Phenergan with Codeine), and ezogabine (DEA, 2016).

The CSA also establishes a national drug control system to distribute approved medications to patients. The drug control system is a closed system—that is, all enterprises and individuals involved in production, distribution, prescribing, dispensing, possession, research, and disposal of prescription-only controlled substances must be registered with the Drug Enforcement Administration (DEA) and also the state, if required. Conditions of DEA registration include:

- Adhering to laws and regulations that limit medication availability to legitimate medical uses and patients
- Implementing safeguards against diversion
- Reporting to the DEA amounts distributed to all registrants at the retail level, as well as amounts that are lost or stolen (PPSG, 2014a)

Federal controlled substances laws do not supersede FDA-approved uses of medications, and states have the jurisdiction to regulate healthcare professionals and their practice (PPSG, 2014a).

Physicians can lose their DEA registration and be subject to criminal or civil penalties if they issue prescriptions for non-medical purposes or outside the usual course of medical practice. Many states have policies that acknowledge a practitioner's need to understand and comply with relevant federal and state laws when prescribing controlled substances (PPSG, 2014a).

Intractable Pain Treatment Acts

Intractable pain is commonly defined as "a pain state. . . which in the generally accepted course of medical practice no relief or cure of the cause of the pain is possible. . ." (PPSG, 2014b).

Intractable Pain Treatment Acts (IPTA) are statutes originally intended to improve access to pain management by providing physicians immunity from regulatory sanctions for prescribing opioids to patients with intractable pain. The first IPTA was adopted by Texas in 1989 (PPSG, 2014b).

IPTAs are a product of the time in which they were first created, typically the late 1980s and 1990s. At that time, many physicians felt that their regulatory authorities viewed opioid use for chronic pain as being outside legitimate medical practice, and they worked with legislators to develop IPTAs to protect their practice from disciplinary action by placing it squarely within legitimate medical practice (PPSG, 2014b).

A potential consequence of such a policy is that prescribing controlled substances, if viewed as outside the IPTA, could be considered a violation of federal and state controlled substances law or regulatory policy. In addition, IPTAs were probably not intended to formalize the use of opioids for pain as being within medical practice only when meeting the IPTA standards. The IPTA language was often ambiguous and was not consistent with the recognition that pain management, including the use of opioid medications, is part of general medicine and is a legitimate professional practice (PPSG, 2014b).

A number of states have recognized these contradictions and have worked to remove confusing language from their IPTAs. For example, in 2001 Michigan became the first state to delete the term *intractable pain* from its statute, thus making its provisions applicable to pain in general. More recently, both California (the state with the second-oldest IPTA) and Rhode Island repealed a number of restrictive provisions from their IPTAs, including removing the term and definition of *intractable pain* (PPSG, 2014b).

In states where IPTAs still exist, state policies can require (without exception) the physician to obtain a consultation from a specialist for every patient with intractable pain as a means to qualify for immunity from discipline before prescribing opioids to that patient, regardless of the clinical situation or practitioner qualifications. Such a requirement may be inappropriate if the practitioner is knowledgeable or has relevant expertise, and appears to regulate pain management excessively as well as the entire class of patients who have "intractable" pain (PPSG, 2014b).

Although IPTAs are intended to improve access to pain relief, such policies may instead discourage pain management or limit patient access because of the increased time and administrative burden for the physician, a lack of available consultation resources, as well as the possibility of increased cost for the patient. Also, when a state policy requires a consultation, the liability is unclear for a physician who prescribes an opioid in the course of treating a patient with pain and who does not obtain the consultation (PPSG, 2014b).

The Central Principle of Balance

The **Central Principle of Balance** represents a government's dual obligation to establish a system of drug controls that prevent abuse, trafficking, and diversion of narcotic drugs while ensuring the adequate medical availability of needed medications. Opioids, including those in the therapeutic group of morphine, should be accessible to patients who need opioids for the relief of pain (PPSG, 2014b).

The Central Principle of Balance encourages governments to ensure the adequate availability of opioids for medical and scientific purposes. This includes empowering medical professionals to provide opioids in the course of professional practice, allowing them to prescribe, dispense, and administer according to the individual medical needs of the patient, and ensuring that a sufficient supply of opioids is available to meet medical demand (PPSG, 2014b).

The evaluation of state pain policies by the University of Wisconsin Pain and Policies Study Group has shown continual improvement in state policies. A state's grade represents the quality of its policies affecting pain treatment, based on the Central Principle of Balance, and is calculated from the total number of provisions in a state fulfilling the evaluation criteria; higher grades mean more balanced state policies influencing pain management, including the medical use of opioid analgesics. In 2013, Alabama, Georgia, Idaho, Iowa, Kansas, Maine, Massachusetts, Michigan, Montana, Oregon, Rhode Island, Vermont, Virginia, Washington, and Wisconsin received an "A" rating, meaning these states have the most balanced pain policies in the country. The 15 states achieving an A comprise 22% of the total U.S. population (PPSG, 2014a).

The Physiology of Pain

Pain plays an important in the survival of all animals. It acts as a signal, alerting us to potential tissue damage, and leads to a wide range of actions to prevent or limit further damage.

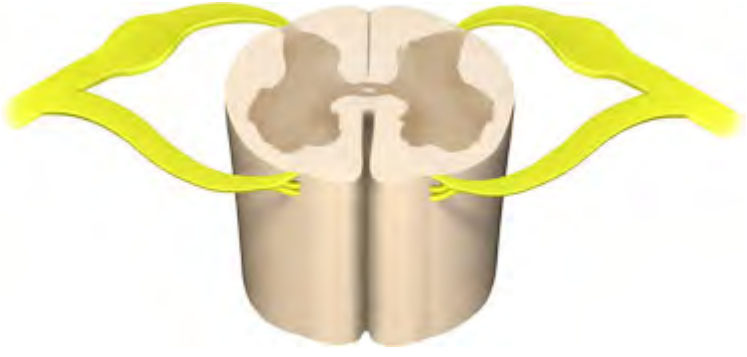
Physiologically, pain occurs when sensory nerve endings called **nociceptors** (also referred to as pain receptors) come into contact with a painful or noxious stimulus. The resulting nerve impulse travels from the sensory nerve ending to the spinal cord, where the impulse is rapidly shunted to the brain via nerve tracts in the spinal cord and brainstem. The brain processes the pain sensation and quickly responds with a motor response in an attempt to cease the action causing the pain.

Nociceptive Pathways

The classic nociceptive pathway involves three types of neurons:

- **Primary sensory neurons** in the peripheral nervous system, which conduct painful sensations from the periphery to the dorsal root of the spinal cord
- **Secondary sensory neurons** in the spinal cord or brainstem, which transmit the painful sensation to the thalamus
- **Tertiary sensory neurons**, which transmit the painful sensation from the thalamus to the somatosensory areas of the cerebral cortex.

Sensory Nerves Entering the Spinal Cord



A section of a lumbar vertebra showing the sensory nerves (in yellow, with bulge) entering the dorsal part of the spinal cord. Illustration provided by 3DScience.com. Used by permission.

There are two major classes of nerve fibers associated with the transmission of pain:

1. Unmyelinated C fibers

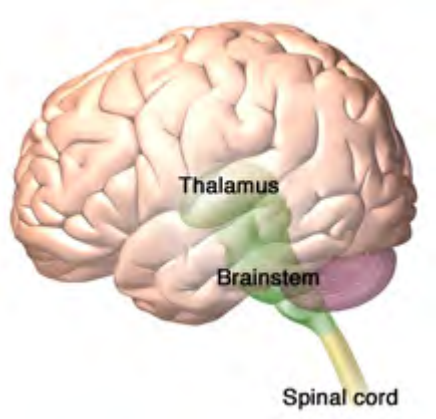
2. Myelinated A-delta fibers

The C fibers are small and conduct impulses slowly. They respond to thermal, mechanical, and chemical stimuli and produce the sensation of dull, diffuse, aching, burning, and delayed pain. A-delta fibers, which are myelinated and thus conduct impulses rapidly, respond to mechanical (pressure) stimulus and produce the sensation of sharp, localized, fast pain.

One of the most important central pain pathways is the **spinothalamic tract**, which originates in the spinal cord and extends to the thalamus. This spinal tract transmits sensory information related to pain, temperature, and crude touch.

Another prominent pathway is the **spinoreticular tract**, which is involved in nociceptive processing. The spino-reticular tract is similar to the spinothalamic tract in that it is excited by similar sensory fibers. Rather than ascending to the thalamus however, spinoreticular neurons terminate within the brainstem.

Destinations of the Spinothalamic and Spinoreticular Tracts in the Brain



The thalamus is the destination of spinothalamic tract—the sensory pathway responsible for processing pain, temperature, and crude touch. The brainstem reticular formation, which forms a diffuse, central core within the brainstem is the destination of the spinoreticular tract. Source: 3DScience.com. Used by permission.

Mechanisms of Pain

Pain can be caused by a mechanical, chemical or inflammatory, or thermal mechanism. Pain of *mechanical* origin can be caused by acute trauma, injury, or overuse. It may be constant, variable, or intermittent in nature and is affected by movement and position.

Pain of *chemical* or *inflammatory* origin is associated with arthritis and other inflammatory disorders. It is often constant but responds to positioning, therapy, rest, and gentle movement. Medications are usually a part of the management regimen for chemical or inflammatory pain.

Pain of *thermal* origin is the result of excessive heat or cold.

If an acute pain sensation is intense enough, it can cause system-wide responses: increased alertness; focused attention; the suppression of feeding, sleep, and reproduction; and increased vascular tone, respiration, and blood sugar levels. If pain persists or becomes chronic it can even change the circuitry in the central nervous system.

Using Neuroimaging to Understand Pain

Our understanding of how the brain changes in response to chronic pain or to pharmacologic or other therapeutic interventions has been significantly improved as a result of neuroimaging techniques. Until the advent of these techniques, the living brain was largely invisible to clinicians and researchers. The development of computed tomography (CT) and, soon thereafter, magnetic resonance imaging (MRI), allowed researchers to look into the living brain and gain some understanding of the parts of the brain affected by certain types of pain. The development of positron emission tomography (PET) has allowed researchers, for the first time, to investigate neuronal activity throughout the entire brain (Casey, 2015).

Functional magnetic resonance imaging (fMRI), positron emission tomography (PET), magnetoencephalography (MEG), and scalp electroencephalography (EEG) have been used to study the neural bases of pain. Other magnetic resonance-based measures such as diffusion tensor imaging, spectroscopy, and volumetric imaging are being used to assess pain-related changes in the brain's wiring, chemistry, and structure; this will help gain further insights into the neurobiology of pain, particularly chronic pain (Lee & Tracey, 2013).

As a result, we now know that pain sensation is more complex than previously thought and involves diverse regions of the brain. Imaging techniques have allowed us to understand that pain results from activation of a number of brain regions such as the amygdala, insula, or the anterior cingulate cortex. We are learning that pain is a result of complex interactions between the immune, nervous (both CNS and autonomic nervous system), and endocrine systems (Zouikr et al., 2016).

In a study of patients with chronic low back pain, neuroimaging showed significant differences in brain function. Compared to healthy controls, chronic low back pain patients showed activation in pain-related brain regions during administration of experimental pain, differences in activation during emotional decision-making tasks, and changes in specific brain regions during a simple visual attention task (Kong et al., 2013).

Other imaging studies have reported structural changes in the brains of patients with chronic low back pain. One study found that these patients showed 5% to 11% less neocortical gray matter volume than control subjects and that the decreased volume was related to pain duration. These studies indicate that chronic low back pain is also associated with structural pathologic changes in the brain (Kong et al., 2013).

Neuroimaging studies are also being used to predict which patients might transition from acute to chronic pain. Using MRI scans in people with acute low back pain, researchers at Northwestern University Feinberg School of Medicine found abnormalities in the white matter in areas of the brain associated with the processing of pain and emotion. After one year, study participants were scanned again, and those with persistent pain showed the same abnormalities identified at the onset of the injury. In patients with ongoing low back pain, these abnormalities may be an indication of which patients will go on to develop chronic low back pain (Paul, 2013).

In patients with chronic pain, a number of research groups have reported significant changes in pain processing at a functional level including **allodynia*** (a stimulus not normally painful is perceived as painful), functional plasticity, and alterations in basic processes in the brain and brainstem. Alterations in neurotransmitters have also been reported in chronic pain patients using magnetic resonance spectroscopy. Such approaches have been applied to migraine, back pain, and spinal cord injury. The approach can be used to define neuronal and axonal markers, including specific metabolites such as glutamate, aspartate, glycine, and GABA (Borsook et al., 2007).

*Allodynia is a clinical feature of neuropathies, complex regional pain syndrome, post-herpetic neuralgia, migraine, and fibromyalgia.

At a macroscopic level, a number of studies have shown changes in volume in brain regions in patients with chronic neuropathic pain, complex regional pain syndrome, and fibromyalgia. This insight has been seminal in transforming our approach and thinking on chronic pain, since these changes indicate the potential of chronic pain being a neurodegenerative disease. At a microscopic level, changes in dendritic spine density or alterations in neuronal count have been observed in pain and stress. Such changes also have implications for the development of co-morbid disease such as depression (Borsook et al., 2007).

Sensitization

We can become sensitized to pain. **Sensitization** is a neurophysiologic term that describes the increased responsiveness of nociceptive neurons (the pain pathways become more sensitive). This can include a drop in the threshold for activating nociceptors and an increase in the frequency of firing for all stimuli (IASP, 2012). **Hyperalgesia** (exaggerated responses to stimuli) and allodynia (see above) are clinical markers used to detect the presence of sensitization (Zouikr et al., 2016).

In sensitization, stimuli that would not normally cause pain, such as the light touch of a sheet on the skin, can cause intense pain. Sensitization can also cause tenderness and soreness, particularly when deep tissue such as joints and hollow viscera are affected.

There are two types of sensitization: peripheral and central. **Peripheral sensitization** occurs in response to the release of inflammatory molecules such as histamine, prostaglandins, and pro-inflammatory cytokines. These substances sensitize (increase the excitability of) nociceptors by creating an "inflammatory soup" environment that enhances pain sensitivity by reducing the threshold of nociceptors activation (Zouikr et al., 2016). Under normal circumstances, peripheral hypersensitivity returns to normal when inflammation subsides or the source of the injury is removed (Kyranou & Puntillo, 2012).

In **central sensitization**, nociceptive-specific neurons may progressively increase their response to repeated non-painful stimuli, develop spontaneous activity, and increase the area of the body that is involved with the pain. The hyperalgesia of central sensitization usually develops as part of ongoing pathology (ie, damage to peripheral or central nerve fibers, cancer, rheumatoid arthritis) and is considered maladaptive (Kyranou & Puntillo, 2012).

Physiologic Effects of Unrelieved Pain

Unrelieved pain is a stressor that can lead to physiologic changes and negative effects on the endocrine, cardiovascular, gastrointestinal, and immune systems. The endocrine system reacts to unrelieved pain by releasing an excessive amount of hormones, ultimately resulting in carbohydrate, protein, and fat catabolism, poor glucose utilization, and other harmful effects. This reaction combined with inflammatory processes can produce weight loss, tachycardia, increased respiratory rate, fever, shock, and death.

The cardiovascular system responds to the stress of unrelieved pain by activating the sympathetic nervous system. Following a surgical procedure, for example, this can include hypercoagulation and increased heart rate, blood pressure, cardiac workload, and oxygen demand. Since the stress response causes an increase in sympathetic nervous system activity, intestinal secretions and smooth muscle sphincter tone increase, and gastric emptying and intestinal motility decrease. This response can cause temporary impairment of gastrointestinal function and increase the risk of ileus (intestinal obstruction). Aggressive pain control may be needed to reduce these effects and prevent thromboembolic complications.

Unrelieved pain may be especially harmful for patients with metastatic cancers. Stress and pain can suppress immune function, including the natural killer cells that play a role in preventing tumor growth and controlling metastasis.

Defining and Categorizing Pain

One of the most common definitions of pain comes from the International Association for the Study of Pain (IASP), which describes pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." When we are exposed to something that causes pain, if able, we quickly or reflexively withdraw. The sensory feeling of pain is called **nociception**.

In the absence of an objective measure, pain is a subjective individual experience. How a person responds to pain is related to his or her genetic features and cognitive, motivational, emotional, and psychological state. Pain response is also related to gender, experiences and memories of pain, cultural and social influences, and general health (Sessle, 2012).

Factors Influencing the Experience of Pain	
Physiologic/biologic factors	▪ Site of injury or source of painful stimuli ▪ Intensity of stimulation/degree of tissue damage ▪ Type and density of receptors present ▪ Biologically based individual differences in pain threshold and sensitivity
Psychological factors	▪ Emotional status of the individual ▪ Individual beliefs and expectations regarding the experience of pain ▪ People's belief regarding their ability to establish control over the pain ▪ The individual's history of pain experiences and pain sensations (cultural and learning effects) ▪ General physical health of the person with pain

Source: Veteran's Health Administration, 2015.

Acute Pain

Acute pain comes on quickly and can be severe, but lasts a relatively short time (IOM, 2011). It can be intensely uncomfortable. It usually has a well-defined location and an identifiable painful or noxious stimulus from an injury, brief disease process, surgical procedure, or dysfunction of muscle or viscera. Acute pain alerts us to possible injury, inflammation, or disease and can arise from somatic or visceral structures.

Acute pain is often successfully treated with patient education, mild pain medications, environmental changes, and stress reduction, physical therapy, chiropractic, massage therapy, acupuncture, or active movement programs. Acute pain is usually easier to treat than chronic pain.

The Institute of Medicine (IOM) has targeted improved treatment of acute pain as an area of significant healthcare savings. The IOM states that better treatment of acute pain, through education about self-management and better clinical treatment, can avoid its progression to chronic pain, which is more difficult and more expensive to treat (IOM, 2011).

Chronic Pain

Chronic pain generally refers to pain that exists for three or more months and does not resolve with treatment. The three-month time frame is not absolute and some conditions may become chronic in as little as a month.

Chronic pain is common; it affects 1 in 5 adults, is more prevalent among women and elders, and is associated with physically demanding work and lower level of education (King & Fraser, 2013). Chronic pain is a silent epidemic that reduces quality of life, negatively impacts relationships and jobs, and increases rates of depression (Sessle, 2012).

Chronic pain is a symptom of many diseases. Up to 70% of cancer patients suffer from chronic pain and, among individuals living with HIV/AIDS, pain has been reported at all stages of infection (Lohman et al., 2010).

Chronic pain is also costly. A 2011 IOM report places this cost at more than $500 billion per year in the United States, creating an economic burden that is higher than the healthcare costs for heart disease, cancer, and diabetes combined. These economic costs stem from the cost of healthcare services, insurance, welfare benefits, lost productivity, and lost tax revenues (Sessle, 2012).

Chronic pain is a multidimensional process that must be considered as a chronic degenerative disease not only affecting sensory and emotional processing, but also producing an altered brain state (Borsook et al., 2007). Chronic pain persists over time and is resistant to treatments and medications that may be effective in the treatment of acute pain.

Aspects of Chronic Pain

When pain becomes chronic, sensory pathways continue to transmit the sensation of pain even though the underlying condition or injury that originally caused the pain has healed. In such situations, the pain itself may need to be managed separately from the underlying condition. Other aspects of chronic pain include:

- Chronic pain may express itself as a consequence of other conditions. For example, chronic pain may arise after the onset of depression, even in patients without a prior pain history.
- Chronic pain patients are often defined as "difficult patients" in that they often have neuropsychologic changes that include changes in affect and motivation or changes in cognition, all of which rarely predate their pain condition.
- In some conditions such as complex regional pain syndrome (CRPS), manifestations of dysautonomia, movement disorders, and spreading pain (ipsilateral and contralateral) are all indicative of complex secondary changes in the CNS that can follow a relatively trivial peripheral nerve injury.
- Chronic opioid therapy results in a hyperalgesic state (an increased sensitivity to pain) in both experimental and clinical pain scenarios, implying changes in central processing.
- Opioids fail to produce pain relief in all individuals, even at high doses. This implies the development of "analgesic resistance," a consequence of complex changes in neural systems in chronic pain that complicates the utility of opioids for long-term therapy. (Borsook et al., 2007)

Chronic pain can be difficult to distinguish from acute pain and, not surprisingly, clinicians have less success treating chronic pain than treating acute pain. Chronic pain does not resolve quickly and opioids or sedatives are often needed for treatment, which complicates the clinician-patient relationship. Because medical practitioners often approach chronic pain management from a medication perspective, other modalities are sometimes overlooked.

Chronic pain can affect every aspect of life. It is associated with reduced activity, impaired sleep, depression, and feelings of helplessness and hopelessness, and about one-fourth of people with chronic pain will experience physical, emotional, and social deterioration over time.

Acute pain can progress to chronic pain. Whether this occurs can depend on a number of factors, including the availability of treatment during the acute phase. Factors from birth, childhood, adolescence, and adulthood can also affect whether pain becomes chronic.

Lifespan Factors Affecting the Development of Chronic Pain	
From birth	▪ Genetics ▪ Female gender ▪ Minority race or ethnicity ▪ Parental anxiety ▪ Irregular feeding and sleeping ▪ Temperament and personality
Childhood	▪ Childhood physical/sexual abuse ▪ Low socioeconomic status ▪ Hyperactivity ▪ Serious illness or injury
Adolescence	▪ Learned reactions to pain ▪ Injuries ▪ Obesity ▪ Low levels of fitness
Adulthood	▪ Vivid recall of childhood trauma ▪ Learned reactions to pain ▪ Lack of social support ▪ Overuse of joints and muscles ▪ Occupational exposure, job dissatisfaction ▪ Chronic disease ▪ Aging

Source: IOM, 2011.

Musculoskeletal pain, especially joint and back pain, is the most common type of chronic pain (IOM, 2011). Although musculoskeletal pain may not correspond exactly to the area of injury, it is nevertheless commonly classified according to pain location. However, most people with chronic pain have pain at multiple sites (Lillie et al., 2013).

Describing Chronic Pain According to Pathophysiology

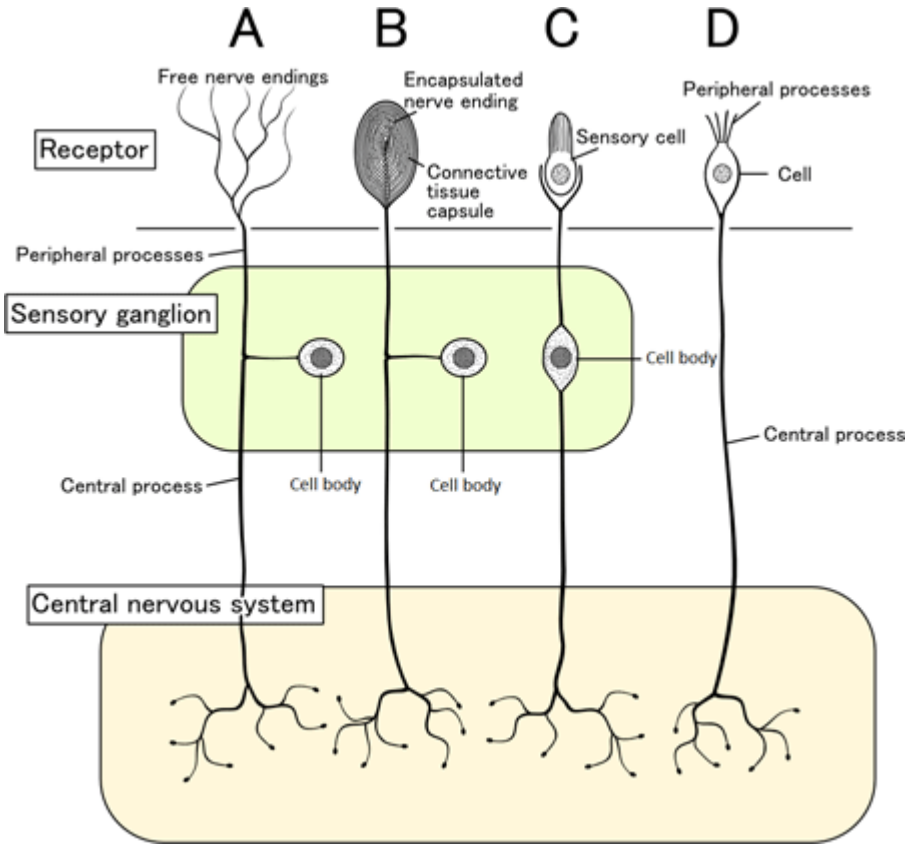
When chronic pain is classified according to **pathophysiology**, three types have been described by the International Association for the Study of Pain (IASP):

- **Nociceptive pain:** caused by stimulation of pain receptors
- **Neuropathic pain:** caused by damage to the peripheral or central nervous system
- **Psychogenic pain:** caused or exacerbated by psychiatric disorders

Nociceptive pain is caused by activation or sensitization of peripheral nociceptors in the skin, cornea, mucosa, muscles, joints, bladder, gut, digestive tract, and a variety of internal organs. Nociceptors differ from mechanoreceptors, which sense touch and pressure, in that they are responsible for signaling potential damage to the body. Nociceptors have a high threshold for activation and increase their output as the stimulus increases.

Nociceptors respond to *physical stimulation* or *chemical stimulation*. In the physical response, the free nerve endings of the nociceptor (cell A in the diagram below) will become deformed by a sufficiently strong and deep stimulus, and in response send a pain signal. An injury triggers a complex set of chemical reactions as damaged cells release certain chemicals while immune cells reacting to the damage release additional chemicals. The nociceptor is exposed to this chemical "soup," and continues to send pain signals until the levels of these pain-generating chemicals are lowered over time as the wound heals. A very similar mechanism is at work with itching sensations (Wikiversity, 2015).

Sensory Pathways from Skin to Brain



Schematic of several representative sensory pathways leading from the skin to brain. Source: Shigeru23, Wikimedia Commons.

Neuropathic pain is "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system" (IASP, 2012). It is usually described as a poorly localized, electric shock-like, lancinating, shooting sensation originating from injury to a peripheral nerve, the spinal cord, or the brain. It can cause a sensation of burning, pins and needles, electricity, and numbness. Neuropathic pain can be associated with diabetic neuropathy, radiculopathy, post herpetic neuralgia, phantom limb pain, tumor-related nerve compression, neuroma, or spinal nerve compression.

Neuropathic pain is classified as **central** or **peripheral**. Central pain originates from damage to the brain or spinal cord. Peripheral pain originates from damage to the peripheral nerves or nerve plexuses, dorsal root ganglion, or nerve roots (IASP, 2012).

Neuropathic pain tends to be long-lasting and difficult to treat. Opioids can be effective, although non-opioid medications such as tricyclic antidepressants, SNRI antidepressants, and several anticonvulsant drugs are commonly used as first-line therapies. Use of SNRIs is common and frequently results in improvement, but treatment of neuropathic pain is considered an off-label use for these agents. Simple analgesics have not been shown to be effective for this type of pain (IASP, 2012).

Psychogenic pain is defined as pain that persists despite the lack of any identified underlying physical cause. Although still commonly used, the term *psychogenic pain* it is no longer considered an official diagnostic term. A more correct diagnostic term is **persistent somatoform pain disorder (PSPD).** PSPD is defined in the ICD-10 Version 2016 as

> the predominant complaint is of persistent, severe, and distressing pain, which cannot be explained fully by a physiological process or a physical disorder, and which occurs in association with emotional conflict or psychosocial problems that are sufficient to allow the conclusion that they are the main causative influences. The result is usually a marked increase in support and attention, either personal or medical (ICD-10, Version 2016).

Persistent somatoform pain disorder patients suffer from persistent, severe, and distressing pain without sufficient explanatory pathology. It is believed the pain originates from emotional conflicts or psychosocial problems. This type of pain is usually nonresponsive to a variety of therapies because of its unclear pathology. The absence of effective treatment can result in excessive consumption of medical resources, in addition to social problems. Persistent somatoform pain disorder seriously impacts the quality of life of patients and brings a great burden to society (Huang et al, 2016).

The identification of PSPD as having no physiologic cause has done a great deal of damage to individuals with chronic pain. Many healthcare professionals fail to recognize the complexity of pain and believe it can be explained based on the presence or absence of physical findings, secondary gain, or prior emotional problems. As a result, countless individuals have been informed that "the pain is all in your head." And if these same individuals react with anger and hurt, clinicians sometimes compound the problem by labeling the individual as hostile, demanding, or aggressive (VHA, 2015).

The correspondence between physical findings and pain complaints is fairly low (generally, 40%–60%). Individuals may have abnormal tests (eg, MRI shows a bulging disk) with no pain, or substantial pain with negative results. This is because chronic pain can develop in the absence of the gross skeletal changes we are able to detect with current technology (VHA, 2015).

Muscle strain and inflammation are common causes of chronic pain, yet may be extremely difficult to detect. Other conditions may be due to systemic problems, trauma to nerves, circulatory difficulties, or CNS dysfunction. Yet in each of these cases we may be unable to "see" the cause of the problem. Instead, we have to rely on the person's report of their pain, coupled with behavioral observations and indirect medical data. This does not mean that the pain is psychogenic or has no underlying physical cause. Instead it means that we are unable to detect or understand its cause (VHA, 2015).

Actually, how often healthy individuals feign pain for secondary gain is unknowable. In addition, the presence of secondary gain does not at all indicate that an individual's pain is less "real." In this country most individuals with chronic pain receive at least some type of benefit (not necessarily monetary) for pain complaints. Therefore, exaggeration of pain or related problems is to be expected. Unfortunately, practitioners may use the presence of secondary gain or pain amplification as an indication that the person's pain is not real (VHA, 2015).

Chronic Pain Syndromes

In deciding how to treat chronic pain, it is important to distinguish between chronic pain and a **chronic pain syndrome**. A chronic pain syndrome differs from chronic pain in that people with a syndrome over time develop a number of related life problems beyond the sensation of pain itself. It is important to distinguish between the two because they respond to different types of treatment (VHA, 2015).

Most individuals with chronic pain do not develop the more complicated and distressful chronic pain syndrome. Although they may experience the pain for the remainder of their lives, little change in their daily regimen of activities, family relationships, work, or other life components occurs. Many of these individuals never seek treatment for pain and those who do often require less intensive, single-modality interventions (VHA, 2015).

Symptoms of Chronic Pain Syndrome

Those who develop chronic pain syndrome tend to experience increasing physical, emotional, and social deterioration over time. They may abuse pain medications, and typically require more intensive, multimodal treatment to stop the cycle of increasing dysfunction (VHA, 2015).

Symptoms of Chronic Pain Syndrome

Reduced activity	Pain behaviors
Impaired sleep	Kinesophobia*
Depression	Helplessness
Suicidal ideation	Hopelessness
Social withdrawal	Alcohol abuse
Irritability	Medication abuse
Fatigue	Guilt
Memory and cognitive impairment	Anxiety
Poor self-esteem	Misbehavior by children in the home
Less interest in sex	Loss of employment
Relationship problems	

* Avoidance of certain movements or activities due to fear of re-injury or re-experiencing the pain. Source: VHA, 2015.

Complex Regional Pain Syndrome

Complex regional pain syndrome (CRPS) is a general term for a severe chronic neuropathic pain condition that, in the past, was referred to by several other names. *Causalgia*, from the Greek meaning heat and pain, was the founding term for the syndrome. Causalgia was first used to represent the burning nature of the pain, as seen within American Civil War casualties suffering traumatic bullet wounds (Dutton & Littlejohn, 2015). In the 1940s the term *reflex sympathetic dystrophy* was introduced when it was thought the sympathetic nervous system played a role in the disease.

In 1994 a working group for the IASP held a conference to develop a more neutral term, to address the widespread inconsistency in terminology, and to avoid unsubstantiated theory on causation and etiology. From this meeting came the officially endorsed term *complex regional pain syndrome*, intended to be descriptive, general, and not imply etiology. The term was further divided into "CRPS 1" and "CRPS 2." The current terminology represents a compromise and remains a work in progress. It will likely undergo modifications in the future as specific mechanisms of causation are better defined (Dutton & Littlejohn, 2015).

CRPS I is characterized by intractable pain that is out of proportion to the trauma, while CRPS II is characterized by unrelenting pain that occurs subsequent to a nerve injury. The criteria for diagnosing CRPS is difficult because of the vast spectrum of disease presentations. They can include:

- Intractable pain out of proportion to an injury
- Intense burning pain
- Pain from non-injurious stimulation
- An exaggerated feeling of pain
- Temperature changes in the affected body part
- Edema
- Motor/trophic disturbances, or
- Changes in skin, hair, and nails; and abnormal skin color.

The pain in CRPS is regional, not in a specific nerve territory or dermatome, and it usually affects the hands or feet, with pain that is disproportionate in severity to any known trauma or underlying injury. It involves a variety of sensory and motor symptoms including swelling and edema, discoloration, joint stiffness, weakness, tremor, dystonia, sensory disturbances, abnormal patterns of sweating, and changes to the skin (O'Connell et al., 2013).

The acute phase of the condition is often characterized by edema and warmth and is thought to be supported by neurogenic inflammation. Alterations in CNS structure and function may be more important to the sustained pain and neurocognitive features of the chronic phase of the CRPS (Gallagher et al., 2013).

Complex Regional Pain Syndrome (CRPS) in Hand and Wrist

Source: Wikimedia Commons. Used by permission.

CRPS usually develops following trauma and is thought to involve both central and peripheral components. Continuous pain is the most devastating symptom of CRPS and has been reported to spread and worsen over time. Pain is usually disproportionate to the severity and duration of the inciting event (Alexander et al., 2013).

CRPS has high impact in terms of individual, healthcare, and economic burden, yet continues to lack a clear biologic explanation and predictable, effective treatment. Despite its sizable disease burden, its long history of identification, and a concentrated research effort, many significant challenges remain. These relate to issues of terminology, diagnostic criteria, predisposing factors, triggers, pathophysiology, and the ideal treatment path. There is also the challenge of the well-guarded notion that CRPS is not a true disease state, but rather a condition with psychological foundations (Dutton & Littlejohn, 2015).

While acute CRPS sometimes improves with early and aggressive physical therapy, CRPS present for a period of one year or more seldom spontaneously resolves. The syndrome encompasses a disparate collection of signs and symptoms involving the sensory, motor, and autonomic nervous systems, cognitive deficits, bone demineralization, skin growth changes, and vascular dysfunction (Gallagher et al., 2013).

Although numerous drugs and interventions have been tried in attempts to treat CRPS, relieve pain, and restore function, a cure remains elusive. Two analyses have attempted to develop evidence-based guidelines for the treatment of CRPS. One covers trials in the period between 1980 and June 2005; the second covers the period from June 2000 to February 2012. The earlier review identified the following treatments that had varying degrees of positive therapeutic effect:

- Sub-anesthetic ketamine intravenous infusion
- Gabapentin
- Dimethyl sulphoxide cream
- N-acetylcysteine
- Oral corticosteroids
- Bisphosphonates (eg, alendronate)
- Nifedipine
- Spinal cord stimulation (in selected patients)
- Various physical therapy regimens (Inchiosa, 2013)

Positive findings to varying degrees in the more recent analysis were as follows:

- Low-dose ketamine infusions

- Bisphosphonates
- Oral tadalafil
- Intravenous regional block with a mixture of parecoxib, lidocaine, and clonidine
- Intravenous immunoglobulin
- Memantine 40 mg per day (with morphine)
- Physical therapy

Spinal cord stimulation and transcranial magnetic stimulation improved symptoms, but only transiently (Inchiosa, 2013).

In the past it was common to explain the etiology of complex regional pain syndrome using the psychogenic model. Now however, neurocognitive deficits, neuroanatomic abnormalities, and distortions in cognitive mapping are known to be features of CRPS pathology. More important, many people who have developed CRPS have no history of mental illness. With increased education about CRPS through a biopsychosocial perspective, both physicians and mental health practitioners can better diagnose, treat, and manage CRPS symptomatology (Hill et al., 2012).

Video (2:31): What is Chronic Pain?

https://www.youtube.com/watch?v=GTmE5X8NcXM

Pain Management Approaches

The management of pain can be, and is, approached in a number of ways. Many people suffering from pain, particularly acute pain, successfully self-manage their pain. If this fails, a trip to primary care physician, emergency department, pain specialist, or complementary practitioner may help. If none of these solves the problem, surgery may be considered.

Broadly speaking, pain has been managed with either of two models: self-management or pain medicine. The self-management model—especially for chronic pain—is supported by strong evidence and has the benefit of involving patients in their own care. The pain medicine model, which includes primary and specialty care, is supported by relatively weak evidence, particularly in chronic pain care, and often fails to involve the recipient as an active participant. Although the pain medicine model has weaker demonstrated efficacy, it is widely used because of a strong business model, industry support, and focus of training in healthcare professionals (NIH, 2013).

Three Approaches to Pain Management

1. The Self-Management Model
2. The Pain Medicine Model
3. The Integrative Medicine Model

Increasingly, however, pain medicine approaches are being combined with self-management and complementary practices into what is referred to as **integrative medicine**. In this model, pain is viewed holistically, and assessed and treated in conjunction with psychological, medical, social, spiritual, and environmental influences. Currently, an integrative approach to pain care is encouraged for all patients (PPSG, 2014b).

Self-Management of Pain

Self-management is defined as a strategy used by the patient to manage or minimize the impact of a chronic condition on everyday life. The basic tenets of self-management include:

- Active participation by the patient
- Treatment of the whole person, not just the disease
- Empowerment of the patient (NIH, 2013)

Although some people seek professional help immediately, most try to self-manage their pain. Self-management approaches include talking to friends, searching the internet, or attending group classes or programs intended to educate a person about pain management. Self-management also includes exercise, ice, heat, positioning, limiting activity, over-the-counter (OTC) medications, and education. In many cases, self-management is highly successful.

Pain Medicine Model

The pain medicine model is widely accepted and widely used. It is based upon the idea that pain is an acute, treatable disease. This approach usually begins with the primary care physician. Primary care physicians may make a referral to a pain specialist or pain clinic.

Primary Care

Primary care practitioners are an early step in the pain care journey, treating 52% of chronic pain patients in the United States based on a national mail survey of primary care physicians, physician pain specialists, chiropractors, and acupuncturists (IOM, 2011).

Primary care involves several management strategies, usually coordinated by a general medicine specialist. Primary care clinicians provide the initial assessment or diagnosis and serve as a starting point for specialty services, including prescription medications and referrals to imaging, physical and occupational therapy, or other integrative practitioners (IOM, 2011).

Once the primary care clinician has completed the initial assessment, effective medical management, especially with chronic pain, ideally involves a multi-disciplinary team. The development of a comprehensive treatment plan is important, utilizing appropriate pharmacologic and nonpharmacologic interventions. Treatments should be regularly re-evaluated for effectiveness, adjusted as needed, with side effects quickly addressed. The treatment plan should include a complete assessment and a clearly written plan of care (PPSG, 2014b).

Primary care clinicians assist patients in making decisions about specialty services and elective procedures. They are also responsible for the majority of pain medicine prescriptions. In 2007 analgesics were the drug category most frequently mentioned in data on office visits to physicians. In 2008 analgesics constituted 10.1% of all drugs prescribed for adults (ranking a close second to antidepressants, at 10.8%) (IOM, 2011).

Specialty Care

Specialty practice in pain management is a growing part of the medical profession, and the American Medical Association recognizes pain medicine as a discrete specialty. Most pain specialists come from anesthesiology, with a smaller number coming from physical and rehabilitation medicine, occupational medicine, psychiatry, and neurology (IOM, 2011). Physicians who are board certified in these specialty areas can become certified in pain medicine.

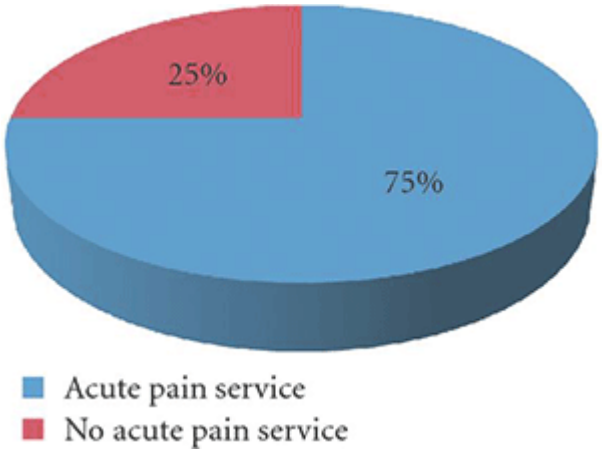
From 2000 to 2009, pain medicine certificates were issued to 1,874 anesthesiologists, 1,337 physiatrists, and 277 psychiatrists and neurologists, based on a common curriculum and a jointly developed examination administered by the American Board of Anesthesiology (IOM, 2011).

Acute Pain Services

Many hospitals have developed acute pain services (APS), the goal of which is to provide consistent pain management for individual patients throughout the course of their hospital stay. Hospitals with formally organized acute pain services are more likely to follow a formal written post operative pain protocol than hospitals without acute pain services (Nasir et al., 2011).

A survey of the structure and function of acute pain services in 200 non-teaching and 101 teaching hospitals throughout the United States found that acute pain services vary significantly, with university/academic institutions being more likely to offer these services than private or Veteran’s Administration (VA) hospitals. However, even in those hospitals with formal acute pain services, many lacked consensus regarding the use of pain management protocols as well as optimal outcome measures for assessing post operative pain therapy (Nasir et al., 2011).

Percentage of Hospitals with Acute Pain Service



Percentage of responding hospitals with an organized acute pain service. Source: Nasir et al., 2011.

The personnel comprising the typical acute pain service included:

- Anesthesiologists (95%)
- Advanced practice nurses (45%), registered nurses (32.5%), pharmacists (11.3%)
- Physician assistants (8.8%)
- Physical medicine and rehabilitation physicians (6.3%)
- Surgeons (5%)
- Neurologists (3.8%)
- Others (oncologists, social workers, and psychologists) (Nasir et al., 2011)

Treating Pain in the Emergency Department

The emergency department has become a common place to seek treatment for pain. The very nature of the ED means that in most cases the average emergency medicine specialist is primarily concerned with differential diagnosis, ruling out life-threatening disease, and providing stabilizing interventions. For the patient, though, the priorities are likely to include pain management (Thomas, 2013).

In a telephone survey of 500 adults, the American Chronic Pain Association sought to understand the ED experience of those with chronic or recurrent pain. Almost one-half reported "complete" or "a great deal" of pain relief during the ED visit, while 78% endorsed as "somewhat or definitely true" that "the ED staff understood how to treat my pain." Although more than three-fourths of patients felt that receiving additional information on pain management or referrals to specialists was extremely or very important, only one-half reported receiving them. A significant minority (11%) reported that the "ED staff made me feel like I was just seeking drugs." The majority (76%) were somewhat to completely satisfied with their treatment, while 24% were neutral or completely dissatisfied. Age, recurrent pain, waiting time, imaging, receiving analgesics, and pain relief predicted patient satisfaction (Todd et al., 2010).

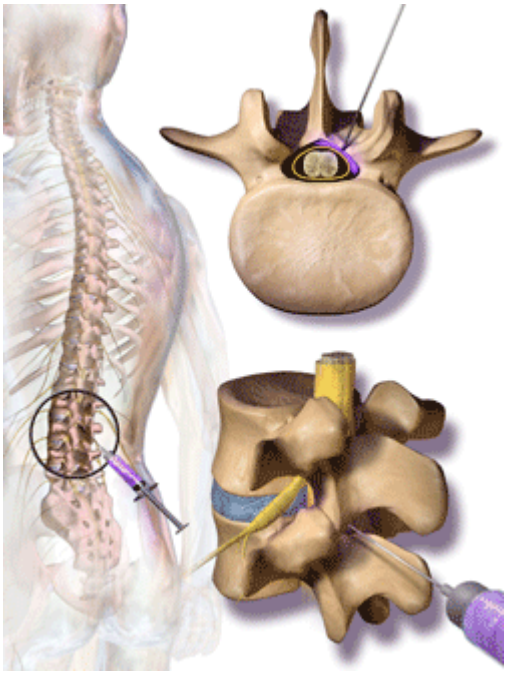
When older adults are treated for pain in the ED, the usual issue is less one of assessment than one of concern for side effects; older patients are simply more likely than younger patients to suffer untoward side effects of many popular ED analgesics such as opioids. A balancing of the risks and benefits of analgesia in older patients is important, and should be discussed with patients and families. The challenge of geriatric analgesia can often be overcome through use of opioid-sparing analgesic regimens or employment of specific therapies (eg, regional nerve blocks for hip fractures) (Thomas, 2013).

Interventional and Surgical Treatments

Interventional techniques are minimally invasive procedures that place drugs in targeted areas or ablate target nerves. This category includes some surgical techniques such as laser or endoscopic discectomy, intrathecal infusion pumps, and spinal cord stimulators, used for the diagnosis and management of chronic, persistent, or intractable pain (Manchikanti et al., 2010).

Epidural injections, in which steroids and anti-inflammatories are injected directly into the epidural space of the spinal cord are the most commonly performed procedures in interventional pain management, comprising 46% of all interventional techniques. The most commonly performed procedures are lumbosacral interlaminar or caudal epidural injections. Facet joint interventions are the second most commonly performed procedures, constituting 38% of all interventional techniques in 2011 (Manchikanti et al., 2010).

Conventional thermal radiofrequency (CT-RF) is another minimally invasive procedure in which a thermal lesion is created by applying radiofrequency energy through an electrode placed in the vicinity of the target neural structure. It has been used for some time in cardiac electrophysiology and tumor ablation although its use in the treatment of pain is recent. A variation—water-cooled radiofrequency (WC-RF) ablation—allows a larger volume of the tissue to be heated and the resultant thermal lesion is substantially larger than with conventional thermal radiofrequency (Malik et al., 2011). These techniques are most commonly applied to the intervertebral disc and sacroiliac joints.



Steroids are injected into the cerebrospinal fluid in the canal surrounding the spine. Nerves branch out from the spine. The nerve roots, which may be compressed, are at the base of the nerves. Source: Blausen.com staff. "Blausen gallery 2014." Wikiversity Journal of Medicine.

There is growing evidence of a disproportionate increase in these interventional techniques and the usefulness of some has been criticized. Analysis of various spinal interventional techniques indicates that there has been an overall increase in interventions of 177% per 100,000 Medicare fee-for-service population with the highest increases seen for sacroiliac joint injections at 331%, facet joint interventions at 308%, epidurals at 130% (Manchikanti et al., 2013).

A systematic review of interventional therapies for low back and radicular pain concluded: "Few nonsurgical interventional therapies for low back pain have been shown to be effective in randomized, placebo-controlled trials." A systematic review of 18 randomized controlled trials found no strong evidence for or against using injection therapy to treat subacute or chronic low back pain (IOM, 2011).

A review of 30 trials determined that corticosteroid injections (and traction) were not found to be beneficial and are not recommended for lumbosacral radicular syndrome (IOM, 2011). Implantation of spinal cord stimulation and intrathecal drug delivery systems (so-called pain pumps) require routine monitoring, replacement of devices over time, refilling of drug reservoirs, and a balancing of high costs and maintenance requirements against benefits (IOM, 2011).

Although interventional techniques are often considered to be surgical procedures, more invasive procedures such as joint replacement, spinal fusion, and disc replacement are also commonly and successfully used to relieve pain. These types of surgeries often occur after other conservative treatments have failed to relieve the pain.

Common Pain Conditions

Despite the difficulty in classifying and understanding various mechanisms of pain, certain pain syndromes are pervasive. Low back pain, headache pain, post operative pain, cancer pain, and pain associated with arthritis are some of the most common reasons patients seek medical care for pain. A National Health Interview Survey of adults during 1997–2014 found that in the three months prior to an interview, participants reported:

- 28% had experienced pain in the lower back
- 16% had experienced a migraine or severe headache
- 14% had experienced pain in the neck area (NCHS, 2016)

Low Back Pain

Low back pain (LBP) is one of the most common types of disability affecting individuals in Western countries. Low back pain affects approximately 80% of people at some stage in their lives, and if it becomes chronic it often results in lost wages and additional medical expenses and can increase the risk of incurring other medical conditions (Chou et al., 2016). Chronic low back pain has been estimated to cost 2% of the gross domestic product in developed countries (Sit et al., 2015).

In the United States, the total indirect and direct costs due to low back pain are estimated to be greater than $100 billion annually (Wang et al., 2012). It is the fifth most common reason for all physician visits. Approximately one-quarter of U.S. adults reported having low back pain lasting at least 1 day in the past 3 months, and 7.6% reported at least one episode of severe low back pain in the previous year.

Clinically, the natural course of low back pain is usually favorable; acute low back pain frequently disappears within 1 to 2 weeks. In some cases acute low back pain becomes chronic and difficult to treat. Any of the spinal structures, including intervertebral discs, facet joints, vertebral bodies, ligaments, or muscles could be an origin of back pain, which is, unfortunately, difficult to determine. In those cases in which the origin of back pain cannot be determined, the diagnosis given is **nonspecific low back pain** (Aoki et al., 2012).

Assessing Low Back Pain

The vast majority of low back pain patients who present to primary care have pain that cannot be reliably attributed to a specific disease or spinal abnormality. Spinal imaging abnormalities such as degenerative disc disease, facet joint arthropathy, and bulging or herniated intervertebral discs are extremely common in patients with or without low back pain, particularly in older adults, and such findings are poor predictors for the presence or severity of low back pain (Chou et al., 2016).

Low back pain symptoms can arise from many anatomic sources, such as nerve roots, muscle, fascia, bones, joints, intervertebral discs, and organs within the abdominal cavity. Symptoms can also be caused by aberrant neurologic pain processing, a condition called neuropathic low back pain. The diagnostic evaluation of patients with low back pain can be challenging and requires complex clinical decision-making. Nevertheless, the identification of the source of the pain is of fundamental importance in determining the therapeutic approach (Allegri et al., 2016).

The location of pain, frequency of symptoms, duration of pain, history of previous symptoms, previous treatments, and response to treatment should be assessed. The possibility of low back pain due to pancreatitis, nephrolithiasis, or aortic aneurysm, or systemic illnesses such as endocarditis or viral syndromes, should also be considered. Low back pain can be influenced by psychological factors, such as stress, depression, or anxiety. History should include substance use exposure, detailed health history, work habits, and psychosocial factors (Allegri et al., 2016).

Back pain can be **referred** or felt at a site distant from the source of the pain. Pain can be local or referred from a painful stimulus occurring in an internal organ. An example of referred pain is when a heart attack occurs and pain in felt in the jaw, shoulder, or arm.

Pain may also be felt in the territory of a *dermatome*, an area of skin supplied by a single sensory nerve. This is referred to as radiating pain and can be quite confusing for patients. If the nerve root is irritated or inflamed, pain can be evoked by any motion that stretches or compresses the root of the nerve. This is referred to as *radicular pain*, which can occur in patients with serious or progressive neurologic deficits or underlying conditions requiring prompt evaluation, as well as patients with other conditions that may respond to specific treatments.

Patients with back and leg pain have a fairly high sensitivity for herniated disc, with more than 90% of symptomatic lumbar disc herniation occurring at the L4/L5 and L5/S1 levels. A focused examination that includes straight leg–raise testing and a neurologic examination that includes evaluation of knee strength and reflexes (L4 nerve root), great toe and foot dorsiflexion strength (L5 nerve root), foot plantar flexion and ankle reflexes (S1 nerve root), and distribution of sensory symptoms should be done to assess the presence and severity of nerve root dysfunction.

Imaging tests such as magnetic resonance imaging (MRI) should be considered only in the presence of clinical elements that are not definitely clear or in the presence of neurologic deficits or other medical conditions. The recommendation of the American College of Radiology is to *not* do imaging for low back pain within the first 6 weeks unless red flags are present. Red flags include recent significant trauma or milder trauma at age older than 50 years, unexplained weight loss, unexplained fever, immunosuppression, history of cancer, intravenous drug use, prolonged use of corticosteroids, osteoporosis, age older than 70 years, and focal neurologic deficits with progressive or disabling symptoms (Allegri et al., 2016).

Treating Low Back Pain

Despite the negative impact and increasing prevalence of low back pain, patients are regularly ignored and their complaints are often misunderstood. As a result, they often do not receive timely or effective treatment. This issue poses considerable challenges and frustrations for healthcare providers and can create a feeling of mistrust among patients. Ample evidence demonstrates that clinicians' attitudes and beliefs regarding low back pain seem to affect the beliefs of their patients. Physicians' attitudes and beliefs also appear to influence their recommendations regarding activities and work (Sit et al., 2015).

Multiple treatment options for acute and chronic low back pain are available. Broadly, these can be classified as pharmacologic treatments, noninvasive nonpharmacologic treatments, injection therapies, and surgical treatments. Pharmacologic treatments include nonsteroidal anti-inflammatory (NSAID) drugs, acetaminophen, opioids, muscle relaxants, anti-seizure medications, antidepressants, and corticosteroids (Chou et al., 2016).

Nonpharmacologic treatments include exercise and related interventions, complementary and alternative therapies, psychological therapies, physical modalities, low-level laser therapy, interferential therapy, superficial heat or cold, back supports, and multidisciplinary rehabilitation (Chou et al., 2016).

Migraine Headaches

A migraine is a very painful headache thought to result from vasodilation of blood vessels in the brain. Migraines cause intense, pulsing or throbbing pain on one or possibly both sides of the head. People with migraine headaches often describe pain in the temples or behind one eye or ear. Migraine sufferers may also have symptoms of nausea, vomiting, and sensitivity to light and sound. Some people see spots or flashing lights or have a temporary loss of vision that forewarn of an impending headache. If a migraine occurs more than 15 days each month for 3 months, it is considered chronic.

Migraines often start in the morning, and the pain can last from a few hours up to two days. These headaches can occur as often as several times per week for some patients or as infrequently as once or twice a year. For many with migraines, the quality of life and activity is greatly diminished during attacks, and their frequency can interfere with the ability to work or to perform activities of daily living. Migraine headaches are still under-diagnosed and under-treated because they can have features in common with other types of headache.

Over time, episodes of migraine headache afflict patients with increased frequency, longer duration, and more intense pain. While episodic migraine may be defined as 1 to 14 attacks per month, there are no clear-cut phases defined, and those patients with low frequency may progress to high frequency episodic migraine and the latter may progress into chronic daily headache (>15 attacks per month) (Maleki et al., 2011).

Numerous imaging studies of migraine patients have described multiple changes in brain functions as a result of migraine attacks: these include enhanced cortical excitability, increased gray matter volume in some regions and decreased in others, enhanced brain blood flow, and altered pain modulatory systems (Maleki et al., 2011).

Migraine has no cure. Drug therapies are broadly divided into two groups: (1) those designed to treat acute occurrences, and (2) those that are prophylactic (preventive) in nature. Many people with migraine use both forms of treatment. The goal is to treat migraine symptoms as soon as possible and to minimize the number of migraine occurrences by avoiding triggers.

The treatment of an individual migraine attack once it has occurred ("acute treatment"), is commonly referred to as **abortive therapy**. Four major medications are used for abortive therapy:

1. The triptans
2. Ergotamine
3. Dihydroergotamine

4. Midrin, a combination of isometheptene mucate, dichloralphenazone, and acetaminophen

Other medications include CGRP receptor antagonists and, among herbals, feverfew.

For relatively mild migraine symptoms, over-the-counter (OTC) pain medications such as aspirin, acetaminophen (Tylenol), or NSAIDs like ibuprofen (Advil, Motrin), may be sufficient. Some combination medicines are sold specifically for migraines (eg, Excedrin Migraine, which contains aspirin, acetaminophen, and caffeine) but these are usually not strong enough for severe migraines. The patient needs to understand that taking migraine medications more than 3 days a week may lead to **rebound headaches**—headaches that keep coming back, in part because of the medications.

Many migraine medicines work by narrowing blood vessels to counteract vasodilation in the vessels of the brain. Caution is advised if the patient has risk for heart attacks or has heart disease. Ergots should not be given if the patient is pregnant or planning to become pregnant.

Pain Following Surgery

Pain following surgery is very common. In the United States, nearly 100 million surgeries take place annually—about 46 million inpatient and about 53 million outpatient procedures. Good post surgical pain management is associated with patient satisfaction, earlier mobilization, shortened hospital stays, and reduced costs.

Post operative pain can be caused by tissue damage, the presence of drains and tubes, post operative complications, prolonged time in an awkward position, or a combination of these factors. Post operative pain is often under-estimated and under-treated, leading to increased morbidity and mortality, mostly due to respiratory and thromboembolic complications, increased hospital stay, and impaired quality of life (EAU, 2013).

There is a pressing need for improvements in post operative pain management—about 70% of post surgical patients report pain that is moderate, severe, or extreme (EAU, 2013) and fewer than half of those patients report adequate post surgical pain control (IOM, 2011). Failure to adequately control post operative pain drives up costs and is thought to be a factor in the development of chronic pain (Chapman et al., 2012).

Good post operative pain management requires good pain assessment and measurement in all post operative patients. Assessment should focus on the patient’s response to surgery as well as respiratory and cardiac complications. Assessment should occur at scheduled intervals, in response to new pain, and prior to discharge (EAU, 2013).

Although much of the focus on post operative pain management is on hospitals, about 60% of surgical procedures in community hospitals are performed on an outpatient basis, and persistent problems exist with pain management after discharge (IOM, 2011). This may be because there is not enough time to assess post surgical pain prior to discharge or to establish a pain management program at home.

Psychological factors such as anxiety and depression can be important predictors in the development of post operative pain. Age has also been found as a predictor, with younger individuals being at higher risk for moderate to intense pain. Patients at high risk for severe post operative pain should be provided with special attention. Patients with good analgesia are more cooperative, recover more rapidly, and leave the hospital sooner. They also have a lower risk for prolonged pain after surgery (Ene et al., 2008).

Persistent Post Surgical Pain

The International Association for the Study of Pain (IASP) refers to post operative pain that continues for more than 2 months and cannot be explained by other causes "persistent post surgical pain" (Kehlet & Rathmell, 2010). A percentage of post operative patients (10%–50%) develop persistent pain following common surgical procedures such as groin hernia repair, breast and thoracic surgery, leg amputation, and coronary artery bypass surgery, often due to nerve damage during the procedure (IOM, 2011).

Many patients suffer from moderate to severe post operative pain despite recent improvements in pain treatment. Severe pain is associated with decreased patient satisfaction, delayed post operative ambulation, the development of chronic or persistent post operative pain, increased incidence of pulmonary and cardiac complications, and increased morbidity and mortality (Ghoneim & O'Hara, 2016).

Chronic or persistent post surgical pain is a serious clinical problem. It is a common reason for early retirement and unemployment and represents an extensive drain on societies' resources. The factors that seem to affect its incidence include the extent of preoperative pain, trauma during surgery, and anxiety and depression. Cancer patients seem particularly susceptible (Ghoneim & O'Hara, 2016).

In a systematic review of the psychosocial predictors and correlates for chronic post surgical pain, depression was a strong predictor. Comorbidity of pain and depression provokes worsening of both conditions. It is important therefore to identify patients at high risk for its development and optimize their management (Ghoneim & O'Hara, 2016).

Chronic, persistent post surgical pain influences patients' quality of life (even after minor surgical procedures) and is currently regarded as an important outcome reflecting the quality of perioperative care provided to patients. A recent study just confirmed that moderate-to-severe persistent post surgical pain is common after outpatient surgery (ie, ambulatory and short-stay procedures), and inguinal hernia repair is a very common surgical procedure, often performed on an ambulatory base (Bugada et al., 2016).

Among risk factors for persistent post surgical pain development, the severity of acute post operative pain is often mentioned, which implies that individuals prone to suffer intense post operative pain may be the most vulnerable to persistent post surgical pain. However, not every patient with severe post operative pain will later develop persistent post surgical pain (Bugada et al., 2016).

To identify the scope of a person's pain following surgery, especially pain persisting more than 2 to 3 months after surgery, a careful clinical evaluation is needed. This includes history, physical examination, and appropriate special tests in order to identify or exclude reversible underlying conditions (Gilron & Kehlet, 2014). Be aware of risk of persistent pain following surgery in the following instances:

- If the patient was previously pain free but has now developed a new chronic pain syndrome
- If previous pain at the site of surgery still remains
- If the patient previously suffered from a chronic pain syndrome—unrelated to the surgery—and the pain persists (Gilron & Kehlet, 2014)

Pain in the ICU

Most, if not all, patients in intensive care units (ICUs) will experience pain at some point during their ICU stay. Pain can be related to injury, surgery, burns, or comorbidities, such as cancer, or from procedures performed for diagnostic or treatment purposes. Some patients may even experience substantial pain at rest. Despite increased attention to assessment and pain management, pain remains a significant problem for ICU patients (Kyranou & Puntillo, 2012).

Unrelieved pain in adult ICU patients is far from benign. Medical and surgical ICU patients who recalled pain and other traumatic situations while in the ICU had a higher incidence of chronic pain and post traumatic stress disorder symptoms than did a comparative group of ICU patients. Concurrent or past pain may be the greatest risk factor for development of chronic pain (Kyranou & Puntillo, 2012).

Pain Associated with Cancer

Pain occurs in 20% to 50% of patients with cancer (NCI, 2016). It is one of the most severe, feared, and common symptoms of a variety of cancers and is a primary determinant of the poor quality of life in cancer patients (Bali et al., 2013). Cancer-associated pain—particularly neuropathic pain—has been shown to be resistant to conventional therapeutics whose application may be severely limited due to widespread side effects (Bali et al., 2013).

Pain from cancer tends to increase in severity as the cancer advances, and patients often experience pain at multiple sites concurrently. The highest prevalence of severe pain occurs in adult patients with advanced cancer. There may be multiple mechanisms with distinct patterns, such as continuous pain, movement-related pain, and spontaneous breakthrough pain.

As cancer reaches the advanced stage, moderate to severe pain affects roughly 80% of patients. Younger patients are more likely to experience cancer pain and pain flares than are older patients (NCI, 2016).

Research from Europe, Asia, Australia, and the United States indicates that cancer patients are repeatedly undertreated for pain, both as inpatients and outpatients—sometimes receiving no analgesia at all. Regardless of what stage the cancer has reached, it is necessary to determine the prevalence of pain in specific cancer types, both to raise awareness among clinicians and to improve patient management (Kuo et al., 2011).

Classifying Cancer Pain

Classifying cancer pain can be a challenge because the pain often does not have a single cause. Pain can be acute or chronic and can vary in intensity over time. Acute pain is typically induced by tissue injury and diminishes over time as the tissue heals. Chronic pain persists after an injury has healed or becomes recurrent over months; or results from lesions unlikely to regress or heal (NCI, 2016). Tumors, which occupy space, can also cause pain by pressing on skin, nerves, bones, and organs.

Breakthrough pain is common in cancer patients. It is a temporary increase or flare of pain that occurs in the setting of relatively well-controlled acute or chronic pain. **Incident pain** is a type of breakthrough pain related to certain activities or factors such as vertebral body pain from metastatic disease. Breakthrough and incident pain are often difficult to treat effectively because of their episodic nature. In one study, 75% of patients experienced breakthrough pain; 30% of this pain was incidental, 26% was non-incidental, 16% was caused by end-of-dose failure, and the rest had mixed etiologies (NCI, 2016).

Pain can be a side-effect of therapies used to treat cancer. A systematic review of the literature identified reports of pain occurring in 59% of patients receiving anti-cancer treatment and in 33% of patients after curative treatments (NCI, 2016). Some pain syndromes that can be caused by cancer therapies include:

- **Infusion-related pain syndromes** (venous spasm, chemical phlebitis, vesicant extravasation, and anthracycline-associated flare)
- **Treatment-related mucositis**
- **Chemotherapy-related musculoskeletal pain** (diffuse arthralgias and myalgias in 10% to 20% of patients)
- **Dermatologic complications and chemotherapy** (acute herpetic neuralgia, tingling or burning in their palms and soles, rash)
- **Pain from supportive care therapies** (osteonecrosis, avascular necrosis)
- **Radiation-induced pain** (mucositis, mucosal inflammation in areas receiving radiation, pain flares, and radiation dermatitis) (NCI, 2016)

The Pain Ladder

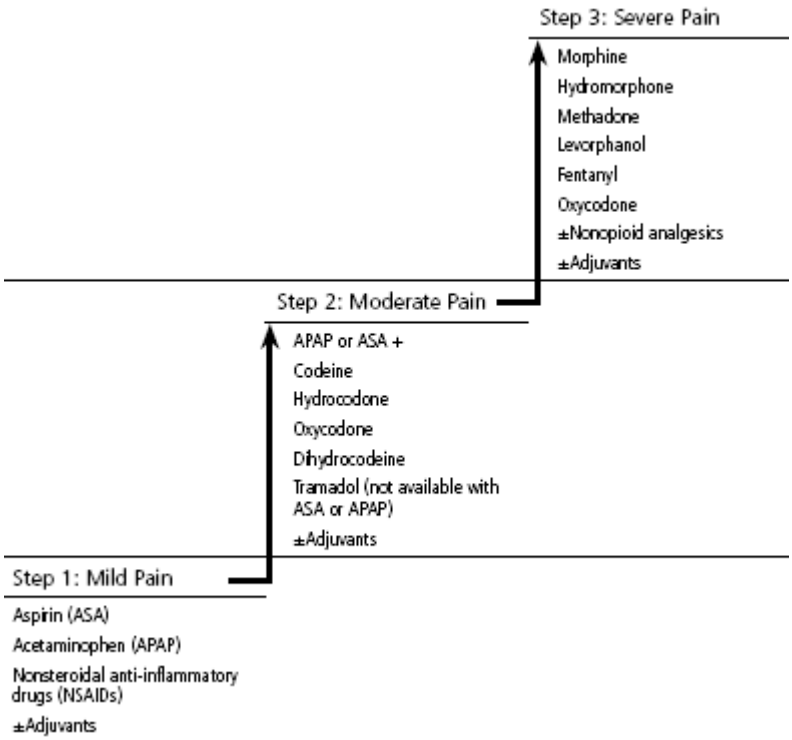
Although cancer pain or other symptoms often cannot be entirely eliminated, available therapies can effectively relieve pain in most patients. Good pain management improves a patient's quality of life throughout all stages of the disease. Patients with advanced cancer may experience multiple concurrent symptoms with pain. In these patients, a thorough assessment of symptoms and appropriate management is needed for optimal quality of life (NCI, 2016).

The Pain Ladder was developed by the World Health Organization (WHO) in the context of cancer care. The WHO three-step analgesic ladder presents a stepped approach based on pain severity. If the pain is mild, begin with Step 1. This involves the use of analgesics such as acetaminophen or an NSAID, while keeping in mind potential renal and gastrointestinal adverse effects (WHO, 2016).

If pain persists or worsens despite appropriate dose increases, a change to a Step 2 or Step 3 analgesic is indicated. Most patients with cancer pain will require a Step 2 or Step 3 analgesic. Step 1 can be skipped in favor of Step 2 or Step 3 in patients presenting at the onset with moderate-to-severe pain. At each step, an adjuvant drug or modality such as radiation therapy may be considered in selected patients. World Health Organization recommendations are based on worldwide availability of drugs and not strictly on pharmacology (WHO, 2016).

In general, analgesics should be given "**by mouth, by the clock, by the ladder, and for the individual**" and should include regular scheduling of the analgesic, not just on an as-needed basis. In addition, rescue doses for breakthrough pain should be added. The oral route is preferred as long as a patient is able to swallow. Each analgesic regimen should be adjusted for the patient's individual circumstances and physical condition (NCI, 2013).

World Health Organization Analgesic Ladder



Source: Adapted from WHO, 1986. Used with permission.

Clinical management of cancer pain is complex, driven by patient's response, and the need to have both shorter and longer acting preparations and equi-analgesic dose ratios. The process of combining or switching opioids is complex for the clinician, who must understand the different half-life, receptors, and conversion ratios of these opioids, which can vary greatly among individuals, opioids, and even by opioid dose (Gao et al., 2014).

Adjuvants medications can enhance the analgesic effect of opioid drugs in patients with cancer. Concurrent use of adjuvants is recommended by the World Health Organization and has been recognized as one of the effective strategies in improving the balance between analgesia and side effects. However, consistent evidence suggests an under-utilization of adjuvants in cancer pain management, which may contribute to unnecessary opioid switching or rotation (Gao et al., 2014).

Pain Associated with Arthritis

Arthritis and other rheumatic conditions are a leading cause of disability in adults in the United States. The negative consequences of arthritis and other rheumatic conditions, including pain, reduced physical ability, depression, and reduced quality of life, can impact the physical functioning and psychological well-being of those living with the conditions (Schoffman et al., 2013).

Treatment of arthritis and other rheumatic conditions is costly, and given the growing number of people in the United States over the age of 65, arthritis and other rheumatic conditions are expected to be a large burden on the healthcare system in the coming years. The number of Americans with arthritis and other rheumatic conditions is expected to reach about 67 million by 2030, meaning that 25% of Americans will have arthritis and other rheumatic conditions (Schoffman et al., 2013).

Osteoarthritis

Osteoarthritis (OA) is a joint disorder, characterized by degeneration of joint cartilage. It causes joint pain and stiffness that worsens over time. OA is the most common form of arthritis and affects close to 27 million Americans. After the age of 65, 60% of men and 70% of women experience OA (Van Liew et al., 2013).

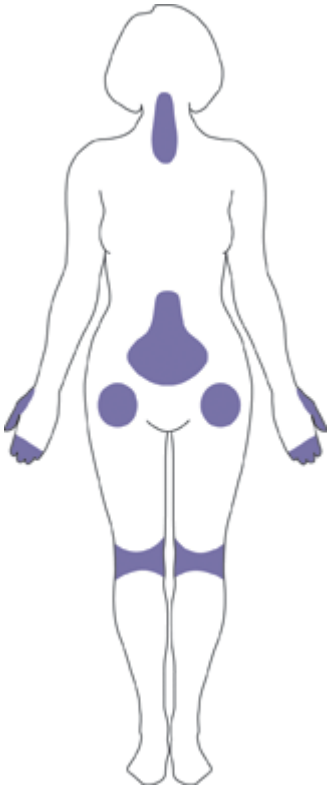
In a healthy joint, the ends of bones are encased in smooth cartilage. They are protected by a joint capsule lined with a synovial membrane that produces synovial fluid. The capsule and fluid protect the cartilage, muscles, and connective tissues. With osteoarthritis, the cartilage becomes worn away. Spurs grow out from the edge of the bone, and synovial fluid increases, causing stiffness and pain (NIAMS, 2015).

Hip Joint Showing Osteoarthritis Progression

Left: Normal hip joint. Right: Hip joint with osteoarthritis. Source: Wikimedia Commons.

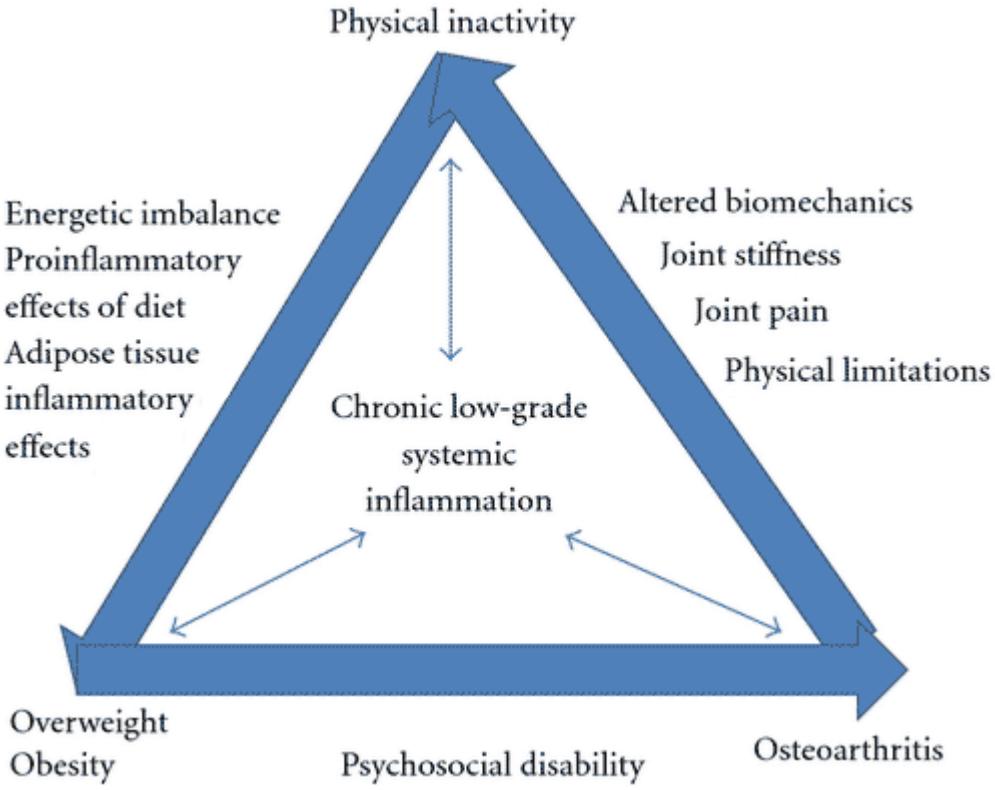
Although the prevalence of osteoarthritis increases with age, younger people can also develop it, usually as the result of a joint injury, a joint malformation, or a genetic defect in joint cartilage. Before age 45, more men than women have osteoarthritis; after age 45, it is more common in women. OA is more likely to occur in people who are overweight and in those with jobs that stress particular joints. The joints most commonly affected by OA are those at the ends of the fingers, thumbs, neck, lower back, knees, and hips (NIAMS, 2015).

Best practice guidelines for chronic osteoarthritis focus on self-management: weight control, physical activity, and pharmacologic support for inflammation and pain. Although low-grade inflammation underlies chronic osteoarthritis, it has not been a focus of best practice guidelines, particularly of its nonpharmacologic management. Obesity is an independent risk factor for osteoarthritis and there is an interactive relationship among osteoarthritis, obesity, and physical inactivity (see figure below). Although the mechanisms for this association are not completely understood, biomechanical loading and metabolic inflammation associated with excess adipose tissue and lipids may have a role (Dean & Hansen, 2012).



Osteoarthritis most often occurs in the hands (at the ends of the fingers and thumbs), spine (neck and lower back), knees, and hips. Source: NIAMS, 2015.

Etiology of Chronic Low-Grade Systemic Infection



Relationships among osteoarthritis, obesity, and physical inactivity and association with the etiology of chronic low-grade systemic inflammation. Source: Dean & Hansen, 2012. Used by permission.

Pain associated with osteoarthritis can lead to decreased physical activity, which is an independent risk factor for inflammation, likely due to the reduced expression of anti-inflammatory mediators. Physical inactivity also reduces daily energy expenditure and promotes weight gain (Dean & Hansen, 2012).

Approximately 80% of adults with OA have some movement limitations that affect daily activities; this is related to reduced quality of life and lower self-confidence. Having high levels of self-confidence is associated with higher quality of life, decreased pain, and increased activity for all people including those with OA (Van Liew et al., 2013).

Physical exercise is widely recommended for individuals with OA. A meta-analysis on treatments for OA found that exercise programs reduced pain, improved physical functioning, and enhanced quality of life among individuals with OA (Van Liew et al., 2013). Despite this, close to 44% of adults with arthritis report not engaging in exercise.

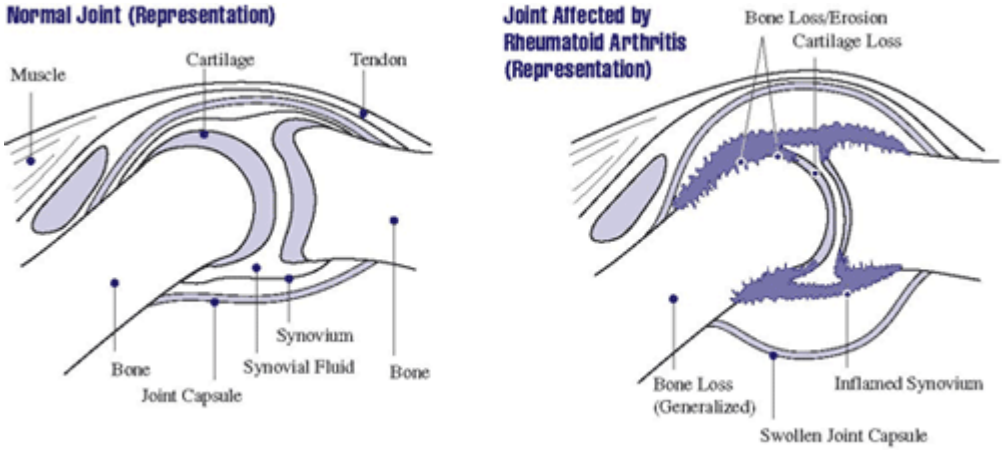
Psychological distress is an important factor associated with exercise and quality of life among people with OA. Evidence suggests that anxiety and depression lead to reduced functioning and to lower levels of physical activity. Although depression may pose barriers to activity engagement, physical activity has been shown to improve its symptoms and is a common focus of behavioral therapies. Conversely, improvements in depression are also likely to lead to increases in activity levels and quality of life (Van Liew et al., 2013).

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is among the most disabling forms of arthritis and it affects about 1% of the U.S. adult population (about 2 million people). RA is an autoimmune disease that involves inflammation of the synovium, a thin layer of tissue lining the joint space. As the disease worsens, there is a progressive erosion of bone, leading to misalignment of the affected joint, loss of function, and disability. Rheumatoid arthritis tends to affect the small joints of the hands and feet in a symmetric pattern, but other joint patterns are often seen.

Because of its systemic pro-inflammatory state, RA can damage virtually any extra-articular tissue. Cardiovascular disease is considered an extra-articular manifestation and a major predictor of poor prognosis. Traditional risk factors such as obesity, dyslipidemia, type 2 diabetes, metabolic syndrome, hypertension, physical inactivity, advanced age, male gender, family history of cardiovascular disease, hyperhomocysteinemia, and tobacco use have been associated with cardiovascular disease in RA patients. In fact, seropositive RA may, like diabetes, act as an independent risk factor for cardiovascular disease (Sarmiento-Monroy et al., 2012).

Joint Affected by Rheumatoid Arthritis



In rheumatoid arthritis, the synovium becomes inflamed, causing warmth, redness, swelling, and pain. As the disease progresses, the inflamed synovium invades and damages the cartilage and bone of the joint. Surrounding muscles, ligaments, and tendons become weakened. Rheumatoid arthritis can also cause more generalized bone loss that may lead to osteoporosis (fragile bones that are prone to fracture). Source: NIAMS, 2016.

Women are nearly three times more likely than men to develop rheumatoid arthritis—it can start at any age (mean age at the onset is 40 to 60 years). The precise cause of rheumatoid arthritis is unknown; like other autoimmune diseases it arises from a variable combination of genetic susceptibility, environmental factors, and the inappropriate activation of the immune responses. Multiple genes are associated with disease susceptibility, with the HLA locus accounting for 30% to 50% of the overall genetic risk (Fattahi & Mirshafiey, 2012).

Despite the well-documented negative impact of chronic pain on quality of life and functional outcomes, the best way to measure pain in patients with RA has not been adequately studied. Most research on the measurement of pain in RA focuses on the reliability of measures rather than their utility in predicting the course of illness. Therefore, there is little evidence to help guide clinicians and researchers on how best to assess RA pain with a focus on treatment and intervention in patients who are most likely to have impaired function over time (Santiago et al., 2016).

Studies that explore the role of pain as a predictor of functional disability typically focus on concurrent pain, or treat pain as a variable when examining predictors of future function. Since factors other than pain are the main predictors of interest, these studies fail to fully characterize the association of pain with future function and, more important, do not explore how different measures of pain and the time periods they reference may impact results (Santiago et al., 2016).

In the context of clinical trials for pain in general, the *Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials* (IMMPACT) recommendations outline pain intensity as one key outcome measure, recommending primarily the use of a 0 to 10 numerical scale for rating pain. Recommendations also suggest use of a verbal rating scale that may be easier for some patients to complete (Santiago et al., 2016).

Psoriatic Arthritis

Psoriatic arthritis is an inflammatory joint disease characterized by stiffness, pain, swelling, and tenderness of the joints as well as the surrounding ligaments and tendons. It affects men and women equally, typically presents at the age of 30 to 50 years, and is associated with psoriasis in approximately 25% of patients. Cutaneous disease usually precedes the onset of psoriatic arthritis by an average of 10 years in the majority of patients but 14% to 21% of patients with psoriatic arthritis develop symptoms of arthritis prior to the development of skin disease. The presentation is variable and can range from a mild, nondestructive arthritis to a severe, debilitating, erosive joint disease (Lloyd et al., 2012).

Psoriatic arthritis affects fewer people in the United States than rheumatoid arthritis. It has a highly variable presentation, which generally involves pain and inflammation in joints and progressive joint involvement and damage. There are multiple clinical subsets of psoriatic arthritis:

- Monoarthritis of the large joints
- Distal interphalangeal arthritis
- Spondyloarthritis, or a symmetrical deforming polyarthropathy similar to that of rheumatoid arthritis (Lloyd et al., 2012)

Left untreated, a proportion of patients may develop persistent inflammation with deforming progressive joint damage which leads to severe physical limitation and disability (Lloyd et al., 2012).

In many patients articular patterns change or overlap in time. **Enthesitis** (an inflammation of the area where tendons, ligaments, joint capsules, or fascia attach to bone) may occur at any site, but more commonly at the insertion sites of the plantar fascia, the Achilles tendons, and ligamentous attachments to the ribs, spine, and pelvis (Lloyd et al., 2012).

Dactylitis, an important feature of psoriatic arthritis, is a combination of enthesitis of the tendons and ligaments and synovitis involving all joints in the digit. The severity of the skin and joint disease frequently does not correlate with each other. Other manifestations of psoriatic arthritis include conjunctivitis, iritis, and urethritis (Lloyd et al., 2012).

Nonsteroidal anti-inflammatory drugs help with symptomatic relief, but they do not alter the disease course or prevent disease progression. Intra-articular steroid injections can be used for symptomatic relief. Physical or occupational therapy may also be helpful in symptomatic relief (Lloyd et al., 2012).

Disease-modifying anti-rheumatic drugs are the mainstay of treatment for patients suffering from psoriatic arthritis. Currently, the most effective class of therapeutic agents for treating psoriatic arthritis is the TNF-α inhibitors; however, these drugs show a 30% to 40% primary failure rate in both randomized clinical trials and registry-based longitudinal studies (Lloyd et al., 2012).

Pain in Special Populations

The extremes of age, as well as specific diseases such as cancer, provide special challenges to pain care. Infants and children, older adults, people with dementia, and cancer patients have little in common physiologically, but they share a propensity toward under-medication for pain. There is some evidence that the under-treatment of pain in these patient populations is improving, but acute care clinicians should pay particular attention to pain assessment and care in these patients (Thomas, 2013).

Pain in Infants, Children, and Adolescents

Although skepticism towards infant pain characterized much of the twentieth century, it is now well understood that an infant's pain transmission pathways are fully developed by 22 to 24 weeks of gestation. In addition, pain inhibitory pathways are not fully developed in infants, suggesting that infants may feel even more pain than older children (Waxman et al., 2016).

In spite of its frequency, pain in infants, children, and adolescents is often underestimated and under-treated. It has been shown that infants and children who experience pain in early life show long-term changes in terms of pain perception and related behaviors (Srouji et al., 2010).

In infants, improper management of acute pain has been associated with negative short- and long-term consequences. Increased metabolic rate during painful experiences has been associated with increased potential for chronic pain, delayed wound healing, increased risk of infection, and alterations in pain sensitivity. Long-lasting consequences include delays in motor and brain development, as well as deficits in cognition and emotional regulation (Waxman et al., 2016).

In an international survey of pain in adolescents, almost three-quarters of adolescents experienced headache, stomachache, or backache at least monthly. These pain conditions commonly coexist and are more prevalent in girls and older adolescents. While there was some variation in pain prevalence across the 28 countries surveyed, there were no countries where these three pains were uncommon (Swain et al., 2014).

In adolescents, pain is an important predictor of future pain. A Danish twins study found adolescents with persistent low back pain were 3.5 times more likely to have low back pain in adulthood. Co-occurrence of low back pain and headache in adolescence further increases the risk of developing future pain (Swain et al., 2014).

Barriers to pain management in children are numerous and include inaccuracies regarding pathophysiologic mechanisms of pain, fears regarding the use of pharmacologic agents, and deficits in knowledge of pain assessment. Personal values and beliefs also prevent adequate identification and alleviation of pain for all children (Srouji et al., 2010).

Did You Know . . .

Pain management in infants and children is an example of the influence of tradition, personal bias, persistence myths, and resistance to change. There is a substantial gap between evidence and practice, and some authors suggest that pediatric nursing, rooted deeply in tradition and ritual, is particularly resistant to evidence-based practice changes (Susan Lacey, 2008).

Chronic Pain in Children

A significant percentage of children and adolescents (25%–33%) experience chronic pain, with prevalence increasing with age and occurring slightly more commonly in girls than boys. The most commonly reported *locations* of pain in children and adolescents are:

- Head
- Stomach
- Arms
- Legs (Carter & Threlkeld, 2012)

The most common chronic pain *conditions* in children include:

- Migraine
- Recurrent abdominal pain
- General musculoskeletal pain (Carter & Threlkeld, 2012)

Chronic pain can interfere with developmental functioning, increase levels of emotional distress, and disrupt school attendance. Parents are also adversely affected and must negotiate appointments with multiple providers, including both primary and secondary providers. This can lead to missed school for the child, missed work for parents, and depletion of emotional and financial resources (Gorodzinsky et al., 2012).

Families often report a loss of trust in providers when treatment fails to address the high levels of pain their child is experiencing. Parents may experience frustration with inconclusive medical tests, decreasing their hopes that any provider will be able to do anything for their child. With failure to reduce their child's pain, parents may experience reduced expectations for treatment (Gorodzinsky et al., 2012).

A multidisciplinary approach using a biopsychosocial perspective to assess and treat chronic pain in children is effective in reducing the pain experiences and consequences of pain. Families note that providers in multidisciplinary settings displayed an interest in understanding the pain and increasing the comfort of the families during the appointment. Including the family's perspective during treatment is an example of collaborative healthcare, which improves communication and more effectively implements the plan of care (Gorodzinsky et al., 2012).

Pain in Older Adults

Pain is the number one complaint of older adults and 20% report taking a painkiller regularly. Establishing the prevalence of pain in older adults has been difficult, however, because of variations in pain study parameters and definitions (Lillie et al., 2013). Wide variations in prevalence exist in the literature due to differences in the studies, including country and date of study, type of study, population studied, type of pain examined, pain definitions used, sites of pain examined, methods used, and time period of prevalence examined (Age and Ageing, 2013).

Older adults, because of their elevated chronic disease burden, have a high risk of experiencing daily pain, and their pain experience may produce a wide spectrum of unwanted consequences including reduced quality of life, reduced engagement in social and recreational activities, and an increased risk of falls. The presence of pain also reduces the likelihood for older adults meeting physical activity guidelines even when factoring in chronic health conditions. Older adults with chronic pain conditions, such as back pain, are significantly less physically active compared with their counterparts who do not experience back pain (Ho et al., 2016).

Because of these difficulties, pain is a persistent and costly problem in older adults, raising several potential issues associated with pain management. Physiologic and cognitive changes, medical literacy, low income, co-morbid conditions, and adherence affect the success of a pain management program.

Issues with Pain Management in Older Adults

Aging is associated with clinically important changes in pharmacokinetics and pharmacodynamics. Drug absorption is generally unchanged, but studies of drug distribution reveal increased plasma concentration of water-soluble drugs and increased half-life of fat-soluble drugs in older adults. For all opioids, half-life of the active drug and metabolites is increased in elders (Dalacorte et al., 2011).

Decline in the cognitive function is also an area of concern with aging adults, partly because impaired cognitive function can lower medication literacy. This has been associated with a decrease in the likelihood of reading prescription leaflets or other medication information, a reduction in medication reconciliation (agreement between physicians and patients on what medications are currently being used), patients misinterpreting dosage directions on drug labels, and failure to adhere to verbal counseling by physicians (Taylor et al., 2012).

Older adults with low income, those without adequate prescription drug coverage, and those using high-cost medications are likely to stretch out their medication supply by skipping doses or extending the interval between doses. Taking a lower-than-prescribed dose is especially prevalent in patients taking multiple medications, those prone to medication side effects, and people who resist prescribed treatment due to personal or cultural beliefs.

In older adults with multiple co-morbid conditions, polypharmacy is common and increases the risk of adverse drug reactions, nonadherence, and cost. Several drugs used to treat pain, such as opioids, tricyclic antidepressants, gabapentin, and pregabalin, are among those associated with sedation, dizziness, and falls, particularly in frail or vulnerable elders (Dalacorte et al., 2011).

Managing Adherence

About 20% of community-dwelling adults aged 65 and older take ten or more medications daily. This is a critical issue because polypharmacy has been associated with a higher risk of non-adherence to treatment. Adherence is the extent to which a patient's actual drug regimen—dosage, time, and mode of administration—corresponds to the prescriptions made by the doctor. In older people, poor adherence has been reported in 26% to 59% of cases (depending on the population considered and on the definition of adherence used), and is associated with a decline in clinical status, a greater risk of falls, hospitalization, and death, as well as an increase in health expenditures (Bilotta et al., 2011).

The main barriers to adherence in older adults are:

- Forgetting to take the drug
- Limited organizational skills
- Belief that the drug is ineffective or unnecessary
- Cost (Bilotta et al., 2011)

Managing pain medications is a serious problem for caregivers, who may be required to manage multiple medications, may have difficulty keeping prescriptions filled, and may miss giving doses due to their work schedules. A substantial number of community-dwelling older adults do not recall receiving any instructions on taking their medications and rely on family members or caregivers for help.

In regards to pain management, following the prescribed treatment plan is important for the prevention and control of pain. If opioids are part of the plan of care, healthcare providers should discuss any fears related to side effects and risk of addiction. Family members and patients must be encouraged to tell healthcare providers when they are experiencing pain or when the nature or level of pain changes. Although complete pain relief may not be possible, providers can assure patients and family members that they will work to keep pain at a level that allows patients to engage in activities necessary to recover and return home.

Adherence can be improved by providing additional training for caregivers of older adults who are unable to take their medications properly. Providers can support caregivers by routinely reviewing their patients' medications to ensure that drug regimens are adequate, are being followed, and as simple as possible. There is evidence that better adherence can be obtained if patients and caregivers are engaged in decisions about starting, keeping, or changing a medication. With frail older adults, their desire for involvement is essentially fulfilled by good communication, which does not necessarily extend to the decision-making process (Bilotta et al., 2011).

Pain in People with Dementia

Pain is a very common problem in people with dementia. Its prevalence is high; there is good agreement in both large and small studies that about 50% of the people with dementia regularly experience pain. This is not surprising, considering that advanced age is an important risk factor for developing pain (van Kooten et al., 2015).

Pain in people with dementia is associated with neuropsychiatric symptoms, declines in cognitive functioning, as well as declines in the performance of activities of daily living. Next to neuropsychiatric symptoms, pain is the most cited reason for a decrease in quality of life in dementia. Therefore, recognition and adequate treatment of pain in people with dementia should have high priority (van Kooten et al., 2015).

Pain in Nursing Home Residents

Because cognitive impairment is common in many nursing home residents, assessment and management of pain can be a particularly demanding problem. Communication difficulties in people with cognitive decline leads to both the under-diagnosis and under-treatment of pain (Bauer et al., 2016).

There is evidence that people with advanced cognitive decline receive pain treatment, notably opioids, less frequently or in lower insufficient doses as compared to their cognitively fit counterparts. Unable to properly communicate their pain, changes in behavior run the risk of being misinterpreted as behavioral symptoms, provoking inappropriate prescription of antipsychotics which, in turn, have been associated with compromised cognition, falls and fractures, and increased risk of death. There is broad consensus that the failure to accurately identify pain in cognitively impaired individuals is the primary cause of sub-optimal management of pain (Bauer et al., 2016).

In 2009 the American Geriatric Society recommended a comprehensive, disease-specific assessment to establish adequate pain management on an individual level. While individuals with mild to moderate cognitive impairment are often able to report pain either verbally or by use of rating scales, these options are not applicable for those with advanced cognitive impairment when the ability to communicate is severely impaired. As a result, self-reported pain may not always be reliable in people with advanced cognitive impairment and pain should be indirectly rated using a validated observational instrument. Various numerical and visual scales are available for self-reported experience of pain, all of them lacking soundness in persons with cognitive impairment, due to their subjection on memory, abstract thinking, and speech comprehension (Bauer et al., 2016).

Pain at the End of Life

> Pain control for cancer and palliative care is used when pain and symptom control is important for quality of life. An integrated model of care to address the entire patient, body and mind, is the best approach. This may serve as a bridge to hospice care.
>
> Oregon Pain Guidance, 2016

When a person is living with an advanced illness or coming to the end of life, preventing and relieving pain is often a high priority. Effective pain management is important for many conditions and pain is among the most debilitating and feared symptoms faced by patients and their families. Despite this understanding, many severely ill patients spend the last days of their lives in moderate to severe pain.

From a provider perspective, consistent assessment of pain is critical, as is involving the patient and family in establishing goals for palliative pain management. Patients and family members should be educated about dosing, compliance, addiction, tolerance, and side effects. Good pain management at the end of life involves listening to the patient's subjective measure of pain, properly assessing patients with cognitive impairment, and overcoming myths about opioid therapy related to fear of causing addiction or hastening death.

Palliative Care

Palliative care is an approach that aims to improve the quality of life of patients and their families who are facing the problems associated with life-threatening illness. This is accomplished through the prevention and relief of suffering by means of early identification, assessment, and treatment of pain and other issues.

In 2013 the National Consensus Project (NCS) released updated guidelines for palliative care. The guidelines build upon and expand the definition of palliative care developed by the Centers for Medicare and Medicaid Services. The updated guidelines state, "The goal of palliative care is to relieve physical, psychological, emotional, and spiritual suffering and distress of individuals and families (recognizing family as it is defined by each individual)."

The main tenets of the National Consensus Project guidelines are as follows:

- Palliative care centers on the unique goals, strengths, and needs of each patient and family.
- An interdisciplinary team—including, but not limited to, chaplains, nurses, physicians, and social workers with expertise in palliative care—provides services in a collaborative manner.
- The team strives to promote continuity of care across various settings and providers.
- Equitable access to palliative care and the availability of palliative care from the time of diagnosis onward is essential.

The new guidelines are organized according to the following domains: structure and processes of care; physical, psychological, and psychiatric aspects of care; spiritual, religious, existential, and cultural aspects of care; care of patients at the end of life; and ethical and legal aspects of care. *Clinical Practice Guidelines for Quality Palliative Care* (3rd edition, 2013) is available at http://www.nationalconsensusproject.org.

Cancer Pain at the End of Life

Under-treatment and inequitable access to pain treatment have been described among many cancer patients presenting with pain. The reported prevalence of moderate to severe pain in advanced cancer is approximately 64%, with a sharp increase to as high as 80% to 90% at the end of life (Gao et al., 2014).

A study evaluating the characteristics of patients with advanced cancer presenting to a palliative care service found the primary tumor as the chief cause of pain in 68% of patients. Most pain was somatic, and pain was as likely to be continuous as intermittent (NCI, 2016).

The traditional mainstay of pain management since the 1980s has been the World Health Organization's three-step "ladder" approach, involving recommendation of a single strong opioid for moderate to severe cancer pain. Increasingly over the treatment course, patients may be switched (sometimes called *rotated*) from one opioid to another because of side effects or concerns regarding effectiveness of the initial opioid. In addition, patients may be prescribed combinations of opioids, usually when they are receiving long-acting and short-acting compounds or compounds by different routes, especially if one compound is not available in the required formulation or route (Gao et al., 2014).

Musculoskeletal Pain at the End of Life

Although palliative care has, in the past, focused on cancer, it has recently expanded to include other conditions, including musculoskeletal pain at the end of life. Population-based studies indicate that musculoskeletal pain is such a common and significant issue at the end of life that musculoskeletal disease may have as much, if not more, effect on whether a person dies in pain than the condition that is the cause of death (Lillie et al., 2013).

Gender Differences in Pain Sensitivity

Evidence suggests men and women experience and report pain differently (Horn et al., 2014). Specifically, women have been shown to have a lower pain threshold and pain tolerance and stronger responses to analgesics than do men. These differences are present in community-dwelling and clinical samples. It is often difficult to discern whether well-documented differences in pain reports among women and men are biology based (sex) or shaped by social and cultural expectations (gender) (Ho et al., 2016).

Evidence suggests that differing biologic and psychosocial factors may account for gender differences in pain sensitivity. It is well-known that psychosocial factors can influence the perception and evaluation of pain. One commonly studied psychosocial factor is pain-related fear, which includes fear of the sensation of pain, fear of movement or re-injury, and fear of physical activities that are assumed to cause pain. Pain-related fear may contribute to the shift from acute low back pain to chronic low back pain, and numerous studies have demonstrated the association of pain-related fear with disability in patients with chronic and acute low back pain, hip and knee osteoarthritis, and foot and ankle dysfunction (Horn et al., 2014).

The differences in psychosocial factors (such as pain-related fear) may contribute to differences in the pain reports between men and women. Several lines of research using experimentally induced pain have begun to shed light on these sex differences. For example, an experimental pain study using electrical stimuli found the increased pain experienced by women during a movement task was accounted for by higher reports of fear among women compared to men. In addition to pain-related fear, Robinson and colleagues found women to be more willing to report pain and consider themselves to be more sensitive to pain compared to males. Conversely, some males believe that they have higher pain endurance than women and as compared to the typical male (Horn et al., 2014).

Clinically, gender differences are relevant because a greater percentage of chronic pain sufferers are women. Women also generally report more areas of bodily pain and more pain-related disability compared to men. Given that pain is such a prevalent and debilitating condition with serious health and economic consequences, the Institute of Medicine has stressed the need to improve healthcare delivery of pain management, including individualized treatment approaches (Horn et al., 2014).

Assessing and Documenting Pain

Assessment and documentation of pain, systematically and consistently, guides the identification of pain as well as the effectiveness of treatment. Since the goal of therapy is to alleviate pain and improve function, assessment should focus on pain and functional status.

The most critical aspect of pain assessment is that it be done on a regular basis using a standard format. Pain should be re-assessed after each intervention to evaluate the effect and determine whether interventions should be modified. The time frame for re-assessment should be directed by the needs of the patient and the hospital or unit policies and procedures.

A self-report by the patient has traditionally been the mainstay of pain assessment. Family caregivers can be used as proxies for patient reports, especially in situations in which communication barriers exist, such as cognitive impairment or language barriers. It is important to note that family members who act as proxies typically, as a group, report higher levels of pain than patient self-reports, although there is individual variation.

Both physiologic and behavioral responses can indicate the presence of pain and should be noted as part of a comprehensive assessment, particularly following surgery. Physiologic responses include tachycardia, increased respiratory rate, and hypertension. Behavioral responses include splinting, grimacing, moaning or grunting, distorted posture, and reluctance to move. A lack of physiologic responses or an absence of behaviors indicating pain may not mean there is an absence of pain.

Good documentation allows communication among clinicians about the current status of the patient's pain and responses to the plan of care. The Joint Commission requires that pain be documented as a means of prompting clinicians to re-assess and document pain whenever vital signs are obtained. Documentation is also used as a means of monitoring the quality of pain management within the institution.

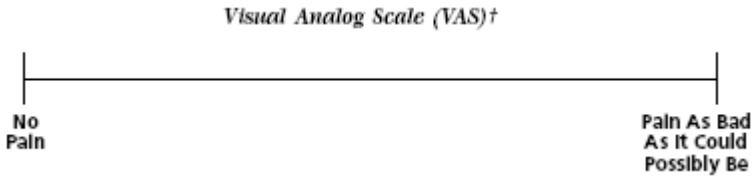
Pain Assessment Tools

Selecting a pain assessment tool should be, when possible, a collaborative decision between patient and provider to ensure that the patient is familiar with the tool. If the clinician selects the tool, consideration should be given to the patient's age; physical, emotional, and cognitive status; and personal preferences. Patients who are alert but unable to talk may be able to point to a number or a face to report their pain. The pain tool selected should be used on a regular basis to assess pain and the effect of interventions; it should not, however, be used as the sole measure of pain (AHRQ, 2008).

Pain Scales

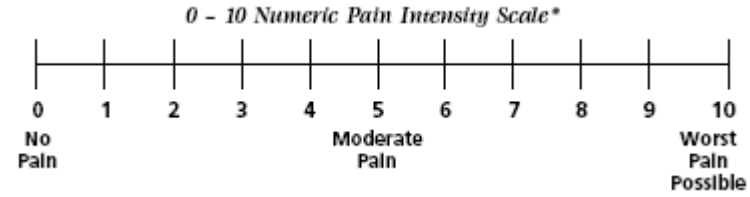
Many pain intensity measures have been developed and validated. Most measure only one aspect of pain (ie, pain intensity) and most use a numeric rating. Some tools measure both pain intensity and pain unpleasantness and use a sliding scale that allows the patient to identify small differences in intensity. The following illustrations show some commonly used pain scales.

Visual Analog Scale



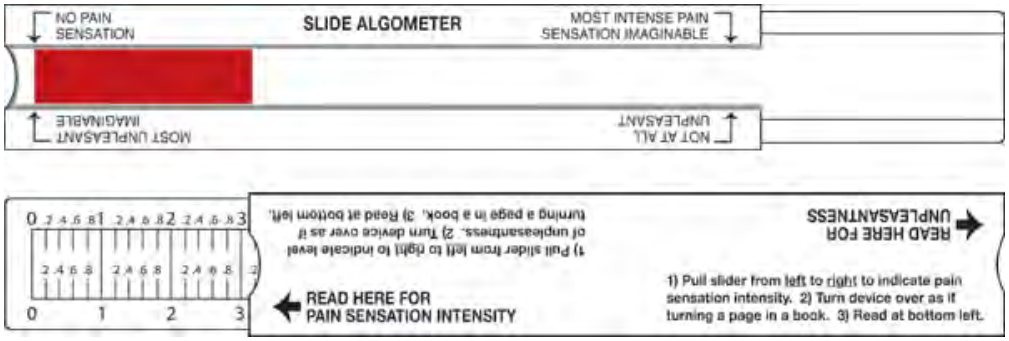
The Visual Analog Scale. The left endpoint corresponds to "no pain" and the right endpoint (100) is defined as "pain as intense as it can be."
†A 10-cm baseline is recommended for VAS scales.
Source: Adapted from Acute Pain Management Guideline Panel, 1992 (AHCPR, 1994). Public domain.

Numeric Rating Scale



The Numeric Rating Scale. Indicated for adults and children (>9 years old) in all patient care settings in which patients are able to use numbers to rate the intensity of their pain. The NRS consists of a straight horizontal line numbered at equal intervals from 0 to 10 with anchor words of "no pain," "moderate pain," and "worst pain." Source: Adapted from Acute Pain Management Guideline Panel, 1992 (AHCPR, 1994). Public domain.

The Pain Scale for Professionals



The Pain Scale for Professionals. The patient slides the middle part of the device to the right and left and views the amount of red as a measure of pain sensation. The arrow at the left means "no pain sensation" and the arrow at the right indicates the "most intense pain sensation imaginable." The sliding part of the device is moved on a different axis for the unpleasantness scale. The arrow at the left means "not at all unpleasant" and the arrow at the right represents pain that is the "most unpleasant imaginable." Source: The Risk Communication Institute. Used with permission.

Simpler tools such as the verbal rating scale (VRS) classify pain as mild, moderate, or severe. Some studies indicate that older adults prefer to characterize their pain using the VRS. The description can be translated to a number for charting (see following table) and works particularly well if everyone on the unit uses the same scale.

Verbal Rating Scale (VRS)	
Description	Points Assigned
No pain	0
Mild pain	2
Moderate	5
Severe	10

For patients with limited cognitive ability, scales with drawings or pictures, such as the Wong-Baker FACES™ scale, are useful. Patients with advanced dementia may require behavioral observation to determine the presence of pain.

Wong-Baker FACES™ Pain Rating Scale

The Wong-Baker FACES scale is especially useful for those who cannot read English and for pediatric patients. Source: Copyright 1983, Wong-Baker FACES™ Foundation, www.WongBakerFACES.org. Used with permission.

Pain Questionnaires

Pain questionnaires typically contain verbal descriptors that help patients distinguish different kinds of pain. The McGill Pain Questionnaire, developed by Melzack in 1971, asks patients to describe subjective psychological feelings of pain. Pain descriptors such as pulsing, shooting, stabbing, burning, grueling, radiating, and agonizing (and more than seventy other descriptors) are grouped together to convey a patient's pain response. The McGill Pain Questionnaire combines a list of questions about the nature and frequency of pain with a body-map diagram to pinpoint its location. The questionnaire uses word lists separated into four classes (sensory, affective, evaluative, and miscellaneous) to assess the total pain experience. After patients are finished rating their pain words, the administrator allocates a numerical score, called the "Pain Rating Index." Scores vary from 0 to 78, with the higher score indicating greater pain (Srouji et al., 2010).

The Brief Pain Inventory (BPI), developed by the World Health Organization, also uses the questionnaire format to measure pain. The ability to resume activity, maintain a positive affect or mood, and sleep are relevant functions for patients. The BPI uses a numeric rating scale to assess difficulties with walking, general activity, mood, and sleep.

Assessing Pain in Children

Despite decades of research and the availability of effective analgesic approaches, many children continue to experience moderate to severe pain, especially after hospitalization. Greater research efforts are needed to identify the factors that facilitate effective pain management. Overall, the factors affecting children's pain management are influenced by cooperation (nurses, doctors, parents, and children), child (behavior, diagnosis, and age), organization (lack of routine instructions for pain relief, lack of time, and lack of pain clinics), and nurses (experience, knowledge, and attitude) (Aziznejadroshan et al, 2016).

Pain evaluation in small children can be a difficult task, since it is a multidimensional experience that possesses sensory and affective components often hard to discriminate by the existing scores. Previous experiences, fear, anxiety, and discomfort may alter pain perception; thus, poor agreement between instruments and raters is often the norm. It has been suggested that, in children younger than 7 years of age and in cognitively impaired children, evaluation of pain intensity through self-report instruments can be inaccurate due to poor understanding of the instrument and poor capacity to translate the painful experience into verbal language; therefore, complementary observational pain measurements should be used to assess pain intensity (Kolosovas-Machuca et al., 2016).

Three methods are commonly used to measure a child's pain intensity:

1. **Self-reporting**: what a child is saying, using age-appropriate numeric scales, pictorial scales, or verbal scales.
2. **Behavioral measures**: what a child is doing using motor response, behavioral responses, facial expression, crying, sleep patterns, decreased activity or eating, body postures, and movements. These are more frequently used with neonates, infants, and younger children where communication is difficult.
3. **Physiologic measures**: how the body is reacting using changes in heartrate, blood pressure, oxygen saturation, palmar sweating, respiration, and sometimes neuroendocrine responses. They are generally used in combination with behavioral and self-report measures, as they are usually valid for short-duration acute pain and differ with the general health and maturational age of the infant or child. In addition, similar physiologic responses also occur during stress,

which results in difficulty distinguishing stress versus pain responses (Srouji et al., 2010).

Children's capability to describe pain increases with age and experience, and changes throughout their developmental stages. Although observed reports of pain and distress provide helpful information, particularly for younger children, they are reliant on the individuals completing the report (Srouji et al., 2010).

Assessing Pain in Infants

The major challenge with infant pain assessment is that neonates cannot self-report their subjective experience of pain. Moreover, there is a lack of agreement on the best proxy modality of assessing infant pain, whether it is cortical, biochemical, physiologic, or behavioral. Recent work has suggested discordance not only among modalities, but also within an assessment modality. For example, the validity and reliability of physiologic measures of infant pain are presently disputed because these measures are influenced by additional variables that have not been properly taken into account (eg, infection and respiratory rate) (Waxman et al., 2016).

Cardio-physiologic indices of pain, such as heart rate and heart rate variability, are pervasive in the hospital setting. Recently, a group of Canadian researchers looked at the development of cardiovascular responses to acutely painful medical procedures over the first year of life in both preterm and term-born infants. Researchers noted the following:

- Extremely pre-term infants (born at less than 28 weeks gestational age) displayed a blunted heart rate response to acute pain in the first week of life.
- In infants born between 28 and less than 32 weeks gestational age, mean heart rate was found to significantly increase following an acutely painful procedure from birth to four months of age.
- In infants born at 32 to less than 37 weeks gestational age, mean heart rate was found to increase in response to acute pain during the first postnatal week of life; however, the magnitude of responses was variable.
- During the first four postnatal months of life, full-term infants displayed an increase in mean heart rate in response to acute pain; however, the magnitude of responses was variable (Waxman et al., 2016).

The most common pain measures used for infants are behavioral. These measures include crying, facial expressions, body posture, and movements. The quality of these behaviors depends on the infant's gestational age and maturity. Preterm or acutely ill infants, for example, do not elicit similar responses to pain due to illness and lack of energy. Interpretation of crying in infants is especially difficult, as it may indicate general distress rather than pain. Cry characteristics are also not good indicators in preterm or acutely ill infants, as it is difficult for them to produce a robust cry (Srouji et al., 2010).

Assessing Pain in Toddlers

In toddlers, verbal skills remain limited and quite inconsistent. Pain-related behaviors are still the main indicator for assessments in this age group. Nonverbal behaviors such as facial expression, limb movement, grasping, holding, and crying are considered more reliable and objective measures of pain than self-reports. Most children of this age are capable of voluntarily producing displays of distress, with older children displaying fewer pain behaviors (ie, they cry, moan, and groan less often) (Srouji et al., 2010).

Most 2-year-old children can report the incidence and location of pain, but do not have the adequate cognitive skills to describe its severity. Three-year-old children, however, can start to differentiate the severity of pain, and are able to use a three-level pain intensity scale with simple terms like "no pain," "little pain" or "a lot." Children in this age group are usually able to participate in simple dialogue and state whether they feel pain and "how bad it is" (Srouji et al., 2010).

Assessing Pain in Preschoolers

By the age of four years, most children are usually able to use 4- to 5-item pain discrimination scales. Their ability to recognize the influence of pain appears around the age of five years, when they are able to rate the intensity of pain. Facial expression scales are most commonly used with this age group to obtain self-reports of pain. These scales require children to point to the face that represents how they feel or the amount of pain they are experiencing (Srouji et al., 2010).

Assessing Pain in School-Aged Children

Healthcare professionals depend more comfortably on self-reports from school-aged children. Although children at this age understand pain, their use of language to report it is different from adults. At roughly 7 to 8 years of age children begin to understand the quality of pain. Self-report, visual analog, and numerical scales are effective in this age group. A few pain questionnaires have also proven effective for this age (eg, pediatric pain questionnaire, adolescent pediatric pain tool) (Srouji et al., 2010).

Assessing Pain in Adolescents

Adolescents tend to minimize or deny pain, especially in front of friends, so it is important to provide them with privacy and choice. For example, they may or may not choose to have parents present. They expect developmentally appropriate information about procedures and accompanying sensations. Some adolescents regress in behavior under stress. They also need to feel able to accept or refuse strategies and medications to make procedures more tolerable. To assess pain, specifically chronic pain, the adolescent pediatric pain tool (APPT) or the McGill pain questionnaire are helpful (Srouji et al., 2010).

Assessing Pain in Cognitively Intact Adults

For the cognitively intact adult, assessment of pain intensity in the clinical setting is most often done by using the 0 to 10 numeric rating scale or the 0 to 5 Wong-Baker Faces scale, or the VRS. Once patients know how to use a pain intensity scale, they should establish "comfort-function" goals. With the clinician's input, patients can determine the pain intensity at which they are easily able to perform necessary activities with the fewest side effects.

The American Geriatrics Society (AGS) and the British Geriatrics Society have issued guidelines for the management of pain in older adults, which begins with an accurate assessment and includes the impact of pain on the patient's daily activities. When analgesic treatment and pain-modulating drugs are used, co-morbidities and other risk factors must be carefully considered. The least invasive method of administration should be used—in most cases the oral route is preferred (Age and Ageing, 2013).

Assessing Pain in Cognitively Impaired Adults

The assessment of pain in patients with cognitive impairment is a significant challenge. Cognitively impaired patients tend to voice fewer pain complaints but may become agitated or manifest unusual or sudden changes in behavior when they are in pain. Caregivers may have difficulty knowing when these patients are in pain and when they are experiencing pain relief. This makes the patient vulnerable to both under-treatment and over-treatment.

In the absence of accurate self-report it has been necessary to develop observational tools to be used in both research and practice, based on the interpretation of behavioral cues to assess the presence of pain. This approach has resulted in a proliferation of pain assessment instruments developed to identify behavioral indicators of pain in people with dementia and other cognitive impairment (Lichtner et al., 2014).

The most structured observational tools are based on guidance published by the American Geriatrics Society, which describe six domains for pain assessment in older adults:

1. Facial expression
2. Negative vocalization
3. Body language
4. Changes in activity patterns
5. Changes in interpersonal interactions
6. Mental status changes (Lichtner et al., 2014)

In people with dementia, the interpretation of these behaviors can be complex due to overlap with other common behavioral symptoms or cognitive deficits such as boredom, hunger, anxiety, depression, or disorientation. This increases the complexity of accurately identifying the presence of pain in patients with dementia and raises questions about the validity of existing instruments (Lichtner et al., 2014).

As a result, there is no clear guidance for clinicians and care staff on the effective assessment of pain, nor how this should inform treatment and care decision-making. A large number of systematic reviews have been published, which analyze the relative value and strength of evidence of existing pain tools. There is a need for guidance on the best evidence available and for an overall comprehensive synthesis (Lichtner et al., 2014).

In a systematic review of reliability, validity, feasibility and clinical utility of 28 pain assessment tools used with older adults with dementia, no one tool appeared to be more reliable and valid than the others (Lichtner et al., 2014). Patient self-report remains the gold standard for pain assessment but in non-verbal older adults the next best option, from a user-centered perspective, becomes the assessment of a person who is most familiar with the patient in their everyday life in a hospital or other care setting; this is sometimes referred to as a "silver standard" (Lichtner et al., 2014).

A thorough review of pain assessment tools for nonverbal older adults by Herr, Bursch, and Black of The University of Iowa is available here.

Keeping these challenges in mind, three commonly used behavioral assessment tools are examples of tools that are used in assessing pain and evaluating interventions in cognitively impaired adults.

Behavioral Pain Scale

The Behavioral Pain Scale (BPS) was developed for use with critically ill patients in the ICU. It evaluates and scores three categories of behavior on a 1 to 4 scale:

1. Facial expression: 1 for relaxed to 4 for grimacing
2. Upper-limb movement: 1 for no movement to 4 for permanently retracted

3. Ventilator compliance: 1 for tolerating ventilator to 4 for unable to control ventilation

A cumulative score above 3 may indicate pain is present; the score can be used to evaluate intervention, but cannot be interpreted to mean pain intensity. The patient must be able to respond in all categories of behavior—for example, the BPS should not be used in a patient who is receiving a neuromuscular blocking agent.

Pain Assessment Checklist

Pain behavior checklists differ from pain behavior scales in that they do not evaluate the degree of an observed behavior and do not require a patient to demonstrate all of the behaviors specified, although the patient must be responsive enough to demonstrate some of the behaviors. These checklists are useful in identifying a patient's "pain signature"—the pain behaviors unique to that individual.

The *Pain Assessment Checklist for Seniors with Limited Ability to Communicate* (PACSLAC) is a caregiver-administered tool that evaluates sixty behaviors divided into four subscales:

1. Facial expressions (13 items)
2. Activity/body movements (20 items)
3. Social/personality/mood (12 items)
4. Physiological indicators/eating and sleeping changes/vocal behaviors (15 items)

A checkmark is made next to any behavior the patient exhibits. The total number of behaviors may be scored but cannot be equated with a pain intensity score. It is unknown if a high score represents more pain than a low score. In other words, a patient who scores 10 out of 60 behaviors does not necessarily have less pain than a patient who scores 20. However, in an individual patient, a change in the total pain score may suggest more or less pain.

Advanced Dementia Scale (PAINAD)

The *Pain Assessment in Advanced Dementia Scale* (PAINAD) was developed to provide a clinically relevant and easy-to-use observational pain assessment tool for individuals with advanced dementia. The aim of the tool developers was to "develop a tool for measuring pain in non-communicative individuals that would be simple to administer and had a score from 0 to 10" (Herr, et al., 2008). This tool is used when severe dementia is present. This tool involves the assessment of breathing, negative vocalization, facial expression, body language, and consolability.

Pain Assessment in Advanced Dementia (PAINAD)				
	0	1	2	Score*
Breathing	Normal	▪ Occasional labored breathing ▪ Short period of hyperventilation	▪ Noisy labored breathing ▪ Long period of hyperventilation ▪ Cheyne-Stokes respirations	
Negative vocalization	None	▪ Occasional moan/groan ▪ Low level speech with a negative or disapproving quality	▪ Repeated, troubled calling out ▪ Loud moaning or groaning ▪ Crying	
Facial expression	Smiling or inexpressive	▪ Sad ▪ Frightened ▪ Frown	Facial grimacing	
Body language	Relaxed	▪ Tense ▪ Distressed ▪ Pacing ▪ Fidgeting	▪ Rigid ▪ Fists clenched ▪ Knees pulled up ▪ Pulling/pushing away ▪ Striking out	
Consolability	No need to console	Distracted or reassured by voice or touch	Unable to console, distract, or reassure	
PAINAD Scoring: 1-3 = Mild; 4-6 = Moderate; 7-10 = Severe * Some institutions have developed policies in which a PAINAD score of four or greater must be addressed in the nursing care plan. Public domain.				Total:

Clinical Assessment of Cancer Pain

Pain assessment in patients with pain secondary to cancer begins with a thorough discussion of the patient's goals and expectations for pain management, including balancing pain levels and other patient goals, such as mental alertness. Comprehensive pain assessment also includes pain history, pain intensity, quality of pain, and location of pain. For each pain location, the pattern of pain radiation should be assessed (NCI, 2016).

A review of the patient's current pain management plan and how he or she has responded to treatment is important. This includes how well the current treatment plan addresses breakthrough or episodic pain. A full assessment also reviews previously attempted pain therapies and reasons for discontinuation; other associated symptoms such as sleep difficulties, fatigue, depression, and anxiety; functional impairment; and any relevant laboratory data and diagnostic imaging. A focused physical examination includes clinical observation of pain behaviors, pain location, and functional limitations (NCI, 2016).

Psychosocial and existential factors that can affect pain must also be assessed and treated. Depression and anxiety in particular can strongly influence the pain experience. Across many different types of pain, research has shown the importance of considering a patient's sense of self-efficacy over their pain: low self-efficacy, or focus on solely pharmacologic solutions, is likely to increase the use of pain medication (NCI, 2016).

Patients who catastrophize pain (eg, patient reports pain higher than 10 on a 10-point scale) are more likely to require higher doses of pain medication than are patients who do not catastrophize. Catastrophizing is strongly associated with low self-efficacy and reliance on chemical coping strategies. Assessing the impact of pain on the individual's life and associated factors that exacerbate or relieve pain can reveal how psychosocial issues are affecting the patient's pain levels (NCI, 2016).

A number of factors can help a provider predict response to pain treatment in a cancer patient. Specifically, a high baseline pain intensity, neuropathic pain, and incident pain are often more difficult to manage. Certain patient characteristics such as a personal or family history of illicit drug use, alcoholism, smoking, somatization, mental health issues such as depression or anxiety, and cognitive dysfunction are associated with higher pain expression, higher opioid doses, and longer time to achieve pain control (NCI, 2016).

Several risk-assessment tools have been developed to assist clinicians, such as the Edmonton Classification System for Cancer Pain (ECS-CP) and the Cancer Pain Prognostic Scale (CPPS) (NCI, 2016).

The ECS-CP considers (1) neuropathic pain, (2) incident pain, (3) psychological distress, (4) addiction, and (5) cognitive impairment. The presence of any of these factors indicates that pain may be more difficult to control. The ECS-CP has been validated in various cancer pain settings. The CPPS (NCI, 2016) considers four variables in a formula to determine the risk score:

1. Worst pain severity (Brief Pain Inventory)
2. Functional Assessment of Cancer Therapy-General (FACT-G) emotional well-being
3. Initial morphine equivalent daily dose (≤60 mg/day; >60 mg/day)
4. Mixed pain syndrome

CPPS scores range from 0 to 17, with a higher score indicating a higher possibility of pain relief (NCI, 2016).

Psychosocial Aspects of Pain Management

Pain perception—the conscious recognition and awareness of a painful stimulus—is modulated and modified by many psychological and personality-related factors. These can include previous pain experiences, emotions and cognition, somatization and catastrophizing, the presence of acute and chronic stressful life events, fatigue, anxiety, fear, boredom, and anticipation of more pain. Pain perception is also influenced by socioeconomic factors such as social support, acceptance, incentives, education, occupation, and quality of life. In addition, pain perception differs among genders and ethnicities, and varies with age (Belfer, 2013).

Chronic pain in particular carries with it personal and economic costs and psychological distress, and psychological factors play a significant role in chronic pain. Pre-existing depression, anxiety, and stress may predispose some individuals to progress to a chronic pain condition, while chronic pain in turn leads to anxiety and depression, creating a vicious cycle (Rice et al., 2016).

Because of the cognitive, emotional, and psychological effects that may be associated with pain, a biopsychosocial concept of pain has emerged over the past two to three decades, along with considerable evidence supporting management approaches that address the psychosocial aspects of a patient with chronic pain (Sessle, 2012).

Within the biopsychosocial model, research on beliefs shows that negative pain beliefs have a detrimental impact on patients' overall health, self-efficacy, and function. Thoughts can *positively* influence beliefs about the pain experience if there is control in managing the pain, confidence that potential harm and possible disability are not threatened, and there are expectations of recovery. Thoughts can *negatively* influence beliefs about the pain experience if control is lacking and recovery is not possible. The consequence can be emotional distress and catastrophizing, as well as excessively negative and pessimistic beliefs and thoughts about pain (Pons et al., 2012).

Beliefs that contribute to poor compliance, motivation, and misunderstanding about pain include catastrophizing, limited control over the pain, and emotional distress. Catastrophizing is associated with persistent pain and it is a predictor of poor outcomes in pain interventions. Although catastrophizing and emotional distress have common characteristics, it is difficult to separate their overall effect (Pons et al., 2012).

Chronic Pain and Depression

It has been estimated that 35% of the chronic pain population has comorbid (associated) depression (Bromley Milton et al., 2013). Pain can be a symptom, a cause, or a consequence of depression. Studies investigating the association between pain and depression suggest that the stress of living with chronic pain can *cause* depression, but there is also evidence that pain develops *secondary to* depression, manifesting as increased pain sensitivity, and that high depression scores are associated with greater risk of developing chronic pain (Schneider et al., 2011). The association between depression and pain appears to increase with the severity of each condition (Bromley Milton et al., 2013).

Failure to treat pain in depressed patients may adversely impact depression treatment outcomes. Recognizing and optimizing the management of pain may be important in enhancing depression remission rates. The presence of severe pain at the start of depression treatment has been seen in those who failed to respond to antidepressants, and a lower overall pain severity score at the outset was associated with higher odds of achieving remission (Schneider et al., 2011).

In a systematic review of studies looking at the psychological factors associated with knee pain, researchers found strong evidence for a positive association between depression and knee pain in adults. The emerging evidence on pathogenesis of depression suggests that it is associated with dysfunction in the inflammatory cytokine production as a response to stressors, dysregulation of the autonomic nervous system, and destabilizing effect on hypothalamic-pituitary-adrenal axis. Each of these mechanisms also contributes to the development of chronic pain syndrome. These findings indicate that physiologic similarities exist between depression and chronic pain (Phyomaung et al., 2014).

Another explanation for the association between depression and knee pain may be reduced physical activity, which could be due to fear of pain or as a consequence of depression. The muscle wasting and reduced joint stability resulting from low activity may have a negative effect on function and the disease outcomes of osteoarthritis (Phyomaung et al., 2014).

Extensive data support the value of tricyclic antidepressants for the alleviation of pain in chronic pain patients, and the newer serotonin and noradrenaline reuptake inhibitors (SNRIs)—duloxetine, venlafaxine, and milnacipran—have shown to be usseful in the treatment of pain and depression. Duloxetine is a SNRI with proven efficacy for painful physical symptoms of depression. Analyses from short-term trials demonstrated that a greater reduction in pain was associated with a higher probability of remission. Furthermore, the efficacy of duloxetine has been proven for the treatment of painful diabetic neuropathy (Schneider et al., 2011).

Chronic Pain and Anxiety

Anxiety is common in chronic pain patients and anxious patients may interpret pain as being more intense than non-anxious patients. The presence of chronic pain makes it difficult to recognize and treat potential psychiatric disorders, and this delay may worsen the prognosis of psychiatric disorders (Mangerud et al., 2013).

In a cross-sectional study of Norwegian adolescents with psychiatric disorders, two-thirds reported chronic pain. Adolescents with mood or anxiety disorders had a significantly higher frequency of chronic pain and pain-related disability than those with hyperkinetic disorders. Adolescents with hyperkinetic and mood or anxiety disorders had a two- to three-fold increased risk of pain-related disability compared to those with hyperkinetic disorders alone (Mangerud et al., 2013).

Research has shown a link between low back pain and psychological factors, particularly depression and anxiety. In relation to low back pain, depression is often described as being atypical and takes the form of a so-called masked depression, often following a traumatic event. Individual psychological intervention is recommended as the primary treatment, with medical treatment secondary (Ellegaard & Peterson, 2012).

Stress

Stress is the physiologic reaction that occurs in animals and people due to threatened or actual damage to the organism, including psychological challenges at the limits of the individual's coping capacity. Stress-inducing factors are collectively called **stressors** (Ellegaard & Peterson, 2012).

A study showed that in psychotherapeutic treatment of patients with chronic nonspecific low back pain and moderate depression, diverse psychological stressors were identified, relating to both the past and present. The study found that when pain, stress, and depression become overwhelming and there are few resources available, stress seems to become prominent. Stressful situations can lower a person's ability to cope with back pain (Ellegaard & Peterson, 2012).

Non-Opioid and Adjuvant Analgesics

A wide variety of non-opioid analgesics are available for the treatment and management of pain. Each has a unique profile and differs in onset, peak action, duration of action, and side effects. A multimodal approach (balanced analgesia), which includes non-opioids, adjuvant medications, and opioids, is recommended.

Non-Opioid Analgesic Agents

The appropriate use of analgesics—the right drug at the right interval—provides good pain relief for the majority of patients. There are dozens, even scores, of drugs that can be used depending on the clinical circumstances. For patients needing "broadly effective analgesia," non-opioid approaches may offer overall safety and efficacy as compared to opioid analgesics. Rather than immediately moving to opioids, a clinician should consider whether non-opioid approaches may be appropriate (Thomas, 2013).

Nonsteroidal Anti-Inflammatories

> A multitude of reports have delineated the risks of using nonsteroidal anti-inflammatory drugs but have not been totally congruent. Meta-analyses of randomized controlled trials sometimes concur regarding gastrointestinal risk and cardiovascular risk but rarely report a balance of these risks for any one drug. Benefits measured in these studies are usually not reported.
>
> Observational data sets, supposedly reflective of "real world" patients, do not always agree with the randomized controlled trial reports. Clinicians need assessments measuring the balance of harms and benefits so that better decisions based on their patients' unique risk factors can be reached.
>
> Lee S. Simon, 2015
> *Non-steroidal Anti-inflammatory Drugs and Their Benefits and Harms*

Nonsteroidal anti-inflammatory drugs (NSAIDs) are medications with anti-inflammatory, analgesic, and antipyretic properties; they are among the most widely used drugs in the world. They are used to reduce short- and long-term pain, decrease stiffness, and improve function in patients with acute and chronic conditions such as arthritis, headache, dysmenorrhea, and post operative pain. Aspirin, the first NSAID, was developed in 1897.

NSAIDs (non-selective NSAIDs, cyclooxygenase 2 inhibitors [coxibs], and semi-selective NSAIDs), are most commonly prescribed to relieve pain and inflammation. They work by inhibiting cyclooxygenase (COX) enzymes from making prostaglandins, some of which cause pain and inflammation. Because certain prostaglandins protect the stomach lining from the stomach acid that helps to digest food, NSAIDs can cause gastrointestinal (GI) complications. A history of prior gastrointestinal symptoms or bleeding, the presence of other risk factors such as advancing age, higher doses of NSAID, duration of NSAID use, and the frailty of the patient all increase the risk for upper GI damage and consequent bleeding (Simon, 2013).

NSAIDs can be classified according to their mechanism of action:

- **Non-selective NSAIDs** like ibuprofen and naproxen inhibit both COX-1 and COX-2 enzymes.
- **Coxibs** such as celecoxib (Celebrex) and rofecoxib* are designed to selectively inhibit COX-2 enzymes.

*Rofecoxib (Vioxx) has been withdrawn from the market.

Semi-selective NSAIDs (indomethacin [Indocin], meloxicam [Mobic], and diclofenac [Voltaren]) has a higher affinity for COX-2 but tend to inhibit the COX-1 pathway also (Ghosh et al., 2015). COX selectivity is one of the determining factors to consider when giving NSAIDs to a patient.

A meta-analysis of more than 700 studies involving the use of certain NSAIDs for pain was conducted by the The Coxib and Traditional NSAID Trialists' (CNT) Collaboration. Researchers looked at the risk of major vascular events, major cardiac events, and upper GI complications from high-dose, long-term use of certain NSAIDs. Concerns about the possible heart risks of NSAIDs, many of which have been on the market for several decades, arose after randomized trials showed that coxibs increased the risk of heart attacks (MRC, 2013).

Diclofenac (Voltaren) is the agent currently in use that is most associated with an increased risk of cardiovascular events: a 40% to 60% higher relative risk of serious cardiovascular events, compared to non-use of NSAIDs, has been reported. This is a rate equivalent to or possibly higher than that of rofecoxib (Vioxx), now withdrawn from the market (McGettigan & Henry, 2013).

In contrast, another traditional NSAID, naproxen, has been found to be relatively benign, with a cardiovascular risk that was observed to be neutral or much lower than that of diclofenac (McGettigan & Henry, 2013). The CNT Collaboration report indicated that naproxen might be safer for patients with cardiovascular risk but that it is one of the worst NSAIDs in terms of risk for a major GI complication (Simon, 2015).

Regardless of their mechanism of action, prolonged exposure to any class of NSAIDs has been shown to have potential adverse cardiovascular effects in patients with or without pre-existing cardiovascular conditions, depending on the duration and dosage of these drugs. Patients with pre-existing cardiovascular conditions such as coronary artery disease, hypertension, and history of stroke are at the greatest risk of cardiovascular events after taking NSAIDs. Patients who have recently had cardiovascular bypass surgery are advised not to take NSAIDs due to a high risk of heart attacks (Ghosh et al., 2015).

NSAID guidelines have been established to increase physician awareness of the complications associated with NSAID use; however, some physicians either do not recognize or do not adhere to such guidelines (Taylor et al., 2012). A recent survey of physicians identified six major barriers that affected their use of established NSAID guidelines:

1. Lack of familiarity with the guidelines
2. Perceived limited validity of the guidelines

3. Limited applicability of the guidelines to specific patient populations
4. Clinical inertia
5. Anecdotal experiences
6. Clinical heuristics (experience-based problem solving, learning by trial and error rather that following a pre-established formula) (Taylor et al., 2012)

Acetaminophen

Acetaminophen, the active ingredient in Tylenol, is also known as paracetamol and N-acetyl-p-aminophenol (APAP), and has been marketed in the United States as an OTC antipyretic and analgesic agent since 1953. It is widely available in a variety of strengths and formulations for children and adults as a single-ingredient product.

Although acetaminophen has been in clinical use for decades, its mechanism of action is not fully understood. It is thought to inhibit cyclooxygenases both centrally and peripherally. Researchers have suggested that the inhibition of cyclooxygenase in the brain is responsible for the antipyretic effect of acetaminophen, suggesting a central mechanism of action. Some have suggested classifying acetaminophen as an *atypical* NSAID (Chavez et al., 2015).

At the same time, research has been conducted showing that acetaminophen is a prodrug,* and indicating that the analgesic effect of acetaminophen arises from the indirect activation of cannabinoid CB_1 receptors. Acetaminophen also has an effect on the descending serotonergic pathway, and may interact with opioidergic** systems or nitric oxide pathways—and also may act as a selective COX-2 inhibitor in humans (Chavez et al., 2015).

*Prodrug. A prodrug is a medication or compound that, after administration, is metabolized into a pharmacologically active drug (Wikipedia, 2016).

**Opioidergic. An opioidergic agent is a chemical that functions to directly modulate the opioid neuropeptide systems (i.e., endorphin, enkephalin, dynorphin, nociceptin) in the body or brain.

Acetaminophen is used in combination with many prescription opioid drugs (Vicodin, Percocet) to give more pain relief while minimizing the dose of the addictive narcotic component. It is generally considered safe at recommended doses, but if more is taken—even just a little more—it can cause serious and even fatal liver damage. In fact, acetaminophen poisoning is a leading cause of liver failure in the United States (Hodgman & Garrard, 2012).

In the United States, acetaminophen is available as 325 mg and 500 mg preparations and as a 650 mg extended-release medication intended for arthritis treatment. It is available in drops, capsules, and pills, as well as various children's dissolvable, chewable, and liquid formulations. To reduce the risk of accidental overdose, in 2014 the FDA announced that medications containing a combination of acetaminophen and an opioid can no longer contain more than 325 mg of acetaminophen per tablet or capsule.

Video (1:53) Prescription Acetaminophen/Opioid Combinations: Making Pain Medicines Safer (2014)

https://www.youtube.com/watch?v=gOuSYNuXHRk

Although acetaminophen is effective as an antipyretic and analgesic, its anti-inflammatory properties are much weaker than those of aspirin and other NSAIDs. It is therefore less effective for chronic inflammatory pain conditions such as rheumatoid arthritis. Acetaminophen is, however, a good choice for osteoarthritis, especially in those patients where aspirin is contraindicated. Acetaminophen lacks the antithrombotic, blood-thinning properties of aspirin and other NSAIDS and therefore does not inhibit coagulation, an important consideration for pain therapy following minor surgical or dental procedures.

From both a GI and cardiovascular perspective, acetaminophen may not be as safe as previously believed—especially at doses higher than 3 g daily. Indeed, a nested case-control study found that use of acetaminophen (any dose) is associated with a small but significant risk of upper GI complications. In addition, although women from the Nurses' Health Study, who reported occasional use of acetaminophen, did not experience a significant increase in the risk of cardiovascular events, those who reported a frequent use (6–14 tablets/week) had a small increased risk (Scarpignato et al., 2015).

Regular acetaminophen has also been associated with an increased risk of hypertension both in women and men. At doses of 3 g daily, acetaminophen induces a significant increase in ambulatory blood pressure in patients with coronary artery disease. These findings are not surprising in the light of the recent discovery that acetaminophen is indeed a selective cyclooxygenase (COX)-2 inhibitor in humans (Scarpignato et al., 2015).

Acetaminophen has been associated with a risk of rare but serious skin reactions. These skin reactions, known as Stevens-Johnson syndrome, toxic epidermal necrolysis, and acute generalized *exanthematous pustulosis*, can be fatal. These reactions can occur with first-time use of acetaminophen or at any time while it is being taken. Other drugs used to treat fever, pain, and body aches (eg, NSAIDS, such as ibuprofen and naproxen) also carry the risk of causing serious skin reactions, which is already described in the warnings section of their drug labels (FDA, 2013b).

Because the risks of acetaminophen-related liver damage are so serious and because the public is often unaware of these risks, the National Council for Prescription Drug Programs, the FDA's Safe Use Initiative, and other stakeholders met in 2011 to form the Acetaminophen Best Practices Task Group. The Task Group recommendations, updated in 2013, are intended to make it easier for consumers to identify whether a prescription pain reliever contains acetaminophen, to compare active ingredients on labels, and to take action to avoid taking two medicines with acetaminophen. The Task Group recommended coordinating prescription container labeling with the labeling that already exists for OTC medicines, providing consistency in labeling across all acetaminophen-containing medicines (FDA, 2013a).

Use of NSAIDs and Acetaminophen in Older Adults

Nonsteroidal anti-inflammatory drugs have been a mainstay for chronic pain management for many years but should be used with caution in older adults (Age and Ageing, 2013). Adverse reactions associated with NSAIDs including GI, cardiovascular, renal, and hematologic side effects, have been known for a long time. Introduction of new drugs into the marketplace and the continual stream of new research data have recently called into question the use and prescribing guidelines of NSAIDs in elders, especially "complex" older patients (Taylor et al., 2012).

Prescribing NSAIDs to older adults requires knowledge of individual patient risk factors, benefits and risks of the NSAID, and patient education. Monitoring for effectiveness and side effects is essential. A recent report demonstrated that more than 50% of patients were not properly informed by a physician or pharmacist on the side effects associated with prescribed or OTC NSAIDs (Taylor et al., 2012).

For older adults, acetaminophen is the first-line treatment for both acute and persistent pain, particular musculoskeletal pain. Acetaminophen has a good safety and efficacy profile as long as the maximum daily dose of 4g/24h is not exceeded (Age and Ageing, 2013).

Nitrous Oxide (N_2O)

Based upon the recent literature, N_2O may be poised for something of a comeback in the acute care setting. The agent is well known, self-administered, safe, and at least moderately effective. It avoids the need for IV access and has a very low risk of side effects. It is excreted unchanged by the lungs so there are no issues with renal or hepatic disease. When the training, technical, and related physical barriers (eg, external venting) to N_2O use in the ED can be overcome, it makes sense for an ED to have this inhaled agent available for analgesia and also as an adjunct for procedural sedation (Thomas, 2013).

As an inhaled, rapid-onset short-acting analgesic in doses used in acute care (generally 50:50 with oxygen but sometimes at higher concentrations for cities at higher altitudes), N_2O has been in effective use in the prehospital and ED settings for many decades. Its onset and offset times of roughly 3 to 5 minutes contribute to N_2O's potential utility in the acute care environment. The gas has been reported useful for analgesia for acute conditions ranging from procedures to acute intensely painful conditions in which traditional analgesia is difficult (Thomas, 2013).

Medical Cannabis

Cannabis has an unrivaled history of continuous cultivation, having started in Neolithic China more than 6000 years ago. A thorough scientific evaluation of the medical use of cannabis goes back to the work of Sir William B. O'Shaughnessy in 1838–1840. Since then cannabis has been intensively investigated. In the early 1960s cannabidiol (CBD) and the most psychoactive cannabinoid delta-9-tetrahydrocannabinol (THC) were identified. By 2009 more than 525 constituents have been identified, among them about a hundred different cannabinoids (Lanz et al., 2016).

In addition to THC, other cannabinoids (and non-cannabinoids, such as terpenoids*) likely contribute to and modulate the overall pharmacologic effects of cannabis. Numerous recent studies have proven the anti-inflammatory and neuroprotective properties of THC and CBD. Cannabidiol is known to reduce the psychotropic effects of THC; in addition, THC and CBD act synergistically (Lanz et al., 2016).

*Terpenoid: a terpene is a hydrocarbon found in the essential oils of many plants, especially conifers and citrus trees. Terpenes are also found in cannabis plants; terpenoids are formed when cannabis is dried and cured. Terpenes are non-cannabinoids and are responsible for the distinctive smell of cannabis.

There is growing evidence that the cannabinoid receptor system plays a central role in the regulation of many key functions to maintain homeostasis. Tetrahydrocannabinol, which is a partial agonist to CB_1 receptors and to a smaller extent to CB_2 receptors, is available in many countries for several indications. It is administered orally to treat pain, nausea, spasticity, and loss of appetite. It has proven to be effective in patients suffering from cancer, multiple sclerosis, amyotrophic lateral sclerosis, chronic pain, and other diseases (Lanz et al., 2016).

All animals except insects have an **endogenous** (made within the body) cannabinoid system, or **endocannabinoid system (ECS).** It has been found that humans make cannabinoids, similar in structure to those of the cannabis plant; further, humans have receptors for these molecules. This newly discovered molecular signaling system is essential for life and helps keep us in balance as we deal with daily stressors (Mathre, 2016).

Cannabinoid receptors in the human brain were first identified in 1988 by American researcher Allyn Howlett and her graduate student William Devane. They named these receptors cannabinoid 1 (CB_1) receptors. In 1992 researchers in Israel discovered an endogenous cannabinoid neurotransmitter, which they called anandamide. By 1993 another group of scientists found cannabinoid receptors in the immune system (CB_2). To date five endocannabinoids have been discovered.

The CB_1 receptors are found mainly on neurons in the brain, spinal cord, and peripheral nervous system, but are also present in other organs and tissues. The low number of CB_1 receptors in the brain stem may help explain the absence of cannabis overdoses due to the depression of respirations. CB_2 receptors are primarily found in immune cells, among them leukocytes, the spleen, and tonsils.

The effectiveness of cannabis in decreasing pain is thought to be related to the role of the CB_2 cannabinoid receptor, which suppresses microglial cell activation and decreases neuro-inflammation. In addition, cannabinoid receptors may couple to other effectors that are critical for the transmission of pain signals (Gadotti et al., 2013).

Pharmaceutical researchers are exploring the potential therapeutic properties of the cannabinoid system while attempting to minimize problematic side effects. A significant problem surrounding the medical use of cannabis-related compounds is a concern regarding their CB_1-mediated psychoactive effects and abuse potential. The interest in developing compounds whose mechanism of action involves CB_2 receptors without CB_1 involvement remains a goal in medical therapeutics. For this reason, selective CB_2 receptor ligands appear as potentially viable compounds for pain management (Gadotti et al., 2013).

Several peer-reviewed studies conducted at University of California, San Diego have shown the value of cannabis for some pain-related conditions. One study looked at the effect of cannabis on HIV-related peripheral neuropathy and found that pain relief was greater with cannabis than placebo. Additionally, mood and daily functioning improved among the group using cannabis for pain relief. In another study, researchers looked at the effect of smoked cannabis on 30 participants with spasticity due to multiple sclerosis. Results indicated that smoked cannabis was superior to placebo in symptom and pain reduction in participants with treatment-resistant spasticity (Corey-Bloom et al., 2012).

The Food and Drug Administration recently approved an investigational new drug study of purified CBD. The new drug, called Epidiolex, is provided by a British company called GW Pharmaceuticals. The drug will be used for the treatment of pediatric epilepsy in small studies at the University of California San Francisco and the NYU School of Medicine.

Adjuvant Medications

Adjuvant analgesics (or *co-analgesics*) are drugs with a primary indication other than pain that have analgesic properties. Although not primarily identified as an analgesic in nature, they have been found in clinical practice to have either an independent analgesic effect or additive analgesic properties when used with opioids (Khan et al., 2011). This group includes drugs such as antidepressants, anticonvulsants, corticosteroids, neuroleptics, and other drugs with narrower adjuvant functions. Adjuvant drugs can be used to enhance the effects of pain medications, treat concurrent symptoms, and provide analgesia for other types of pain. Adjuvant analgesics are particularly useful when evidence of decreased opioid responsiveness is present (Prommer, 2015).

Adjuvants commonly used to enhance the effects of pain medications include:

- Antidepressants
- Anticonvulsants
- Local anesthetics
- Corticosteroids
- Bisphosphonates

Using Opioids to Manage Pain

> Despite low-quality evidence supporting practice change, use of chronic opioid therapy for chronic non-cancer pain increased dramatically over the past two decades. Concurrently, opioid analgesic overdose deaths, addiction, misuse, and diversion have increased markedly.

Physicians for Responsible Opioid Prescribing, 2012

Opioids are chemicals that produce morphine-like effects in the body; they are commonly prescribed for the treatment of both acute and chronic pain and for pain associated with cancer. Opioids have a **narcotic effect**, that is, they induce sedation and are effective for the management of many types of pain.

Adverse events in opioid therapy can include nausea, vomiting, and constipation, as well as central nervous system (CNS) manifestations such as dizziness, confusion, and sleep disturbance. These directly interfere with patient adherence and are attributed to opioid discontinuation in approximately 25% of patients (Xu & Johnson, 2013).

An estimated 20% of patients presenting to physician offices with noncancer pain symptoms or pain-related diagnoses (including acute and chronic pain) receive an opioid prescription. In 2012 healthcare providers wrote 259 million prescriptions for opioid pain medication, enough for every adult in the United States to have a bottle of pills (CDC, 2016b).

Dozens of compounds fall within this class of opioid analgesics, including hydrocodone, oxycodone, morphine, fentanyl, codeine, propoxyphene (recalled in 2010), hydromorphone (Dilaudid), and meperidine (Demerol). In addition to their effective pain-relieving properties, some of these medications are used to relieve severe diarrhea (eg, Lomotil, or diphenoxylate) or severe coughs (codeine).

Opioid receptors are found throughout the nervous system, as well as in vascular, gut, lung airway, cardiac, and some immune system cells. They act by attaching to specific proteins called **opioid receptors**. When these drugs attach to their receptors, they reduce the perception of pain (NIDA, 2014a).

There are three types of opioid receptors, with similar protein sequences and structures: *mu*, delta, and kappa. The *mu* opioid receptors are thought to give most of their analgesic effects in the CNS, as well as many side effects including sedation, respiratory depression, euphoria, and dependence. Most analgesic opioids are agonists on *mu* opioid receptors. Of all the analgesics used in pain control, the most safety issues arise with the use of *mu* opioids, or morphine-like drugs such as morphine, etorphine, methadone, hydromorphone (Dilaudid), sufentanil, and fentanyl.

The *delta* opioid receptors are more prevalent for analgesia in the peripheral nervous system. The *kappa* opioid receptors contribute to analgesia in the spine and may cause dysphoria and sedation, but do not generally lead to dependence.

Regulatory agencies and expert groups have encouraged prescribers to rely on evidence-based guidelines when prescribing opioids. This includes:

1. Use of opioid treatment agreements
2. Regular monitoring for efficacy, safety, and misuse using tools such as urine drug testing and querying prescription monitoring databases and
3. Provision of or referral to addiction treatment if recurrent misuse or opioid use disorder is identified (Becker et al., 2016)

In practice, many primary care providers struggle to follow these guidelines, citing lack of clinical time for opioid management, inadequate training, and low confidence. Use of opioid risk mitigation strategies has been low in primary care, even among patients at high risk for misuse. It is therefore understandable that the most complex cases—those in which individuals on long-term opioids, often at high doses, have persistently poor function, exhibit concerning behaviors such as running out of opioids early, or develop a substance use disorder to an opioid or other drug—are extremely challenging to manage in primary care. Even among experts in the field, there is no consensus regarding how to best address these clinical situations (Becker et al., 2016).

Benefits and Harms of Opioid Therapy

Balance between benefits and harm is a critical factor influencing the strength of clinical recommendations. In recent publications, CDC has considered what is known from the epidemiology research about benefits and harms related to specific opioids and formulations, high-dose therapy, co-prescription with other controlled substances, duration of use, special populations, and risk stratification and mitigation approaches (CDC, 2016b).

CDC also considered the number of persons experiencing chronic pain, numbers potentially benefiting from opioids, and numbers affected by opioid-related harms. Finally, CDC considered the effectiveness of treatments that addressed potential harms of opioid therapy (opioid use disorder) (CDC, 2016b).

Specific formulations of opioids have been shown to be harmful. Serious risks have been associated with the use of extended release/long-acting (ER/LA) opioid formulations. ER/LA opioids are used for management of pain severe enough to require daily, around-the-clock, long-term opioid treatment in patients for whom other treatment options such as non-opioid analgesics or immediate-release opioids are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. Serious risks have also been associated with time-scheduled opioid use, specifically substantially higher average daily opioid dosage than as-needed opioid use (CDC, 2016b).

Several epidemiologic studies examined the association between opioid dosage and overdose risk related to high-dose therapy. Consistent with the clinical evidence review, opioid-related overdose risk is dose-dependent, with higher opioid dosages associated with increased overdose risk. A study involving Veterans Health Administration patients with chronic pain found that patients who died of overdoses related to opioids were prescribed higher opioid dosages than controls. Another recent study of overdose deaths among state residents with and without opioid prescriptions revealed that prescription opioid-related overdose mortality rates rose rapidly up to prescribed doses of 200 MME/day, after which the mortality rates continued to increase but grew more gradually (CDC, 2016b).

Epidemiologic studies suggest that concurrent use of benzodiazepines and opioids might put patients at greater risk for potentially fatal overdose. Three studies of fatal overdose deaths found evidence of concurrent benzodiazepine use in 31% to 61% of decedents. In one of these studies, among decedents who received an opioid prescription, those whose deaths were related to opioids were more likely to have obtained opioids from multiple physicians and pharmacies than decedents whose deaths were not related to opioids (CDC, 2016b).

Regarding duration of use, patients can experience tolerance and loss of effectiveness of opioids over time. Patients who do not experience clinically meaningful pain relief early in treatment (ie, within 1 month) are unlikely to experience pain relief with longer-term use (CDC, 2016b).

Patients with sleep apnea or other causes of sleep-disordered breathing, patients with renal or hepatic insufficiency, older adults, pregnant women, patients with depression or other mental health conditions, and patients with alcohol or other substance use disorders have been found to have an increased risk for harm from opioids. Opioid therapy can decrease respiratory drive and a high percentage of patients on long-term opioid therapy have been reported to have an abnormal apnea-hypopnea index. Additionally, opioid therapy can worsen central sleep apnea in obstructive sleep apnea patients and it can cause further desaturation in obstructive sleep apnea patients not on continuous positive airway pressure (CPAP) (CDC, 2016b).

Reduced renal or hepatic function can lead to a greater peak effect and longer duration of action and reduce the dose at which respiratory depression and overdose occurs. Age-related changes in patients aged ≥65 years, such as reduced renal function and medication clearance, even in the absence of renal disease, result in a smaller therapeutic window for safe dosages. Older adults might also be at increased risk for falls and fractures related to opioids (CDC, 2016b).

Opioids used during pregnancy can be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with birth defects, including neural tube defects, congenital heart defects, gastroschisis, preterm delivery, poor fetal growth, and stillbirth. Moreover, in some cases opioid use during pregnancy leads to neonatal opioid withdrawal syndrome (CDC, 2016b).

Patients with mental health comorbidities and patients with a history of substance use disorders might be at higher risk than other patients for opioid use disorder. Recent analyses found that depressed patients were at higher risk for drug overdose than patients without depression, particularly at higher opioid dosages, although investigators were unable to distinguish unintentional overdose from suicide attempts. In case-control and case-cohort studies, substance abuse/dependence was more prevalent among patients experiencing overdose than among patients not experiencing overdose (CDC, 2016b).

Prescription drug monitoring programs (PDMPs) and urine drug testing provide potential benefits, including the ability to identify patients who might be at higher risk for opioid overdose or opioid use disorder. These strategies may help determine which patients will benefit from greater caution and increased monitoring or interventions when risk factors are present. One study found that most fatal overdoses could be identified retrospectively on the basis of two pieces of information: multiple prescribers and high total daily opioid dosage. Both of these important risk factors for overdose are available to prescribers in the PDMP. However, limited evaluation of PDMPs at the state level has revealed mixed effects on changes in prescribing and mortality outcomes (CDC, 2016b).

There is limited evidence available regarding the benefits and harm of risk mitigation approaches. Although no studies were found to examine prescribing of naloxone with opioid pain medication in primary care settings, naloxone distribution through community-based programs providing prevention services for substance users has been demonstrated to be associated with decreased risk for opioid overdose death at the community level (CDC, 2016b).

Concerns have been raised that prescribing changes such as dose reduction might be associated with unintended negative consequences, such as patients seeking heroin or other illicitly obtained opioids or interference with appropriate pain treatment. With the exception of a study noting an association between an abuse-deterrent formulation of OxyContin and heroin use, showing that some patients in qualitative interviews reported switching to another opioid, including heroin, for many reasons, including cost and availability as well as ease of use, CDC did not identify studies evaluating these potential outcomes (CDC, 2016b).

Finally, regarding the effectiveness of opioid use disorder treatments, methadone and buprenorphine for opioid use disorder have been found to increase retention in treatment and to decrease illicit opioid use among patients with opioid use disorder involving heroin. Although findings are mixed, some studies suggest that treatment effectiveness is enhanced when psychosocial treatments are used in conjunction with medication-assisted therapy; for example, by reducing opioid misuse and increasing retention during maintenance therapy, and improving compliance after detoxification (CDC, 2016b).

Opioid-Induced Hyperalgesia

Apart from potential side effects, tolerance, and addiction, opioid use can be associated with **opioid-induced hyperalgesia**, which is defined as a state of nociceptive sensitization caused by exposure to opioids. It is characterized by a paradoxical response whereby a patient receiving opioids for the treatment of pain actually becomes more sensitive to pain (Suzan et al., 2013).

Opioid-induced hyperalgesia in the post operative period has been reported following the administration of short-acting opioids during surgery. Additional evidence comes from opioid addicts on methadone maintenance therapy, in whom decreased tolerance to cold pain has been reported. Mixed results are found regarding hyperalgesia in patients with chronic pain who receive intermediate-term opioid treatment (Suzan et al., 2013).

Opioid Reassessment

In an effort to support primary care in the management of patients with complex chronic pain on long-term opioid therapy, a multi-disciplinary team designed the Opioid Reassessment Clinic (ORC) at VA Connecticut Healthcare System (Becker et al., 2016).

Located in the primary care setting, the clinic is staffed by an addiction psychiatrist, an internist with addiction and pain training, a behavioral health advanced practice nurse, and a clinical health psychologist. The clinic has served as a learning opportunity for management of complex chronic pain and opioids over the past three years. The following case highlights evidence-based practices as well as approaches based on pragmatic considerations where evidence is lacking (Becker et al., 2016).

Case

This is a 56-year-old patient with bilateral hip pain due to severe osteoarthritis that significantly interfered with functioning, for which the patient was prescribed morphine for several years. Nine months prior to Opioid Reassessment Clinic (ORC) referral, the patient successfully completed a residential treatment program for his long-standing alcohol use disorder while continuing on long-term opioid therapy. Presently, the primary care provider referred the patient to the ORC after two episodes of running out of opioid prescriptions early (without early refill) and a brief return to alcohol use.

In the ORC, clinicians facilitated engagement in outpatient alcohol treatment by making continued opioid therapy contingent upon adherence with followup, and required frequent ORC visits including breathalyzer tests and urine drug screens. Following another return to drinking, the patient was admitted to an intensive outpatient alcohol use disorder treatment program and was simultaneously tapered off morphine, transitioning to tramadol with adjuvant non-opioid medications including an NSAID, gabapentin, and topical lidocaine.

While tramadol, a weak *mu* receptor agonist with more prominent serotonin and norepinephrine reuptake inhibition, was still a risky medication in this patient in recovery, it is classified by the DEA as less risky (schedule V compared to oxycodone and morphine's schedule II designation); plus the patient's tramadol dose was markedly lower in terms of morphine-equivalent daily dose.

Additionally, orthopedics was consulted and agreed to schedule hip replacement surgery contingent upon several months of documented alcohol abstinence. This motivated the patient to adhere to appointments and monitoring as required by both ORC and addiction treatment providers.

While the patient continued to request a switch to a "stronger" opioid, the ORC repeatedly reiterated that this was not an option given the recent history of misuse, the lack of evidence of improved functioning on such medications, and benefit of being on the lowest possible opioid dose prior to surgery. After 6 months of abstinence from alcohol, safe use of tramadol, and engagement in multimodal therapy including ongoing specialty treatment, the patient was discharged from ORC to followup with primary care providers while awaiting scheduled surgery.

Epilogue: The patient underwent total hip replacement and received 2 weeks of full agonist opioid treatment (MSIR 15 mg Q6 PRN) following the surgery. After the 2-week post-operative period, the patient was transitioned back to tramadol. He remains abstinent from alcohol and participates fully in his hip rehabilitation program.

Source: Becker et al., 2016.

Tolerance, Dependence, and Addiction

> Thirty years ago, I attended medical school in New York. In the key lecture on pain management, the professor told us confidently that patients who received prescription narcotics for pain would not become addicted.
>
> While pain management remains an essential patient right, a generation of healthcare professionals, patients, and families have learned the hard way how deeply misguided that assertion was. Narcotics—both illegal and legal—are dangerous drugs that can destroy lives and communities.
>
> Thomas Frieden, MD
> Director, CDC

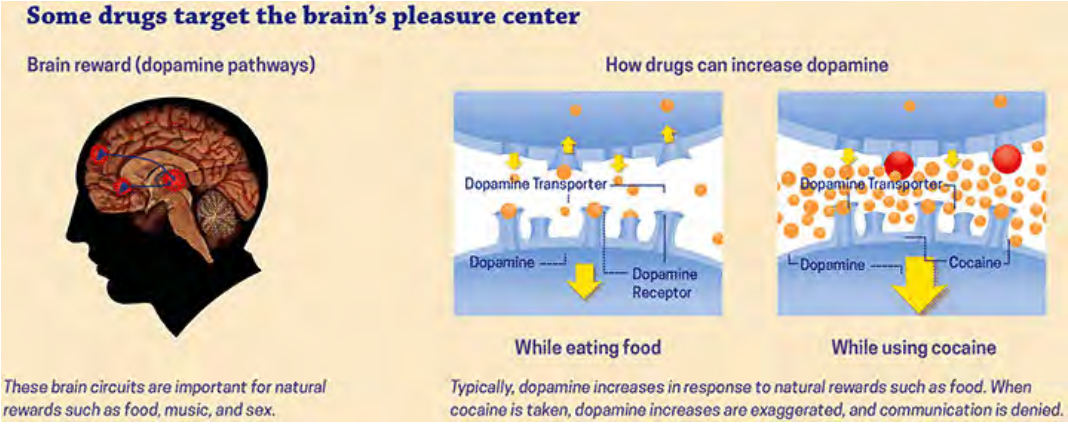
A number of terms and definitions are regularly used to define behaviors that are associated with the misuse and abuse of drugs. These terms are imprecise and at times confusing and can reflect societal attitudes and beliefs about drug abuse. So it is not surprising that medical terminology associated with drug use and abuse is opaque and at times unclear, particularly in the area of prescription drug abuse.

To address this issue and to clarify the terms *dependence* and *addiction*, particularly in opioid-treated patients, new definitions for drug addiction have been included in the 2013 DSM-V update. The term "substance dependence"—used in DSM-III and DSM-IV—has been replaced by the terms "substance use disorder" and "opioid use disorder" (IASP, 2013).

Additional changes in the DSM-V state that two items (not including tolerance and withdrawal) are needed from a list of behaviors suggesting compulsive use to meet the criteria for substance use disorder (SUD). Tolerance and withdrawal are not counted for those taking prescribed medications under medical supervision such as analgesics, antidepressants, anti-anxiety medications, or beta-blockers (IASP, 2013).

Tolerance

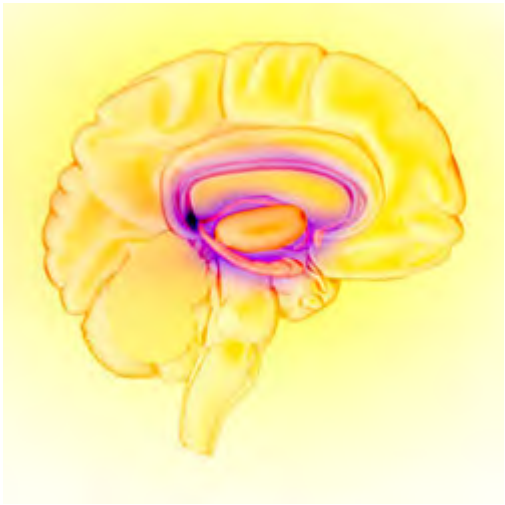
Tolerance is a state of adaptation in which a drug becomes less effective over time, which means a larger dose is needed to achieve the same effect. Tolerance occurs because some drugs cause the brain to release 2 to 10 times the amount of dopamine than natural rewards do. In some cases, this occurs almost immediately—especially when drugs are smoked or injected—and the effects can last much longer than those produced by natural means. The resulting effects on the brain's pleasure circuit dwarfs those produced by naturally rewarding behaviors.



Source: National Institute on Drug Abuse, 2018.

The brain adapts to these overwhelming surges in dopamine by producing less dopamine or by reducing the number of dopamine receptors in the reward circuit. This reduces the user's ability to enjoy not only the drugs but also other events in life that previously brought pleasure. This decrease compels the person to keep abusing drugs in an attempt to bring the dopamine function back to normal, but now larger amounts of the drug are required to achieve the same dopamine high (NIDA, 2016a).

The Brain's Reward Circuit



The limbic system—the brain's reward circuit. Source: National Institute on Drug Abuse.

Dependence

Dependence is a state of adaptation characterized by symptoms of withdrawal when a medication is abruptly stopped, the dose is rapidly reduced, or an antagonist is administered. It is a term often misused as a synonym for addiction, but the two terms are not synonymous. The seriousness of the withdrawal symptoms depends upon the drug being used and the extent of its use (risks increase with higher doses over long periods of time). For some drugs, such as alcohol or benzodiazepines, withdrawal symptoms can be serious and life-threatening.

An example of dependence is a patient who is on morphine for several months for chronic back pain. If the morphine is discontinued all at once, a flu-like syndrome will quickly develop, accompanied by nausea, stomach pains, and malaise. These symptoms of physical dependence will disappear if the morphine is resumed. Once a person has been on opioids for a period of time, the medication must be tapered off to avoid withdrawal symptoms.

Addiction

> It is often said that addiction is easy to recognize, that it rarely arises during the treatment of pain with addictive drugs, and that cases of addiction during pain treatment can be managed in much the same way as other addictions, but such generalizations grossly oversimplify the real situation.
>
> International Association for the Study of Pain

Addiction is defined as a chronic, relapsing disease that is characterized by compulsive drug seeking and use, despite the known, harmful consequences. Addiction involves a psychological craving and is considered a brain disease because drugs change the brain's structure and function. Brain changes can be long lasting and can lead to the harmful behaviors seen in people who abuse drugs. Although taking drugs at any age can lead to addiction, research shows that the earlier a person begins to use drugs the more likely they are to progress to more serious abuse (NIDA, 2014c).

Addiction

The term *addiction* may be regarded as equivalent to *severe substance use disorder* as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5, 2013) (NIDA, 2014c).

Opioids are highly addictive and rates of addiction among patients receiving opioids for the management of pain vary from 1% to 50%, which suggest uncertainty about what addiction really is and how often it occurs (IASP, 2013). Savage and colleagues introduced the four "Cs" criteria for identifying opioid addiction in chronic pain population:

1. Impaired **C**ontrol over drug use
2. **C**ompulsive use
3. **C**ontinued use despite harm
4. Unmanageable drug **C**raving (Chang & Compton, 2013).

A strategy to distinguish between aberrant or misuse behaviors and addiction in chronic pain patients is to assess the relationship between opioid dose titration and functional restoration. In this approach, in response to aberrant "drug-seeking" behaviors (ie, continued complaints of pain or requests for more medication), the clinician increases the opioid dose in an effort to provide analgesia. Improvements in functional outcomes and quality of life, with fewer problematic behaviors, indicate that active addiction is not present. In this case, drug-seeking behaviors may reflect pseudo-addiction, therapeutic dependence, or opioid tolerance. Effective dosing results in functional restoration (Chang & Compton, 2013).

Treating Patients with a History of Substance Abuse

Treating chronic pain with chronic opioid therapy in individuals with a history of a **substance use disorder (SUD),** whether active or in remission, presents a challenge to pain clinicians. This is, in part, due to concerns about the patient relapsing to active substance abuse. In addition, clinicians may confuse "drug-seeking" behaviors with addictive disease, resulting in poor treatment outcomes, such as premature discharge of patients from pain care (Chang & Compton, 2013).

The goal of chronic pain treatment in patients with SUDs is the same as that for patients without SUDs: specifically, to maximize functionality while providing pain relief. However, reluctance to prescribe opioids and poor understanding of the complex relationship between pain and addiction often results in undertreated pain in this population (Chang & Compton, 2013).

When estimating the presence of substance use disorder in chronic pain patients, terminology is important. It is increasingly understood that SUD cannot be defined by physical dependence and tolerance, as these are predictable physiologic consequences of chronic opioid use. Reflecting this, in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V), tolerance and withdrawal are not counted as criteria for the substance use and addictive disorder diagnosis if a patient is taking an opioid analgesic under medical supervision (Chang & Compton, 2013).

A systematic review of literature synthesizing 21 studies published prior to February 2012 showed that the overall prevalence of current substance use disorders in chronic pain patients ranges from 3% to 48% depending on the population sampled. The lifetime prevalence of any substance use disorder ranged from 16% to 74% in patients visiting the ED, with those visiting for opioid refill having the highest rate. It has been reported that 3% to 11% of chronic pain patients *with* a history of substance use disorder may develop opioid addiction or abuse, whereas only less than 1% of those *without* a prior or current history of SUD develop the same (Chang & Compton, 2013).

When screening patients for a history of substance abuse, one of the easiest tools to use is the National Institute on Drug Abuse (NIDA) Drug Use Screening Tool. It begins with a Quick Screen, which recommends that clinicians ask their patients one question: "In the past year, how often have you used alcohol, tobacco products, prescription drugs for nonmedical reasons, or illegal drugs?" Patients are asked to respond on a 5-point continuum: never, once or twice, monthly, weekly, or daily/almost daily. A response of "at least 1 time" when asked about frequency of prescription or illegal drug use is considered a positive result. Recent research has identified that this single-question screening test is highly sensitive and specific for identifying drug use and drug use disorders (NIDA, 2014a).

For those who screen positive for illicit or nonmedical prescription drug use, clinicians are directed to administer the full NIDA-modified Alcohol, Smoking, and Substance Involvement Screening Test (NM-ASSIST). The NM-ASSIST automatically generates a risk level to indicate the level of intervention needed and provides additional resources such as scripts on how to discuss drug use with patients and resources to link patients to specialty care (NIDA, 2016b).

Identifying Risk Level	
High risk Score ≥27	▪ Provide feedback on the screening results ▪ Advise, assess, and assist ▪ Arrange referral ▪ Offer continuing support
Moderate Risk Score 4–26	▪ Provide feedback ▪ Advise, assess, and assist ▪ Consider referral based on clinical judgment ▪ Offer continuing support
Low Risk Score 0–3	▪ Provide feedback ▪ Reinforce abstinence ▪ Offer continuing support

Source: NIDA, 2012a.

Untreated Addiction

In many primary care or pain management settings, the ability to provide the comprehensive services necessary to treat patients with both pain and current addiction are sorely lacking. Some clinicians strongly believe that patients with chronic pain and active addiction, regardless of type of substance abused, are not candidates for chronic opioid therapy (Chang & Compton, 2013).

Patients with an active substance use disorder should be referred to formal addiction treatment. It is incumbent upon the prescribing clinician to maintain a referral network of substance abuse treatment providers willing to collaborate on providing care to patients with co-morbid pain and substance use disorder. After referral, a pain clinician should continue to work closely with the SUD treatment provider to monitor use behaviors and pain outcomes (Chang & Compton, 2013).

Addiction in Remission

For individuals with addiction in remission, the goal of treatment is the same as that as for all chronic pain patients: to improve pain and maintain functionality. Indicators of successful pain management include:

- The patient's ability to comply with regimens
- The ability to engage in cognitive-behavioral pain management strategies
- Utilization of positive coping skills to manage stress and
- The ability to establish better social support systems (Chang & Compton, 2013)

Management of co-morbid neuropsychiatric complications is critical to maximize functionality (Chang & Compton, 2013).

Regardless of the type of substance previously abused, exposure to psychoactive medications can lead to relapse in patients with a recently or poorly treated substance use disorder. Although concerns of relapse may contribute to clinicians' reluctance to prescribe chronic opioid therapy for patients whose addiction is in remission, there is evidence that patients with successfully treated addiction can be effectively treated with opioids for chronic pain (Chang & Compton, 2013).

In patients with substance use disorder in remission, clinicians must assess the patient's relative risk for relapse and monitor for its emergence. The ability to manage a relapse episode is a necessary skill of any chronic opioid therapy prescriber. To assess risk of relapse, a series of questions should be asked of the chronic pain patient regarding the status of SUD remission. Asking these questions at each visit allows for early identification of high-risk situations and potential coping responses to these stressors (Chang & Compton, 2013).

- How long you been in recovery?
- How engaged are you in addiction recovery efforts and treatment (ie, supportive counseling, 12-step program)?
- What types of drugs have you abused?
- What are current stressors that might precipitate relapse (unrelieved pain, sleep disorders, withdrawal symptoms, psychiatric symptoms, interpersonal conflicts)?
- What are your current protective factors against relapse, including improved coping responses and a social support system?
- How stable you feel in recovery? (Chang & Compton, 2013)

A relapse contract can be developed early in treatment, which is individualized to the patient and specifies steps or actions that will be taken by both the patient and clinician if relapse occurs. The patient's behaviors with respect to the opioid analgesic regimen provide the best evidence for the presence of active addiction (Chang & Compton, 2013)

The clinician should keep in mind that seeking a higher dose of a prescribed medication does not necessarily mean that the patient is drug-seeking. However, losing or forging prescriptions, stealing or having others steal for you, visiting multiple providers for duplicate prescriptions, and injecting oral formulations are signs that the patient is not using the medication appropriately.

Management of pain requires a great degree of trust on both sides. Being consistent, open, and fair are important attributes for the provider. Providing positive feedback, reducing harm through education, and attempting to understand individual circumstances are helpful to the patient. If the patient is approaching the end of life, old habits and fears often resurface and more support may be needed.

Children and Opioids

> Thankfully, not many children experience the types of cancer pain, extensive trauma, or surgeries that require long-term pain management. However, few pain management products have specific information on their label about their safety and effectiveness in pediatric patients. This even includes several new pain medications that have been approved for use in adults.
>
> To manage pain in pediatric patients, physicians often have to rely on their own experience to interpret and translate adult data into dosing information for pediatric patients.

Sharon Hertz, MD, Director
FDA, Office of New Drugs
Center for Drug Evaluation and Research,
Division of Anesthesia, Analgesia, and Addiction Products

The use of opioids to treat pain in infants and children presents challenges. First, with rare exceptions, opioids have not been labeled for use in individuals under 18 years of age. There is a dearth of quality studies on pharmacokinetics, pharmacodynamics, safety, and clinical effectiveness. Acute pain problems in pediatrics have many characteristics in common with adult presentations. Persistent, recurrent, and chronic pain in infants, children, and adolescents are often qualitatively different from chronic pain problems in adults. Treatment approaches may vary accordingly (Oregon Pain Guidance, 2016).

In adults, there is a well-recognized epidemic of hospitalizations and deaths related to the increasing use of opioid analgesics. Although there are fewer studies in children, this vulnerable population also appears to be at high risk for opioid toxicity. A study of 960 randomly selected medical records from 12 children's hospitals in the United States identified 107 adverse drug events with more than half attributable to opioid analgesics. Deaths have been reported in young children related to therapeutic use of codeine and hydrocodone in doses within or moderately exceeding recommended pediatric limits (Chung et al., 2015).

Despite their potential for serious adverse events, opioids are increasingly prescribed for adolescents. Opioid prescriptions for patients between 15 and 19 years of age doubled from 1994 to 2007, with estimates that opioids are prescribed in nearly 6% of ambulatory and emergency department visits made by adolescents in the United States (Chung et al., 2015).

Given the large number of pediatric patients receiving prescribed opioids, there is an urgent need for fundamental epidemiologic studies to inform the risk-benefit decisions of prescribers and families. An essential component of these studies is the identification of serious adverse reactions related to opioids. Epidemiologic studies in adults have developed procedures to identify hospitalizations and deaths related to opioid use. However, similar studies in children are lacking (Chung et al., 2015).

Clinical recommendations for chronic non-malignant pain in children and adolescents include (Walco, 2015):

- Prescribe opioids for acute pain in infants and children only if knowledgeable in pediatric medicine, developmental elements of pain systems, and differences in pharmacokinetics and pharmacodynamics in young children.

- Avoid opioids in the vast majority of chronic nonmalignant pain problems in children and adolescents, as evidence shows no indication.
- Opioids are indicated for a small number of persistent painful conditions, including those with clear pathophysiology and when an endpoint to usage may be defined.
- Opioids may be indicated for some chronic pain conditions in children and adolescents, when there is clear pathophysiology, and no definable endpoint.
- Consult or refer to a pediatric pain specialist when chronic pain problems in children and adolescents are complicated or persistent.

Managing Cancer Pain with Opioids

The use of opioids for the relief of moderate to severe cancer pain is considered necessary for most patients. For moderate pain, weak opioids such as codeine or tramadol or lower doses of strong opioids such as morphine, oxycodone, or hydromorphone are often administered and frequently combined with non-opioid analgesics. For severe pain, strong opioids are routinely used. Although no agent has shown itself to be more effective than any other agent, morphine is often considered the opioid of choice because of provider familiarity, broad availability, and lower cost. In one well-designed review, most individuals with moderate to severe cancer pain obtained significant pain relief from oral morphine (NCI, 2016).

Effective pain management requires close monitoring of patient response to treatment. In a review of 1,612 patients referred to an outpatient palliative care center, more than half of patients with moderate to severe pain did not experience pain relief after the initial palliative care consultation. In addition, one-third of patients with mild pain progressed to moderate to severe pain by the time of their first followup visit (NCI, 2016).

For patients with a poor pain prognosis, clinicians may consider discussing realistic goals for alleviating pain, focusing on function, and use of multimodality interventions. Repeated or frequent escalation of analgesic doses without improvement of pain may trigger clinicians to consider an alternative approach to pain (NCI, 2016).

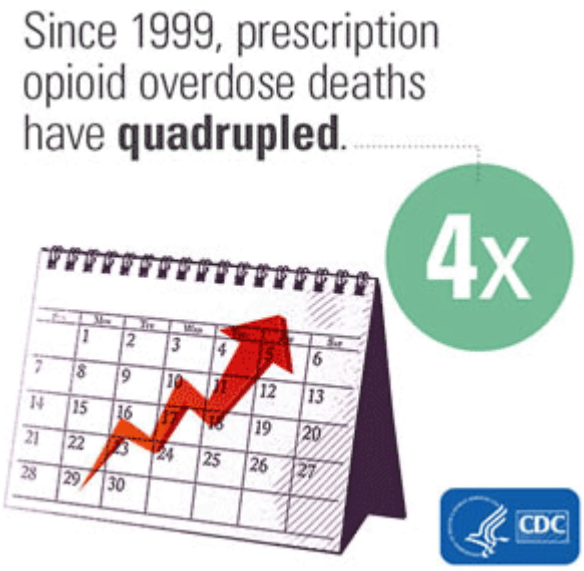
Abuse of Opioid Analgesics

> Here I lie in my hospital bed
>
> Tell me, sister morphine, when are you coming round again?
>
> Oh, I don’t think I can wait that long
>
> Oh, you see that my pain is so strong

> The scream of the ambulance is soundin' in my ear
>
> Tell me, sister morphine, how long have I been lying here?
>
> What am I doing in this place?
>
> Why does the doctor have no face?
>
> Marianne Faithfull, *Sister Morphine*

The United States is in the midst of an unprecedented drug overdose epidemic. Since 1999 prescription drug overdose death rates have quadrupled (CDC, 2016b). In 2009, for the first time in U.S. history, drug overdose deaths outnumbered motor vehicle deaths (CDC, 2013a). Since pain was coined "the fifth vital sign" in the 1990s, sales of prescription opioids in the Unites States have quadrupled (see below) (Bartels et al., 2016).

This increase in the prescription of opioids for pain management has been accompanied by a dramatic rise in prescription opioid-associated morbidity and mortality. In 2010 more than 16,000 deaths were attributed to prescription opioids, making them a leading cause of injury death in the general population (Bartels et al., 2016). There are now more deaths from opioid-related overdoses than from all other illicit drugs combined. Emergency department visits, substance treatment admissions, and economic costs associated with opioid abuse have all soared (CDC, 2013a).

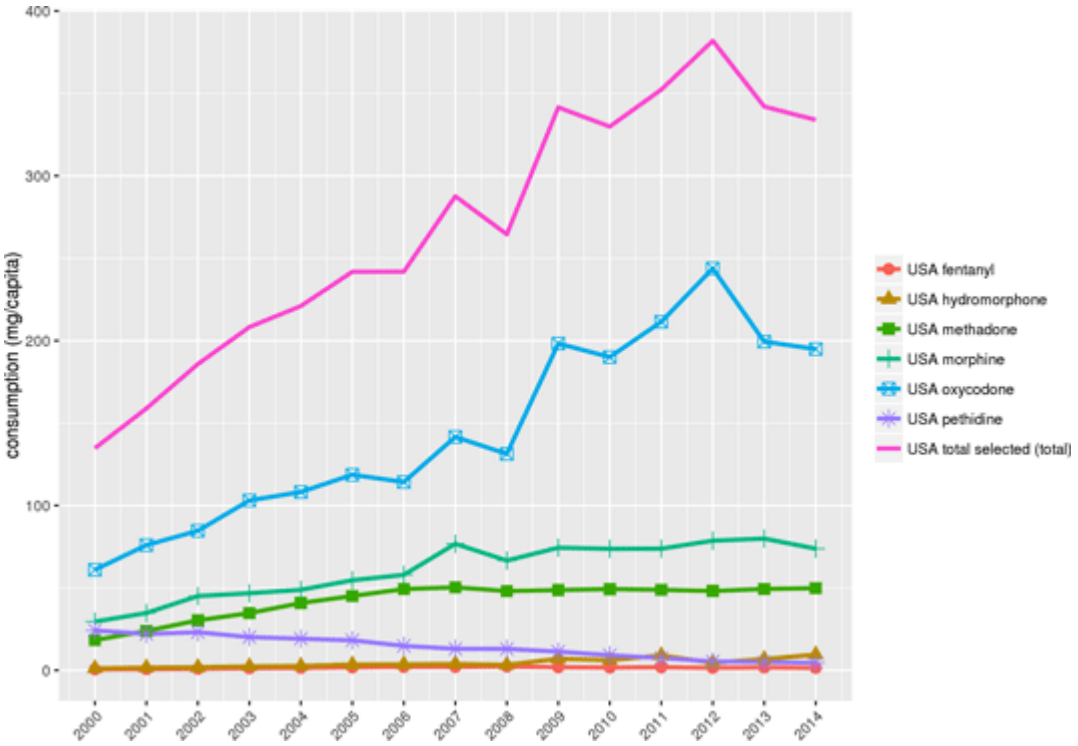


Source: CDC, 2016b.

Some startling statistics illustrate the magnitude of the abuse problem. Between 1997 and 2011 the U.S. population increased only 16%, however the number of prescription pain medications sold by pharmacies increased significantly more than that. Between 1997 and 2011:

- Oxycodone sales increased by 1,259%
- Hydrocodone sales increased by 356%
- Methadone sales increased by 1,099%
- Fentanyl sales increased by 711%
- Morphine sales increased by 246%
- Buprenorphine sales increased from 17 grams in 2002 to 1,639 kg in 2011 (McDonald & Carlson, 2013)

USA Opioid Consumption (mg/capita), 2000–2014



Sources: International Narcotics Control Board; World Health Organization population data
By: Pain and Policy Studies Group, University of Wisconsin/WHO Collaborating Center, 2016.

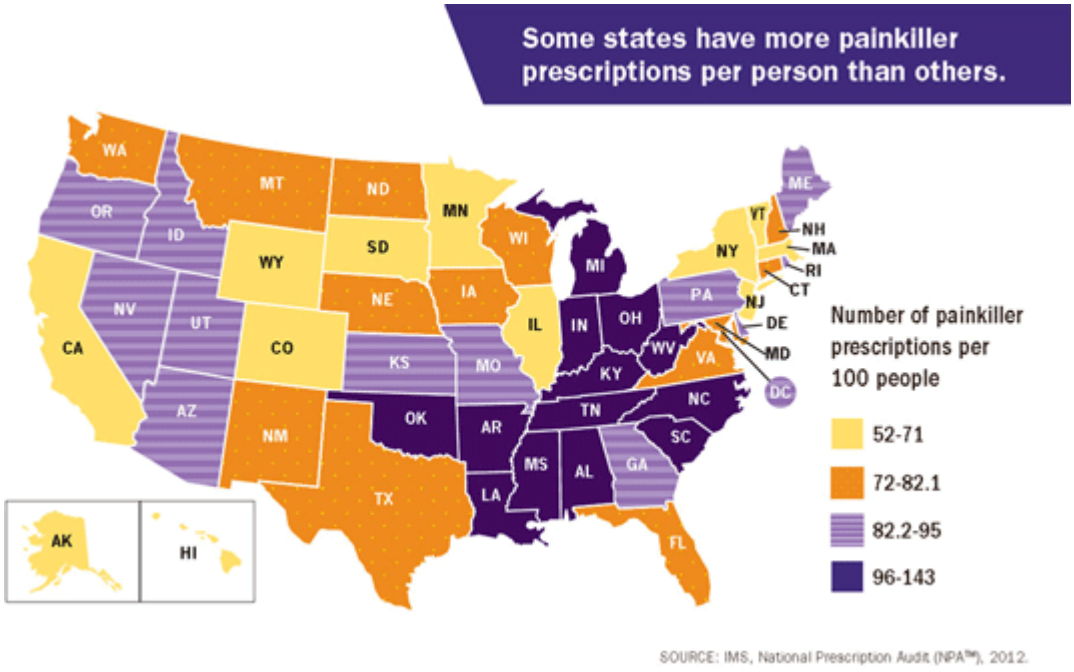
The increased availability of opioid analgesics means they are being used in ways that are unsafe or unintended. OxyContin, for example, which was designed as a slow-release, oral medication is now being crushed, then snorted or injected, with lethal consequences. To combat this, new formulations are being designed to deter some of these abuses. For example, a new formulation of OxyContin releases from 21% to 48% less opioid when tampered with (milled, manually crushed, dissolved, and boiled) than the original version (Raffa et al., 2012).

Paradoxically, despite an enormous rise in spending and prescription, there is limited evidence to support the efficacy of opioids in chronic noncancer pain management. In a European survey on chronic pain, 15% of respondents felt that their medications were not very, or not at all, effective (Xu & Johnson, 2013). A systematic review by Chou and colleagues suggested limited efficacy of long-term opioid therapy over short-term treatment or placebo, while an evidence review by the Institute of Medicine concluded that the effectiveness of opioids as pain relievers, especially over the long term, is somewhat unclear (Xu & Johnson, 2013).

A survey of pain management in sixteen European countries conducted in 2003 found that 28% of survey respondents used prescription opioids. Of particular interest, the countries reporting higher percentage of opioid use were no more satisfied with their pain control than those with lower prevalence of use (Xu & Johnson, 2013).

Prescribing rates for opioids vary widely across states. In 2012 healthcare providers in the highest-prescribing state wrote almost 3 times as many opioid painkiller prescriptions per person as those in the lowest prescribing state (CDC, 2016b). Health issues that cause people pain do not vary much from place to place, and do not explain this variability in prescribing. Some factors that may influence prescribing rates include:

- Healthcare providers in different parts of the country do not agree on when to prescribe opioid painkillers and how much to prescribe.
- Some of the increased demand for prescription opioids is from people who use them non-medically, who sell them, or who obtain them from multiple prescribers.
- Many states report problems with for-profit, high-volume pain clinics (so-called pill mills) that prescribe large quantities of painkillers to people who don't need them medically (CDC, 2016b).



CDC, 2016b

Prescription Drug Abuse

Prescription drug abuse is the use of a medication without a prescription, in a way other than as prescribed, or for the experience or feelings elicited. According to several national surveys, prescription medications, such as those used to treat pain, attention deficit disorders, and anxiety, are being abused at a rate second only to marijuana among illicit drug users. The consequences of this abuse have been steadily worsening, reflected in increased treatment admissions, emergency room visits, and overdose deaths (NIDA, 2014b).

Prescription drug abuse can include taking a drug prescribed for someone else, taking more of the medication than was prescribed, taking medication more frequently than was directed, or altering the formulation (crushing, snorting) so as to obtain a greater amount of active agent than was originally intended (NIDA, 2012b).

Opioid pain medication use presents serious risks, including overdose and opioid use disorder. From 1999 to 2014, more than 165,000 persons died from overdose related to opioid pain medication in the United States. In the past decade, while the death rates for the top leading causes of death such as heart disease and cancer have *decreased* substantially, the death rate associated with opioid pain medication has *increased* markedly. Sales of opioid pain medication have increased in parallel with opioid-related overdose deaths. The Drug Abuse Warning Network estimated that >420,000 ED visits were related to the misuse or abuse of narcotic pain relievers in 2011, the most recent year for which data are available (CDC, 2016a).

Although clinical criteria have varied over time, opioid use disorder is a problematic pattern of opioid use leading to clinically significant impairment or distress. This disorder is manifested by specific criteria such as unsuccessful efforts to cut down or control use and use resulting in social problems and a failure to fulfill major role obligations at work, school, or home. This diagnosis has also been referred to as "abuse or dependence" and "addiction" in the literature, and is different from tolerance (diminished response to a drug with repeated use) and physical dependence (adaptation to a drug that produces symptoms of withdrawal when the drug is stopped), both of which can exist without a diagnosed disorder (CDC, 2016a).

In 2013, on the basis of DSM-IV diagnosis criteria, an estimated 1.9 million people abused or were dependent on prescription opioid pain medication. Having a history of a prescription for an opioid pain medication increases the risk for overdose and opioid use disorder, highlighting the value of guidance on safer prescribing practices for clinicians. For example, a recent study of patients aged 15 to 64 years receiving opioids for chronic noncancer pain and followed for up to 13 years revealed that 1 in 550 patients died from opioid-related overdose at a median of 2.6 years from their first opioid prescription, and 1 in 32 patients who escalated to opioid dosages >200 morphine milligram equivalents (MME) died from opioid-related overdose (CDC, 2016a).

Did You Know. . .

Enough prescription painkillers were prescribed in 2010 to medicate every American adult around-the-clock for one month (CDC, n.d.).

Several factors have been put forth to explain the rise in opioid prescriptions for chronic noncancer pain that began in the 1980s and became dominant one decade later:

- Reservations against alternative pain therapies, especially those related to adverse events associated with long-term use of NSAIDs
- Aggressive and, at times, misleading product marketing by the manufacturers
- A widespread belief that opioid therapy carries a low risk of addiction potential (Xu & Johnson, 2013)

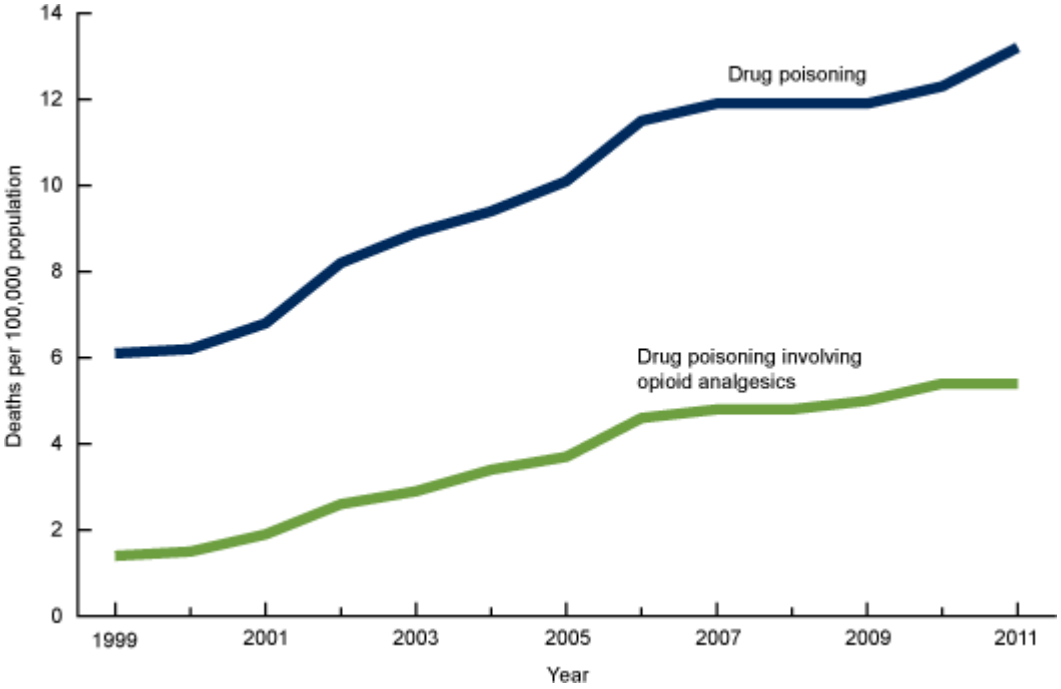
Overdose and Poisoning

> Poisoning is now the leading cause of death from injuries in the United States, and nearly 9 out of 10 poisoning deaths are caused by drugs.
>
> Margaret Warner, 2011

From 1999 to 2011, the age-adjusted rate for opioid-analgesic poisoning deaths nearly quadrupled. However, the increase in rates seems to be slowing. For opioid-analgesic poisoning deaths, there was an 18% increase each year from 1999 through 2006 but only a 3% increase each year from 2006 through 2011 (NCHS, 2014).

Deaths from opioid analgesics often involve other drugs. Benzodiazepines have been reported frequently in deaths involving opioid analgesics. Over the past decade, there has been an upward trend in the presence of benzodiazepines in opioid-analgesic poisoning deaths. In 1999 benzodiazepines were involved in 13% of the opioid analgesic poisoning deaths; by 2011, 31% of the opioid analgesic-related drug-poisoning deaths also involved benzodiazepines (NCHS, 2014).

Age-adjusted drug-poisoning and opioid-analgesic poisoning death rates: United States, 1999–2011



Source: NCHS, 2014.

Intertwined Epidemics: Prescription Opioids and Heroin

The enormous increase in the availability of prescription pain medications is drawing new users to these drugs and changing the geography and age-grouping of opiate-related overdoses. Prescription opioid-related overdoses currently represent the second leading cause of injury-related death in the United States and the leading cause of death for 35- to 54-year-olds. This has led to an increase in healthcare utilization that is troubling for both its high social and healthcare-related costs (Unick et al., 2013).

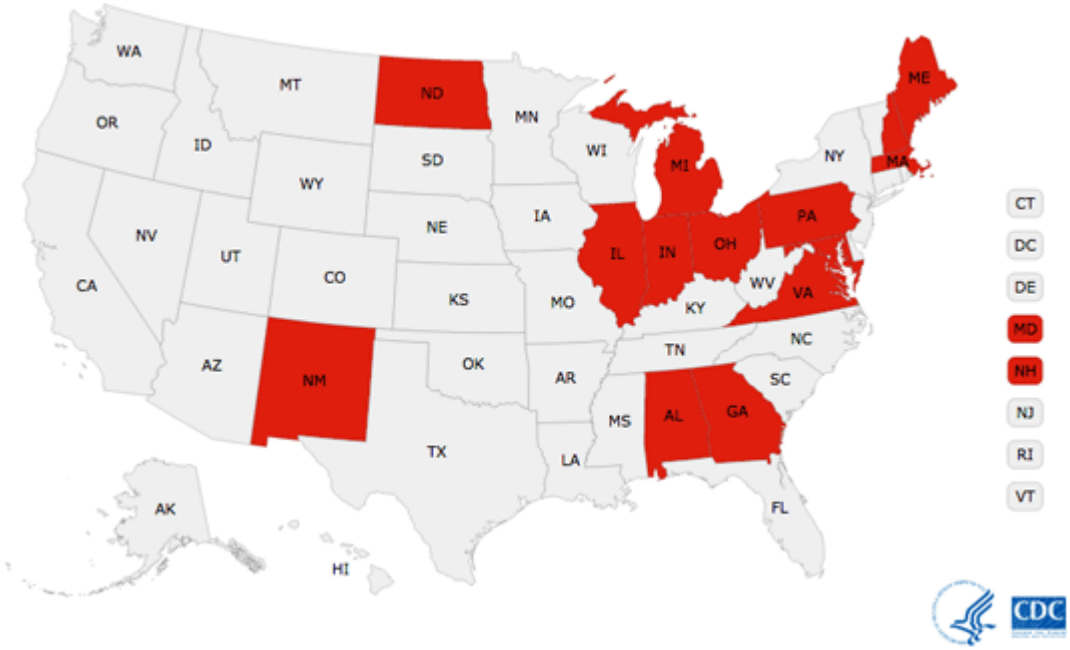
While many drugs and medicines have potential for overdose, the use of both prescription opioids and heroin (often taken in combination with other medicines and drugs) has increased since 1999. With increased use of opioids, communities have seen increases in overdose hospitalizations and deaths and need for treatment. Data on the sales of legally prescribed medicines (opioids in particular) and data on overdose hospitalizations and deaths can be used to illustrate the progression of an epidemic of overdose hospitalizations and deaths (OHA, 2014).

Most of the current cases of opioid-related overdoses can be traced to two fronts: (1) illegal heroin consumption, and (2) the illicit use or misuse of prescription opioids. Given the differences in the sources of opioids and the financial and social costs associated with overdose cases, it is important to understand the dynamics of the opioid-related overdose epidemic and the changing characteristics of opiate abusers (Unick et al., 2013).

The rise in prescription opioid-related overdose deaths has been particularly alarming in rural areas; between 1999 and 2004 prescription opioid-related overdose deaths increased 52% in large urban counties and a staggering 371% in non-urban counties (Unick et al., 2013).

Significant increases in drug overdose death rates were seen in the Northeast, Midwest and South census regions. In 2014 the five states with the highest rates of death due to drug overdose were West Virginia, New Mexico, New Hampshire, Kentucky, and Ohio. States with statistically significant increases in the rate from 2013 to 2014 included Alabama, Georgia, Illinois, Indiana, Maine, Maryland, Massachusetts, Michigan, New Hampshire, New Mexico, North Dakota, Ohio, Pennsylvania, and Virginia (CDC, 2016b).

Drug Overdose Increase, 2013–2014



Statistically significant drug overdose death rate increase from 2013 to 2014, U.S. states.

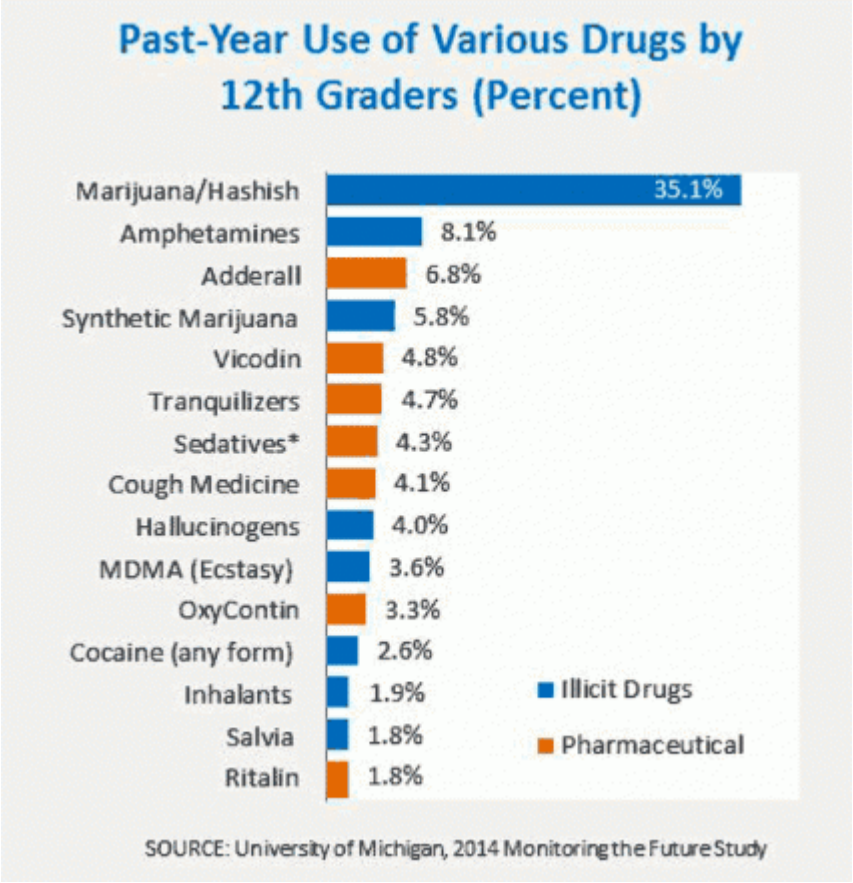
There is an evolving flux between prescription opioid use and heroin use in urban areas. Ethnographic work from Montreal shows that individuals at risk for heroin use have begun shifting to injecting prescription opioids. Additional evidence from Baltimore and Washington State suggests a high prevalence of prescription abuse in injection drug using populations, often preceding heroin use. Interestingly, recent changes to the formulation of OxyContin, the brand name long-acting form of oxycodone, have been linked to a self-reported rise in heroin use. What these studies suggest is that prescription opioid misuse and heroin use are intertwined (Unick et al., 2013).

Abuse Among Adolescents and Young Adults

Adolescents and young adults are especially vulnerable to prescription drug abuse, particularly opioids and stimulants. According to the Monitoring the Future (MTF) survey, an ongoing study of the behavior and attitudes of American youth involving nearly 45,000 8th, 10th, and 12th grade students, with regard to illicit drugs, annual prevalence declined for synthetic marijuana, heroin, MDMA (ecstasy, Molly), sedatives, and nonmedical use of any prescription drug. Annual prevalence of using any illicit drug remained essentially unchanged in all three grades in 2015 (Johnston et al., 2015).

Psychotherapeutic drugs now make up a significantly larger part of the overall U.S. drug problem than was true 10 to 15 years ago. This is in part because use increased for many prescription drugs over that period, and in part because use of a number of street drugs has declined substantially since the mid- to late-1990s. It seems likely that young people are less concerned about the dangers of using these prescription drugs outside of medical regimen because they are widely used for legitimate purposes. (Indeed, the low levels of perceived risk for sedatives and amphetamines observed among 12th graders illustrate this point.) Also, prescription psychotherapeutic drugs are now being advertised directly to the consumer, which implies that they are both widely used and safe to use. Fortunately, the use of most of these drugs has either leveled or begun to decline in the past few years. The proportion of 12th graders misusing any of these prescription drugs (eg, amphetamines, sedatives, tranquilizers, or narcotics other than heroin) in the prior year continued to decline in 2015 down from its high in 2005 (Johnston et al., 2015).

Amphetamine use without a doctor’s orders—currently the second most widely used class of illicit drugs after marijuana—continued a gradual decline in 2015 in all grades, though the one-year declines did not reach statistical significance. Use of narcotics other than heroin without a doctor’s orders (measured only in 12th grade) also continued a gradual decline begun after 2009 (Johnston et al., 2015).



Source: National Institute on Drug Abuse, 2015.

Abuse Among Middle-Aged and Older Adults

Prescription opioid-related overdoses rates are increasing the most in middle-aged individuals. Older adults represent another area of concern. Although older adults currently comprise just 13% of the population, they account for more than one-third of total outpatient spending on prescription medications in the United States. Older patients are more likely to be prescribed long-term and multiple prescriptions, which could lead to misuse or abuse (NIDA, 2014b).

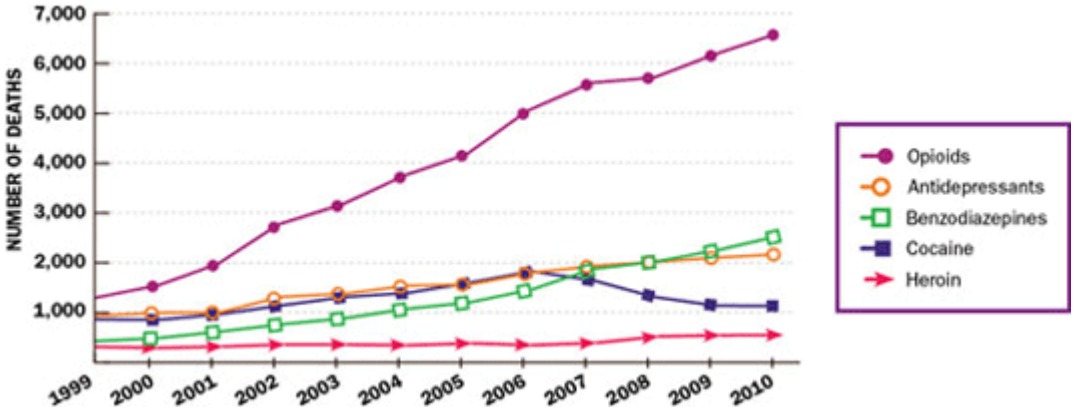
The high rates of comorbid illnesses in older populations, age-related changes in drug metabolism, and the potential for drug interactions may make any of these practices more dangerous than in younger populations. Further, a large percentage of older adults also use over-the-counter medicines and dietary supplements, which (in addition to alcohol) could compound any adverse health consequences resulting from prescription drug abuse (NIDA, 2014b).

Gender Differences in Opioid Abuse

Overall, adult men and women have roughly similar rates of nonmedical use of prescription drugs, although some studies suggest that women are more likely than men to be prescribed prescription drugs, particularly narcotics and anti-anxiety drugs. Adolescent females are more likely than males to use psychotherapeutic drugs nonmedically. Research has also suggested that women are at increased risk for nonmedical use of narcotic analgesics and tranquilizers such as benzodiazepines (CDC, 2013b).

Prescription pain medication overdoses are increasing among women. Although men are still more likely to die of prescription painkiller overdoses (more than 10,000 deaths in 2010), the gap between men and women is closing. Deaths from prescription painkiller overdose among women have risen more sharply than among men; since 1999 the percentage increase in deaths was more than 400% among women compared to 265% in men. This rise relates closely to increased prescribing of these drugs during the past decade (CDC, 2013b).

Deaths of Women from Prescription Painkillers, 1999–2010



Prescription painkiller deaths among women have increased dramatically since 1999.
Source: CDC, 2013b.

Prescription Painkillers: Growing Problem Among Women

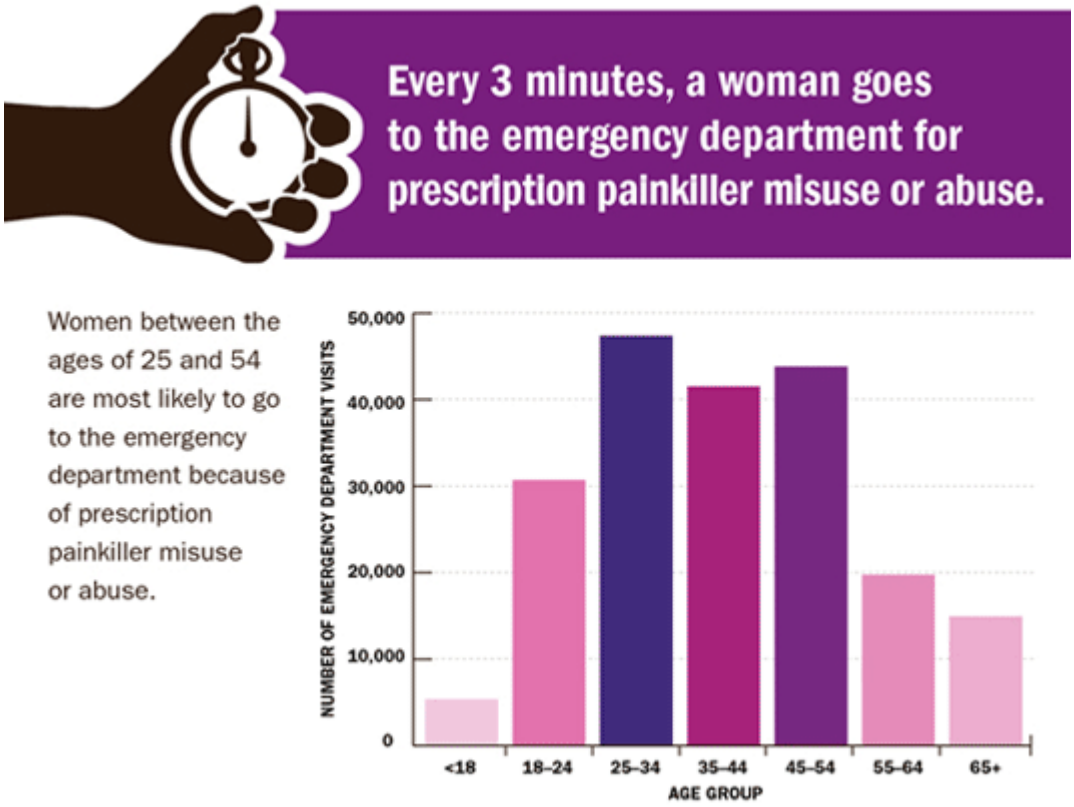
- More than 5 times as many women died from prescription painkiller overdoses in 2010 than in 1999.
- Women between the ages of 25 and 54 are more likely than other age groups to go to the emergency department from prescription painkiller misuse or abuse.
- Women ages 45 to 54 have the highest risk of dying from a prescription painkiller overdose.*
- Non-Hispanic white and American Indian or Alaska Native women have the highest risk of dying from a prescription painkiller overdose.
- Prescription painkillers are involved in 1 in 10 suicides among women.

*Death data include unintentional, suicide, and other deaths. Emergency department visits only include suicide attempts if an illicit drug was involved in the attempt.

Prescription Painkillers Affect Women Differently than Men

- Women are more likely to have chronic pain, be prescribed prescription painkillers, be given higher doses, and use them for longer time periods than men.
- Women may become dependent on prescription painkillers more quickly than men.
- Women may be more likely than men to engage in "doctor shopping" (obtaining prescriptions from multiple prescribers).
- Abuse of prescription painkillers by pregnant women can put an infant at risk. Cases of neonatal abstinence syndrome (NAS)—which is a group of problems that can occur in newborns exposed to prescription painkillers or other drugs while in the womb—grew by almost 300% in the United States between 2000 and 2009.

Source: CDC, 2013b.



Source: CDC.

Opioid Abuse and Chronic Pain

Diagnosed chronic pain patients make up less than 1% of the insured population in the United States but consume about 45% of all prescription opioids. It has been estimated that up to 40% of pain patients on chronic opioid therapy display aberrant drug-related behaviors (Raffa et al., 2012).

Chronic pain is defined as pain that typically lasts >3 months or past the time of normal tissue healing. Chronic pain can be the result of an underlying medical disease or condition, injury, medical treatment, inflammation, or an unknown cause (CDC, 2016b).

Prevention, assessment, and treatment of chronic pain are challenges for health providers and systems. Pain might go unrecognized, and patients, particularly members of racial and ethnic minority groups, women, elders, people with cognitive impairment, and those with cancer and at the end of life, can be at risk for inadequate pain treatment. Patients can experience persistent pain that is not well controlled. There are clinical, psychological, and social consequences associated with chronic pain including limitations in complex activities, lost work productivity, reduced quality of life, and stigma, emphasizing the importance of appropriate and compassionate patient care. Patients should receive appropriate pain treatment based on a careful consideration of the benefits and risks of treatment options (CDC, 2016b).

Chronic pain has been intertwined with substance abuse: 33% of individuals in a substance abuse program reported suffering from chronic pain and individuals in substance abuse treatment programs with chronic pain were significantly more likely to abuse opioids than those not reporting chronic pain. The term **rational abuse** has been put forth to describe chronic pain patients who abuse opioids because of undertreated pain, but very little is known about this population (Raffa et al., 2012).

Sales of opioid pain medication have increased in parallel with opioid-related overdose deaths. The Drug Abuse Warning Network estimated that >420,000 emergency department visits were related to the misuse or abuse of narcotic pain relievers in 2011, the most recent year for which data are available. Although clinical criteria have varied over time, opioid use disorder is a problematic pattern of opioid use leading to clinically significant impairment or distress (CDC, 2016b).

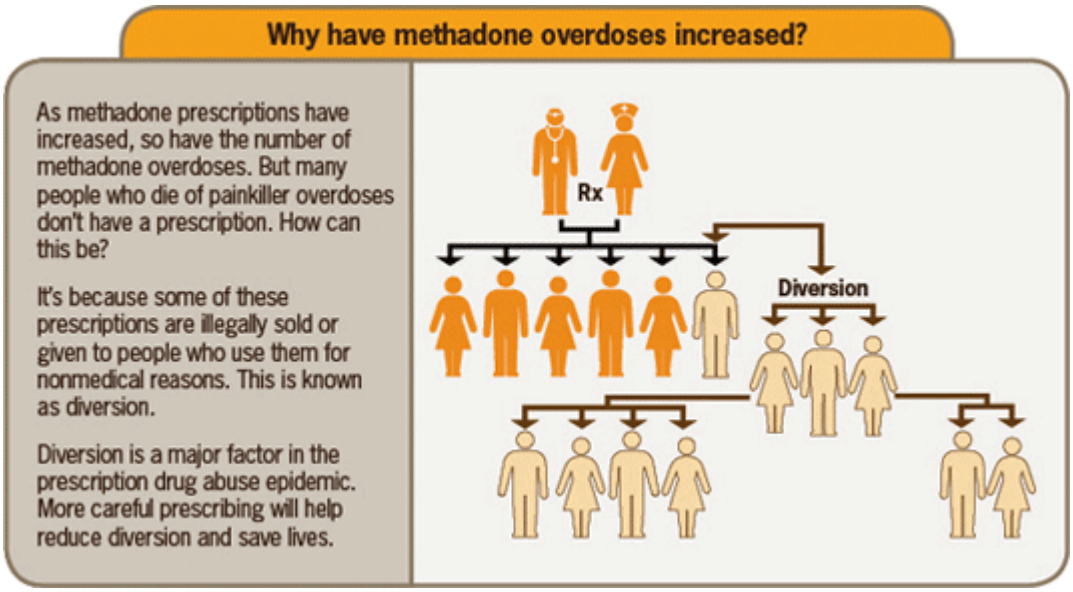
This disorder is manifested by specific criteria, such as unsuccessful efforts to cut down or control use, and use resulting in social problems and a failure to fulfill major role obligations at work, school, or home. This diagnosis has also been referred to as "abuse or dependence" and "addiction" in the literature, and is different from tolerance (diminished response to a drug with repeated use) and physical dependence (adaptation to a drug that produces symptoms of withdrawal when the drug is stopped), both of which can exist without a diagnosed disorder (CDC, 2016b).

Abuse of Methadone

Methadone is a synthetic narcotic first developed by German scientists during World War II to address a shortage of morphine. Methadone was introduced into the United States in 1947 as an analgesic (Dolophinel) and has emerged as a commonly prescribed medication for the management of pain. Methadone is also used for the treatment of opioid dependence, in which case it may be dispensed only in federally approved opioid treatment programs.

Drug Enforcement Administration (DEA) data suggest that abuse of methadone diverted from its intended purpose has contributed significantly to the rise in overdose deaths. Some individuals who abuse other narcotics have turned to methadone because of its availability.

Methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for pain. Methadone has been found to account for as much as a third of opioid-related overdose deaths involving single or multiple drugs in states that participated in the Drug Abuse Warning Network, which was more than any opioid other than oxycodone, despite representing <2% of opioid prescriptions outside of opioid treatment programs in the United States; further, methadone was involved in twice as many single-drug deaths as any other prescription opioid (MMWR, 2016).



Source: CDC, 2012.

Methadone differs from most other opioids because of its long half-life, delayed onset, narrow therapeutic window, and interactions with drugs such as alcohol and benzodiazepines. Methadone is less expensive than other opioids and is increasingly being prescribed as a cost-effective alternative, partly due to pressure from insurance companies.

Abuse of Fentanyl

Fentanyl is a synthetic opioid analgesic that is similar to morphine but is 50 to 100 times more potent. It is a schedule II prescription drug, and it is typically used to treat patients with severe pain or to manage pain after surgery. It is also sometimes used to treat patients with chronic pain who are physically tolerant to other opioids.

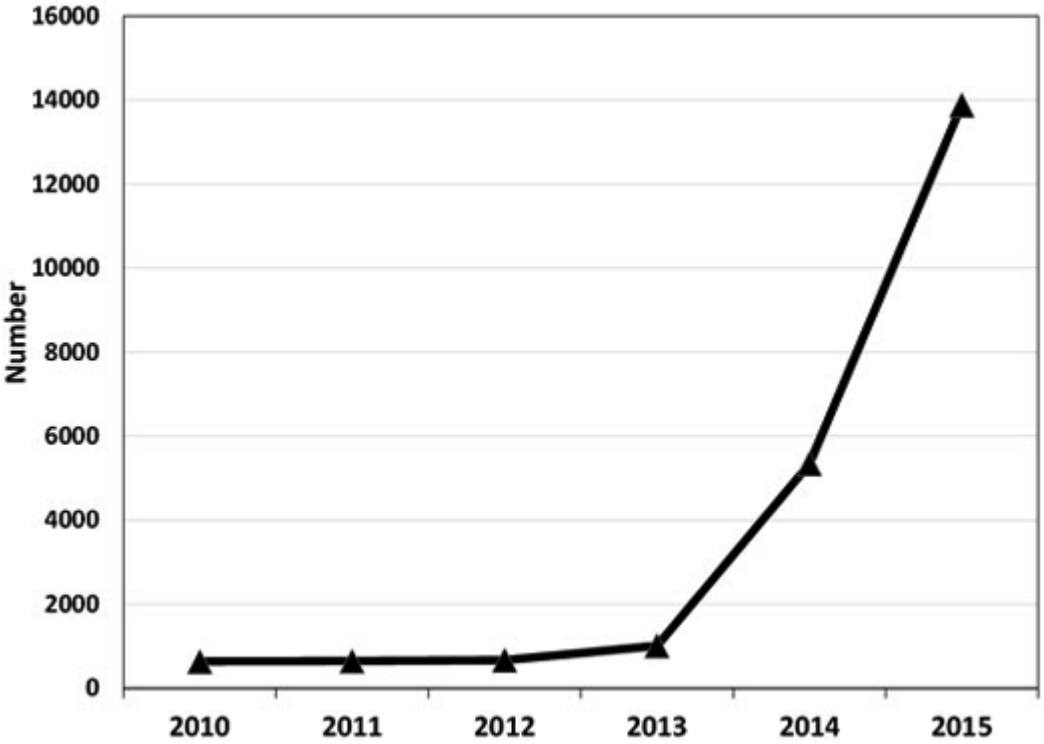
Fentanyl can be absorbed through the skin (fentanyl patch), by IV injection, by mouth (for breakthrough cancer pain), and intranasally. There are two types of fentanyl:

1. Pharmaceutical fentanyl, which is primarily prescribed to manage acute and chronic pain associated with advanced cancer

2. Nonpharmaceutical fentanyl, which is illegally made, and is often mixed with heroin and/or cocaine—with or without the user's knowledge—in order to increase the drug's effect

A sharp increase has been noted in the number of fentanyl overdoses in recent years. Most of the increases in fentanyl deaths over the last three years do not involve prescription fentanyl but are related to illicitly made fentanyl that is being mixed with or sold as heroin —with or without the users' knowledge—and increasingly as counterfeit pills. In July 2016, the DEA issued a new nationwide report indicating hundreds of thousands of counterfeit prescription pills have been entering the U.S. drug market since 2014, some containing deadly amounts of fentanyl and fentanyl analogs. The current fentanyl crisis continues to expand in size and scope across the United States (CDC, 2016b).

Number of Reported Law Enforcement Encounters Testing Positive for Fentanyl in the US: 2010–2015



This graph uses data from the DEA National Forensic Laboratory Information System (NFLIS) on the number of law enforcement drug submissions that test positive for fentanyl from 2014 to 2015 as of July 1, 2016. Source: CDC.

Abuse of Buprenorphine (Subutex) and Suboxone

Buprenorphine (Subutex) and the combination of buprenorphine and naloxone (Suboxone) are used to treat opioid dependence. Buprenorphine alone and the combination of buprenorphine and naloxone work to prevent withdrawal symptoms when someone stops taking opioid drugs by producing similar effects to these drugs. In recent years, buprenorphine has surpassed methadone as a drug of diversion and abuse (Medline Plus, 2016).

Subutex, which contains only buprenorphine, is intended for use at the beginning of treatment. Suboxone, which contains both buprenorphine and naloxone (to decrease the potential for abuse by injection), and is used in the maintenance treatment of opiate addiction.

The National Forensic Laboratory Information System (NFLIS) collects results from law enforcement-encountered drug items submitted to and analyzed by state and local forensic laboratories across the country. In contrast to methadone, the number of buprenorphine reports in the year following its approval to treat opioid dependence increased from 90 in 2003 (one year after it was approved) to 10,537 in 2010. It has increased slowly each year since then, reaching a high of 11,992 in 2013 (CESAR, 2014).

In 2013 the majority of buprenorphine reports were from the Northeast United States census region, while the West had the lowest number (CESAR, 2014).

Curbing Opioid Abuse

Medicine and drug use is highly regulated by the federal government and the states to protect people from harm. Regulations require pharmaceutical companies to place warnings on packaging of OTC and prescribed medicines. Federal and state regulations control who is able to prescribe medicines with a high risk for abuse. Medical training institutions teach students to prescribe controlled substances and OTC medicines safely. Schools of pharmacy teach pharmacists to dispense medicines safely. Pharmaceutical boards regulate the practice of dispensing medicines (OHA, 2014).

Many states require prescriber education on pain and the use of pharmaceutical medicines to control pain. States regulate the age at which individuals can legally purchase and consume alcohol. Federal and state laws establish penalties to control and punish infractions of laws and regulations by individuals (patients, prescribers, and pharmacists), institutions, corporations, and criminal organizations that promote and control drug trade. Yet all of these laws and regulations have not prevented misuse, abuse, addiction, and overdoses due to the use of prescribed medicines, alcohol, and illegal drugs (OHA, 2014).

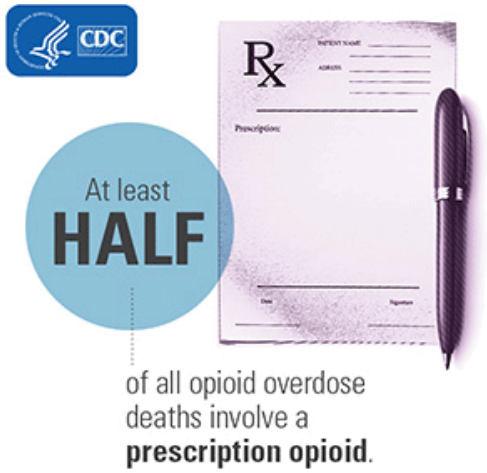
The increase in nonmedical use of pharmaceuticals suggests that previous prevention measures—such as provider and patient education and restrictions on the use of specific formulations—have not been adequate to curb widespread abuse and misuse. Given the societal burden of the problem, additional interventions are needed, such as more systematic provider education, universal use of state prescription drug monitoring programs by providers, routine monitoring of insurance claims information for signs of inappropriate use, and efforts by providers and insurers to intervene when patients use drugs inappropriately (MMWR, 2010).

Preventing Diversion

Diversion is the use of drugs for other than medically necessary or legal purposes or for nonmedical or not-medically-authorized purposes. Diversion involves, but is not limited to, physicians who sell prescriptions to drug dealers or abusers, pharmacists who falsify records and subsequently sell the drugs, employees who steal from inventory and falsify orders to cover illicit sales, prescription forgers, and individuals who commit armed robbery of pharmacies and drug distributors (DEA, n.d.).

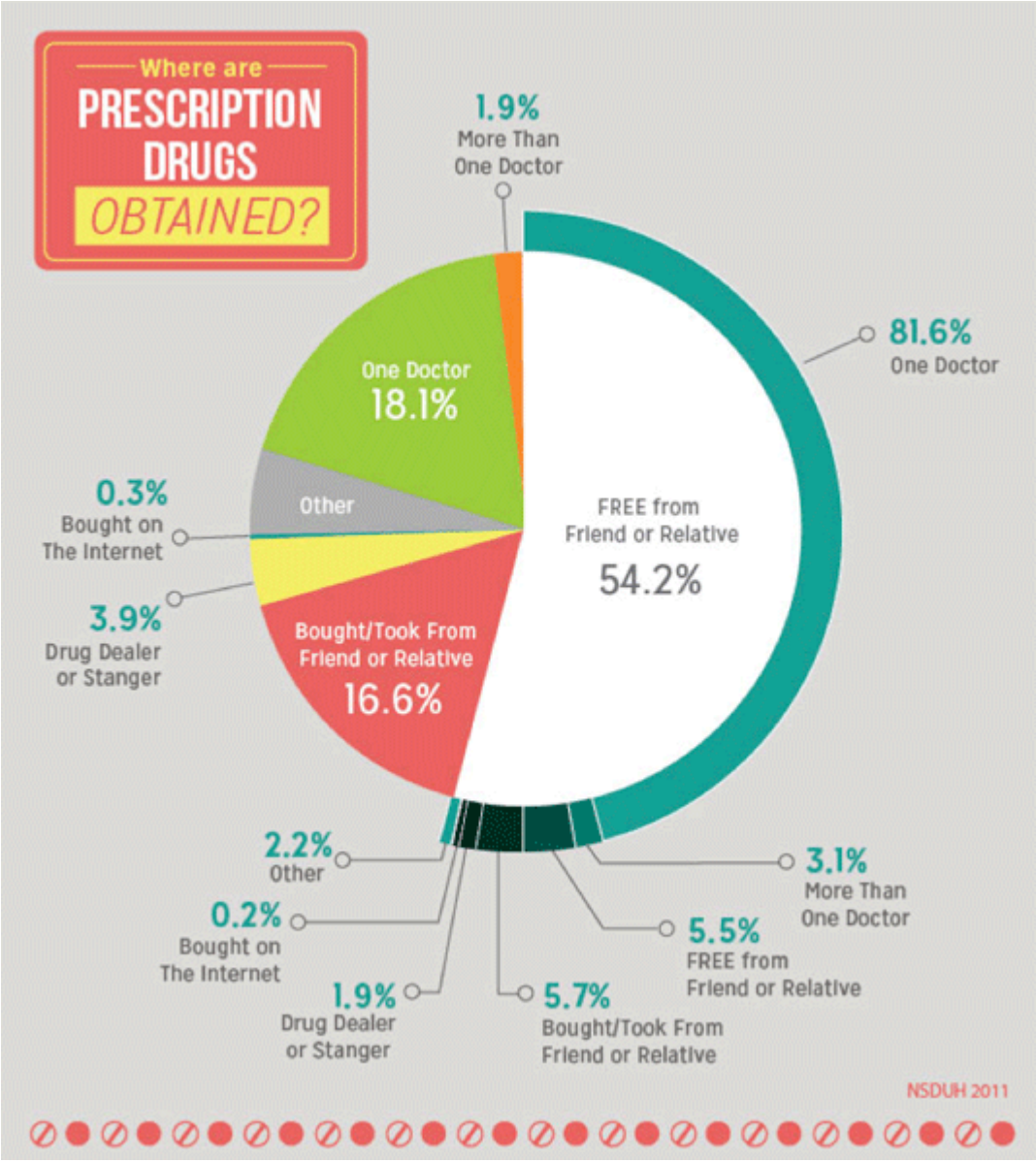
Surveys reveal that diversion of prescription drugs is endemic in communities. Diversion takes place in many contexts, most often when friends and relatives share their prescription pain relievers. Fifty-four percent of those surveyed in the United States reported the source of the pain relievers that they used nonmedically was free from their family and friends (OHA, 2014).

Under federal law, all businesses that import, export, manufacture, or distribute controlled substances; all health professionals licensed to dispense, administer, or prescribe them; and all pharmacies authorized to fill prescriptions must register with the DEA. Registrants must comply with regulatory requirements relating to drug security and recordkeeping. The DEA is obligated under international treaties to monitor the movement of licit controlled substances across U.S. borders and to issue import and export permits for that movement (DEA, n.d.).



Source: CDC.

Almost all prescription drugs involved in overdoses originate from prescriptions; very few come from pharmacy theft. However, once they are prescribed and dispensed, prescription drugs are frequently diverted to people using them without prescriptions. More than 3 out of 4 people who misuse prescription painkillers use drugs prescribed to someone else. Most prescription painkillers are prescribed by primary care and internal medicine doctors and dentists, not specialists. About 20% of prescribers prescribe 80% of all prescription painkillers (CDC, 2013a).



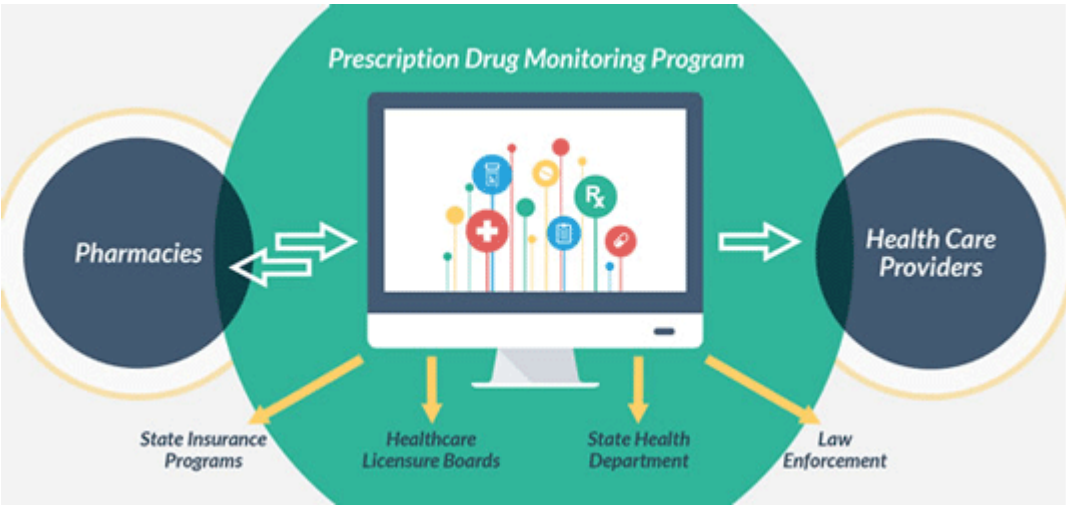
More than half of prescription drugs are obtained from a friend or relative. Source: NIDA, 2014

In addition to other drugs of abuse, today's illicit drug market offers an assortment of purely synthetic drugs, sometimes referred to as designer drugs. The term **designer drugs** in the context of drug abuse refers to substances chemically similar to and/or that mimic the drug-like effects of controlled substances. The term is often used synonymously with *club drugs*, *party drugs,* and *synthetic drugs.* Designer drugs affect the central nervous system and can display stimulant, depressant, and hallucinogenic properties (Volkow, 2013).

A large number of new unregulated substances are being abused for their psychoactive properties, often resulting in violent and unpredictable behavior. This growing phenomenon is particularly challenging, first because of the speed with which rogue chemists can modify existing drugs and market them. and second because of the ease with which the Internet allows for the sharing of information about and purchase of products such as "spice" and "bath salts" (Volkow, 2013).

Prescription Drug Monitoring Programs

Thirty-six states have Prescription Drug Monitoring Programs (PDMP) that can help prescribers and pharmacists identify high-risk patients who would benefit from early interventions. CDC recommends that PDMPs focus their resources on high-risk patients and prescribers who clearly deviate from accepted medical practice in terms of prescription painkiller dosage, numbers of prescriptions for controlled substances, and proportion of doctor shoppers among their patients. CDC also recommends that PDMPs link to electronic health records systems so that PDMP information is better integrated into healthcare providers' day-to-day practices (CDC, 2016b).



Source: cdc.gov.

New research funded by the National Institute on Drug Abuse (NIDA) found that state implementation of PDMPs was associated with a reduction in opioid-related overdose deaths. The study also found PDMPs that monitored a greater numbers of drugs with abuse potential and updated their data more frequently had greater declines in opioid-related overdose deaths than programs without those characteristics (NIDA, 2016b).

Implementation of a PDMP was linked to a decrease of 1.12 opioid-related overdose deaths per 100,000 population. A state with a program that monitored four or more drug schedules and updated their information at least weekly was predicted to have 1.55 fewer opioid-related overdose deaths per 100,000 population annually than a state without a program (NIDA, 2016b).

Providing Naloxone to Laypeople

For many years, community-based programs have offered opioid overdose prevention services to laypeople who might witness an overdose, including people who use drugs, their families and friends, and service providers. Since 1996, an increasing number of programs provide laypeople with training and kits containing the opioid antagonist naloxone hydrochloride (naloxone) to reverse the potentially fatal respiratory depression caused by heroin and other opioids (Wheeler et al., 2015).

In July 2014, the Harm Reduction Coalition (HRC), a national advocacy and capacity-building organization, surveyed 140 managers of organizations in the United States known to provide naloxone kits to laypeople. Managers at 136 organizations completed the survey, reporting on the amount of naloxone distributed, overdose reversals by bystanders, and other program data for 644 sites that were providing naloxone kits to laypeople as of June 2014. From 1996 through June 2014, surveyed organizations provided naloxone kits to 152,283 laypeople and received reports of 26,463 overdose reversals. Providing opioid overdose training and naloxone kits to laypeople who might witness an opioid overdose can help reduce opioid overdose mortality (Wheeler et al., 2015).

Providing naloxone kits to laypeople reduces overdose deaths, is safe, and is cost-effective. U.S. and international health organizations recommend providing naloxone kits to laypeople who might witness an opioid overdose; to patients in substance use treatment programs; to people leaving prison and jail; and as a component of responsible opioid prescribing (Wheeler et al., 2015).

Although the number of organizations providing naloxone kits to laypeople is increasing, in 2013, 20 states had no such organization, and 9 had less than 1 layperson per 100,000 population who had received a naloxone kit. Among these 29 states with minimal or no access to naloxone kits for laypeople, 11 had age-adjusted 2013 drug overdose death rates higher than the national median (Wheeler et al., 2015).

At their annual meeting in June 2016, the AMA adopted new policies that encourage physicians to co-prescribe naloxone to patients at risk of an overdose; promote timely and appropriate access to non-opioid and nonpharmacologic treatments for pain; and support efforts to delink payments to healthcare facilities with patient satisfaction scores relating to the evaluation and management of pain (AMA, 2016a).

The new naloxone policies will promote increased access to the overdose-reversing drug for friends and family members of patients at risk of overdose. The policy also encourages private and public payers to include all forms of naloxone on their preferred drug lists and formularies with nominal or no cost sharing. The policy supports liability protections for physicians and other authorized healthcare professionals to prescribe, dispense, and administer naloxone. Delegates called for policies to enable law enforcement agencies to carry and administer naloxone, as many states have done (AMA, 2016a).

Probuphine: Fighting Opioid Dependence

Medications like buprenorphine and methadone have revolutionized the treatment of people with opioid use disorder, including those with severe disorders (addiction). By controlling cravings and withdrawal symptoms without producing a high, these medications enable the patient to engage in treatment and make healthier choices while balance is gradually restored in brain circuits involved in reward and self-control. In people with severe disorders, these circuits are greatly disrupted (NIDA, 2016c).

One of the challenges with all addiction medications, however, is making sure patients adhere to their prescribed regimen. For the medication to be effective, the patient must take their prescription or show up daily at the clinic. This can be challenging for anyone managing life's responsibilities, especially in times of stress. Failing at this challenge can mean relapse, which may delay recovery (NIDA, 2016c).

In May of 2016, the FDA approved a long-acting buprenorphine implant called **Probuphine**. This subdermal implant delivers a constant low dose of buprenorphine over six months, the first such tool in the treatment of opioid use disorder. The implant is approved for individuals with opioid dependence who have already been treated with, and are medically stable on, existing orally absorbed buprenorphine formulations. It is a valuable new therapeutic tool for this subset of patients (NIDA, 2016c).

Buprenorphine, which in numerous studies has been shown to significantly improve outcomes for patients, has previously only been available in products that must be taken daily. The Probuphine implant, created by marrying buprenorphine to a polymer, delivers the drug steadily in the body at a low dose, eliminating the need for daily dosing (NIDA, 2016c).

AMA Recommendations

The American Medical Association acknowledges that opioid addiction is a national problem that has reached epidemic proportions. They urge physicians to take the following steps to address opioid abuse (AMA, 2016b):

1. Register and use your state prescription drug monitoring program to check your patient's prescription history.
2. Educate yourself on managing pain and promoting safe, responsible opioid prescribing.
3. Support overdose prevention measures, such as increased access to naloxone.
4. Reduce the stigma of substance use disorder and enhance access to treatment.
5. Ensure patients in pain aren't stigmatized and can receive comprehensive treatment.

Video (9:03) All on the Same Team: Managing Chronic Pain

Patients on opioids and providers work to improve their quality of life. Oregon Pain Guidance (2016). https://www.youtube.com/watch?v=2kP10Z228Os&feature=youtu.be

Non-Pharmacologic Approaches to Pain Management

Professionals approaching pain management from a non-pharmacologic perspective use diverse techniques to address the needs of their clients. Those trained within the traditional, Western medical model include physical and occupational therapists, doctors of osteopathy, chiropractors, psychologists, mental health practitioners, physiologists, and athletic trainers and kinesiologists, among others. Many Western-trained practitioners are adding alternative techniques to their practices.

Alternative practitioners make up an ever larger piece of the pain management universe. Most are trained in what would be considered complementary and alternative medicine and many are being included in Western medicine under the increasingly popular and effective approach called **integrative medicine**. Alternative practices include traditional Chinese medicine, acupuncture, cognitive-behavioral practices, meditation, hypnotherapy, massage therapy, and body-based practices such as yoga, Tai Chi, and Feldenkrais, among others.

Approaches overlap and professions argue about who does what and even who *can* do what. For example, physical and occupational therapists are using pain management techniques once exclusively in the domain of chiropractors, acupuncturists, and doctors of osteopathy. Nurses and doctors are encouraging patients to use mindfulness meditation, yoga, and other alternative practices to manage pain. In almost every profession, the amount and breadth of education and training has increased, and with it many innovative approaches and practices are competing with the traditional, pain-medicine model. The development of interdisciplinary, integrative pain management programs, which draw on the expertise of multiple disciplines, is perhaps one of the most encouraging developments in the field of pain management.

Interdisciplinary Pain Rehabilitation

Interdisciplinary pain rehabilitation programs are becoming more common, especially for the treatment of chronic pain. A growing body of literature supports the immediate and long-term benefits of the interdisciplinary rehabilitation approach. In this model, healthcare professionals work from the same facility, with daily meetings about the patients' progress, sharing the same treatment vision and passing the same message to the patients (Kurklinsky et al., 2016).

In one such program at the Mayo Clinic Comprehensive Pain Rehabilitation Center in Jacksonville, Florida, the overall goal is to improve function in people with chronic pain. The physical therapy component focuses on general reconditioning with graded exposure to activity, gradual reduction of fear-avoidance behaviors, and incremental elimination of other pain behaviors. Daily exercise sessions include a morning stretch group, which incorporates 15–20 minutes of whole-body active range of motion, gentle dynamic stretching, moderate static stretching, balance, and coordination training. Cardio and strength groups are also performed. During cardio group, each patient's goal is to complete 20–30 minutes of moderate conditioning activities within an age determined target heart rate zone followed by 5–10 minutes of static stretching. During strength group, each patient uses free weights, resistance bands, or body weight resistance to complete a whole-body strengthening and stability circuit (Kurklinsky et al., 2016).

The occupational therapy component focuses on the role of moderation and balance in daily activities. The overall goal is to increase functional independence and improve participation in life roles. Group lecture topics include home safety and modification, body mechanics and ergonomics, cleaning and yard work strategies, cognitive strategies, driving, fall prevention, self-care, shopping, time management, and vocational training. Each Friday, the occupational therapists lead a time management session for weekend planning to help patients appropriately moderate their schedule and balance activity during their time away from the structured program. Midway through the program, an OT meets with each patient to begin planning his or her days immediately after the program. There are also three individual biofeedback sessions during which patients learn diaphragmatic breathing and muscle relaxation and how to utilize these strategies during daily activity and functional mobility (Kurklinsky et al., 2016).

A pain psychologist leads up to three group therapy sessions each day. Discussion topics include anger, anxiety, fear, assertiveness, behavior change, central sensitization syndrome, cognitive behavioral therapy, identifying pain cycles, coping with pain and depression, difficult-day planning, distraction, drug interventions, forgiveness, goal setting, grief, maintaining lifestyle changes, pain behaviors, perfectionism, personal responsibility, problems solving, relationships, relaxation, self-esteem, sleep, stress, and withdrawal. There are also weekly question and answer sessions for the group members with no scheduled topic and weekly sessions for family and friends to learn about the pain rehabilitation program and ask questions. There are also work groups for distraction and difficult-day planning, nutrition, posture, and pain rehabilitation program tools (Kurklinsky et al., 2016).

Throughout the three-week program, nurses serve as patient care coordinators. They take the lead in medication management and tapering (under the direction of a physician). With patient authorization, nurses in the program also communicate with primary and specialty care providers outside of the pain rehabilitation team to assist with continuity of care into the future (Kurklinsky et al., 2016).

Physical and Occupational Therapy

Physical and occupational therapists (PTs and OTs) have long been involved in pain management. Starting in World War I, "reconstruction aides" began to develop their profession by tending to soldiers on the battlefield and those returning from war. Since that time, PTs and OTs have significantly expanded their scope of practice, education, and training. As movement specialists, they play a key role in the assessment and management of pain.

Physical and occupational therapists are particularly well-positioned to assume an educational role for patients related to healthy lifestyles and exercise. They encourage a model of care based on health, which includes initiating and supporting behavior change, optimal nutrition, weight reduction, reduced sedentary activity, and increased physical activity. As nonpharmacologic practitioners, therapists integrate health education into practice, including initiating and supporting smoking cessation, improved sleep hygiene, and stress management (Dean & Hansen, 2012).

Physical and occupational therapy generally involves one-on-one sessions, which can include manual therapy, movement analysis, or supportive technologies and equipment that assist the client in mobilizing and strengthening muscles, or improving motion in tendons, joints, and connective tissue. Patient education plays a key role in rehabilitation therapy with emphasis on body mechanics and changing habits and patterns of movement that lead to pain and dysfunction.

Physical and occupational therapists provide expertise in the use of assistive devices, orthotics, braces, as well as positioning devices, which designed to improve function, support areas of weakness, and reduce pain. Patients are referred to rehabilitation therapy following surgery, stroke, accidents, and illness and for education and training, with the goal of helping patients return to or even improve their prior level of function. In some states, a person can see a PT without a doctor's referral, a practice referred to as **direct access**.

Clinical practice guidelines are becoming the standard of practice for physical and occupational therapists. In a review of guidelines for the treatment of low back pain, adherence to physical therapy clinical practice guidelines has been shown to play an important role in certain measures of healthcare utilization and costs. With a few exceptions, those patients with low back pain who were treated by therapists using accepted clinical practice guidelines had lower overall healthcare utilization including fewer PT visits, shorter duration of care, fewer prescription medications, fewer physician or emergency department visits and less use of advanced imaging and injection procedures. Also, decreased costs have been associated with prescription medications, surgical procedures, and total low back pain related costs for those patients with low back pain treated by guideline-adherent physical therapy interventions (Hanney et al., 2016).

Therapeutic Exercise

Both PTs and OTs make extensive use of therapeutic exercise in the treatment of pain. Therapeutic exercise is an active treatment designed to address pain, maintain or improve strength and range of motion, increase blood flow, improve proprioception, and prevent muscle guarding, spasms, and contractures. Exercise programs directed by a physical or occupational therapist are tailored to the individual patient, based on assessment of impairments, patient preference, and co-morbidities.

Low back pain, neck pain, migraine, and other musculoskeletal disorders are 4 of the top 10 causes of disability worldwide (Lancet, 2015). By far, the most common reason for a referral to physical therapy is for low back pain, and often the pain has no structurally identifiable cause. Exercise therapy has been shown to be particularly effective for patients with low back pain. Results indicate that exercise therapy decreases pain intensity, alleviates disability, and improves physical functions for a long period (eg, 12-month followup) (Ishak et al., 2016).

Meta-analyses have also been conducted on the effectiveness of exercise as low back pain treatment. In 2006 researchers systematically reviewed trunk strengthening exercise and revealed that this exercise can alleviate pain and improve functions more effectively than aerobics and other exercises. Others have reported that progressive resistance exercise is effective and safe for patients experiencing muscle force deficiency and pain-related problems and that exercise improves the ability of patients to perform daily life activities (Ishak et al., 2016).

Proprioceptive training, in which passive and active sensory feedback exercises are used to improve motor function, may be more effective than traditional exercise in the treatment of low back and neck pain. Proprioception relates to our conscious awareness of where our body and limbs are in space. Proprioception also has unconscious components, for example it is associated with the control of posture, balance, and muscle tone.

In a systemic review of proprioceptive training techniques, researchers identified five main categories of proprioceptive-based interventions:

1. Active movement/balance training (single-joint active movements, single-joint passive and active movements, multi-joint passive and active movements, multi-joint active movements, and whole body balance training)
2. Passive movement training (passive motion apparatus focused either on single-joint or multi-joint movement)
3. Somatosensory stimulation training (muscle or vibro-tactile vibration ranging from whole-body vibration to local vibration of a single segment, thermal stimulation, multi-somatosensory stimulation, magnetic stimulation, electrical stimulation, and acupuncture)
4. Somatosensory discrimination training (active exploration of objects with the hand, tactile discrimination of textures, wrist or ankle joint position discrimination, and wrist joint velocity discrimination tasks)
5. Combined/multiple system training (multiple components of the three main categories mentioned above or multi-sensory approaches) (Aman et al., 2015)

For patients with musculoskeletal conditions such as chronic neck pain, knee ligament reconstruction, ankle injury, and osteoarthritis, training consisted of active multi-joint or whole body movement as well as whole body balance training. Among the musculoskeletal conditions, proprioceptive training proved most beneficial for improving function in knee osteoarthritis, leading to significant functional improvement (Aman et al., 2015).

Transcutaneous Electrical Stimulation

Transcutaneous electrical nerve stimulation (TENS) is widely used all around the world for relieving a variety of painful conditions. Controlled clinical trials have clearly demonstrated that TENS has a specific antalgic effect (relieves pain), but the intrinsic mechanism remains largely unknown. For this reason, clinically TENS is largely used by trial and error, and the optimal setting of stimulation parameters is still a matter of debate (Buonocore et al., 2013).

TENS Apparatus

The term TENS covers a variety of techniques that use electrical stimulation of the skin for pain control. HF-TPNS (high-frequency transcutaneous peripheral nerve stimulation) is a subtype of TENS, where the trunk of a peripheral nerve is electrically stimulated at high frequency using surface electrodes. Accurate placement of electrodes is commonly considered very important for pain relief (Buonocore et al., 2013).

Transcutaneous Electrical Nerve Stimulator. Source: Wikipedia.

TENS has been shown to relieve pain effectively in cases of musculoskeletal pain, arthritic pain, low back pain, neuropathic pain, and post operative pain. Some studies have reported that the application of TENS improves motor function (Suh et al., 2015).

Therapeutic Ultrasound

Therapeutic ultrasound is among the most commonly used physical modalities for treating soft tissue injuries and pain. It involves the use of ultrasonic sound waves applied directly to a patient's skin, which causes the underlying tissue to vibrate and mildly heat, improving blood flow to the affected tissue. It is delivered using a hand-held, rounded wand in either of two modes: (1) continuous mode, in which the delivery of ultrasound is nonstop throughout the treatment period; and (2) pulsed mode, in which the delivery of ultrasound is intermittently interrupted (Ebadi et al., 2012).

The therapeutic effects of ultrasound are classified as thermal and nonthermal. Ultrasonic energy causes soft tissue molecules to vibrate from exposure to the acoustic wave. This increased molecular motion generates frictional heat and consequently increases tissue temperature. This thermal effect is thought to cause changes in nerve conduction velocity, increase in enzymatic activity, changes in contractile activity of skeletal muscles, increase in collagen tissue extensibility,* increase in local blood flow, increase in pain threshold, and reduction in muscle spasm (Ebadi et al., 2012).

* Extensibility means the ability of muscles to be stretched to their normal resting length and beyond, to a limited degree.

The nonthermal mechanical effects are proposed to be achieved through the application of pulsed, low-intensity therapeutic ultrasound. A number of studies using animal models of cartilage injury to evaluate the effect of therapeutic ultrasound on the rate of cartilage degeneration have shown benefits. In some of these in vitro studies, pulsed low-intensity therapeutic ultrasound—with temporal average intensities achievable using devices widely available in physical therapy practice—has been used with beneficial effects on cartilage repair (MacIntyre et al., 2013).

In other studies, very-low-intensity pulsed therapeutic ultrasound, such as that used in bone healing systems, has been used. Very-low-intensity pulsed ultrasound slowed progression of cartilage degeneration in the guinea pig model of idiopathic osteoarthritis—particularly in those guinea pigs with early rather than established degeneration. The studies in the animal models suggest that very-low-intensity pulsed ultrasound could stimulate the repair of injured cartilage and, if applied at early stages, may slow the progression of knee osteoarthritis (MacIntyre et al., 2013).

Heat/Cold Therapy

The application of heat and cold to reduce pain or promote comfort is a common intervention. However, there are few studies investigating the impact of heat or cold on pain or function. A meta-analysis of heat and cold for low back pain concluded that continued intermittent use of heat (over a 5-day period) reduced pain intensity and improved function.

Cold therapy includes cold packs, cold baths, vapocoolant sprays, cold compression, continuous-flow cold therapy, and ice massage. Cold alters the pain threshold, reduces local swelling, decreases tissue metabolism and bleeding, and decreases muscle spasm and spasticity. Cold may be contraindicated in patients who are hypersensitive to cold (as in Raynaud's phenomenon), have marked hypertension, have arteriosclerosis, or have diminished circulation.

Heat can usually be initiated 48 hours following an operation or injury, and is commonly used in combination with other treatments. Thermal agents are used to apply heat superficially or as deep-heating applications. Superficial methods include hot packs, warm whirlpools, and paraffin. Deep heat, such as ultrasound, can increase the temperature of the tissues 3 to 5 centimeters in depth. Heat has the advantage of inducing relaxation and decreasing joint stiffness, muscle spasm, and guarding. It assists in increasing range of motion and increases superficial circulation.

Dry Needling

Dry needling is the penetration of a needle through the skin without introduction of any drug (Chou et al., 2012). Dry needling uses a thin, flexible needle to stimulate underlying myofascial trigger points,* and muscular and connective tissues for the management of neuro-musculoskeletal pain and movement impairments. Dry needling is used by physical therapists to treat pain and reduce or restore impairments of body structure and function (APTA, 2013).

*Trigger point: a hyperirritable nodule or knot in the fascia surrounding the muscle.

Although there is strong evidence to support the use of dry needling in the treatment of various neuromuscular pain syndromes, the American Physical Therapy Association and several state boards of physical therapy have narrowed their definition of dry needling to an "intramuscular" procedure. More specifically, these professional organizations have equated the procedure of dry needling with the terms *intramuscular manual therapy (IMT)* or *trigger point dry needling (TDN)* (Dunning et al., 2014).

In June 2016 the American Medical Association adopted a policy directing that physical therapists and other non-physicians practicing dry needling should—at a minimum—have standards that are similar to the ones for training, certification, and continuing education that exist for acupuncture. "Lax regulation and nonexistent standards surround this invasive practice. For patients' safety, practitioners should meet standards required for licensed acupuncturists and physicians," announced AMA board member Russell W.H. Kridel (AMA, 2016c).

Manual Therapy

Manual therapy is an important and specialized area within many professions, particularly physical therapy, osteopathy, and chiropractic. Manual therapists use a variety of nonsurgical techniques directed to the patient's spine and extremities for the purpose of assessing, diagnosing, and treating various symptoms and conditions. Manual therapy techniques can be categorized into four major groups: (1) manipulation (thrust manipulation), (2) mobilization (non-thrust manipulation), (3) static stretching, and (4) muscle energy techniques. The definition and purpose of manual therapy varies across healthcare professionals (Clar et al., 2014).

Manual therapists mobilize areas of the spine or other painful joints using their hands, forearms, or elbows to apply a force with a therapeutic intent. Manual therapy approaches and techniques include massage, joint mobilization/manipulation, myofascial release, nerve manipulation, strain/counterstrain, and acupressure (Smith, 2007).

Spinal manipulation and mobilization are commonly used treatment modalities for back pain, particularly by physical therapists, osteopaths, and chiropractors. Their use has been steadily increasing in the West. For example, in the United States, 33% of people with low back pain are treated by a chiropractor. A United Kingdom-based study surveyed the use of chiropractic/osteopathy services for back pain in a randomly selected sample of adults aged 18 to 64 years living in four counties of England. Of the respondents with back pain, 13.4% had consulted with osteopaths or chiropractic practitioners (Clar et al., 2014).

A 2010 review of scientific evidence on manual therapies for a range of conditions concluded that spinal manipulation or mobilization may be helpful for several conditions in addition to back pain, including migraine and neck-related headaches, neck pain, upper- and lower-extremity joint conditions, and whiplash-associated disorders. The review also identified a number of conditions for which spinal manipulation or mobilization appears *not* to be helpful (eg, asthma, hypertension, menstrual pain) or the evidence is inconclusive (eg, fibromyalgia, mid-back pain, premenstrual syndrome, sciatica, temporomandibular joint disorders) (NCCIH, 2012).

Mobilization

Mobilization is a manual therapy technique applied to painful or restricted joints that uses low grade, low velocity, small or large amplitude passive movement and neuromuscular techniques within a patient's range of motion. Mobilization is typically used by physical and occupational therapists and chiropractors, often in conjunction with patient education, heat/cold therapy, and therapeutic exercise.

One such mobilization technique was developed by Geoffrey Maitland, an Australian physiotherapist who developed a system of manual therapy for the treatment of joint and back pain. In this technique, joint mobilization is gently applied by hand following a thorough and detailed subjective and objective physical examination. Mobilization involves a nearly imperceptible (Grade I) or slightly more forceful (Grades II, III, and IV) oscillation of the affected joint.

The gentle oscillations may have an inhibitory effect on the perception of painful stimuli by repetitively stimulating mechanoreceptors that block nociceptive pathways at the spinal cord or brainstem levels. These non-stretch motions help move synovial fluid to improve nutrition to the cartilage (Kumar et al., 2012).

Gentle mechanical force during mobilization may include breaking up of adhesions, realigning collagen, or increasing fiber glide when specific movements stress specific parts of the capsule. Mobilization techniques may increase or maintain joint mobility by inducing biologic changes in synovial fluid (Kumar et al., 2012).

Mobilization has an effect on blood flow in the vessels supplying the nerve fibers and synovial fluid surrounding damaged, avascular articular cartilage. This facilitates an exchange of fluid, which increases venous drainage and disperses chemical irritants. Mobilization causes a reversal of the ischemia-edema-inflammation cycle and reduces joint effusion. It also relieves pain by reducing the pressure over the nerve endings (Kumar et al., 2012).

Manipulation

The velocity of the technique has been the subject of great debate. The merits of high-velocity techniques (thrust techniques) have been compared to low-velocity techniques (non-thrust techniques). Some have described high-velocity techniques as *manipulation* and low-velocity techniques as *mobilization* while others consider these terms synonymous (Smith, 2007).

It is thought that spinal manipulation affects muscles, tendons, ligaments, and fascia, altering orientation or position of anatomic structures, unbuckling some structures, releasing entrapped structures, or disrupting adhesions. In 2007 guidelines, the American College of Physicians and the American Pain Society included spinal manipulation as one of several treatment options for practitioners to consider when low back pain does not improve with self-care. A 2010 Agency for Healthcare Research and Quality (AHRQ) report noted that complementary health therapies, including spinal manipulation, offer additional options to conventional treatments, which often have limited benefit in managing back and neck pain. The AHRQ analysis also found that spinal manipulation was more effective than placebo and as effective as medication in reducing low-back pain intensity (NCCIH, 2013).

Complementary, Alternative, and Integrative Therapies

Complementary, alternative, and integrative health approaches are often used to treat or manage disorders or symptoms associated with acute and chronic pain. Common complementary health approaches include mind and body interventions such as meditation, spinal manipulation, yoga, massage, tai chi, and acupuncture. A variety of natural products, including herbs, dietary supplements, and prebiotic or probiotic products are also commonly used (NCCIM, 2016a).

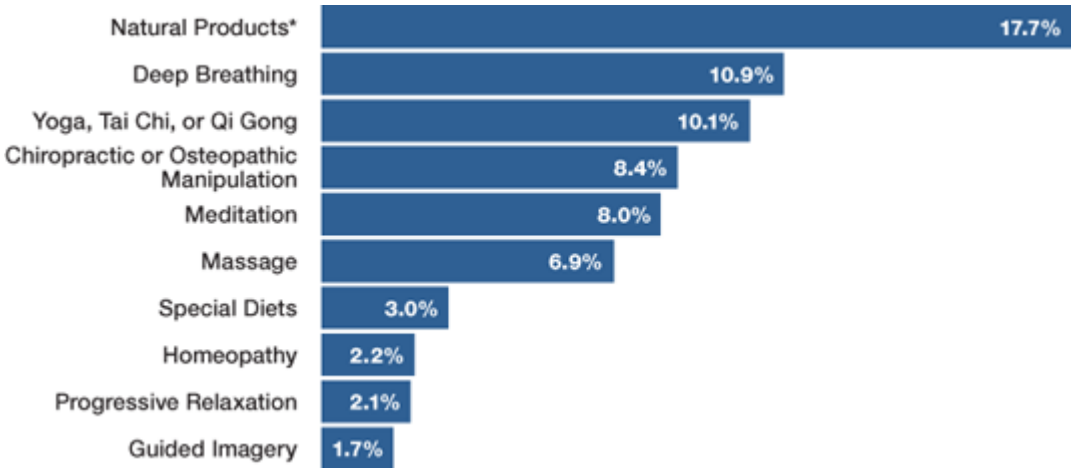
The most current and comprehensive picture of Americans' use of complementary health approaches has been developed under the National Center for Complementary and Integrative Health (NCCIH) through two National Health Interview Surveys (NHIS) conducted by the National Center for Health Statistics at the CDC in 2002, 2007, and 2012.

The surveys showed:

- Non-vitamin, non-mineral dietary supplements were the most commonly used complementary health approach at each of the three time points.
- Whether used independently or as a part of other approaches, deep-breathing exercises were the second most commonly used complementary health approach.

- The use of yoga, tai chi, and qi gong increased linearly over the three time points, beginning at 5.8% in 2002, 6.7% in 2007, and 10.1% in 2012. Yoga was the most commonly used of these three approaches at all three time points.
- There was a small but significant linear increase in the use of homeopathic treatment, acupuncture, and naturopathy.
- The use of chiropractic care or chiropractic and osteopathic manipulation was the fourth most commonly used approach.
- Meditation was used by 7.6% of adults in 2002, 9.4% in 2007, and 8.0% in 2012, keeping it among the top five most commonly used approaches for each time point.
- Ayurveda, biofeedback, guided imagery hypnosis, and energy healing therapy had a consistently low prevalence and had no significant changes across the three time points (Clarke et al, 2015).

10 Most Common Complementary Health Approaches Among Adults—2012



*Dietary supplements other than vitamins and minerals.
Source: Clarke TC, Black LI, Stussman BJ, Barnes PM, Nahin RL. Trends in the use of complementary health approaches among adults: United States, 2002–2012. National health statistics reports; no 79. Hyattsville, MD: National Center for Health Statistics, 2015.

In the United States, more than 30% of adults and about 12% of children use healthcare approaches developed outside of mainstream Western, or conventional, medicine. When describing these approaches, people often use *alternative* and *complementary* interchangeably, but the two terms refer to different concepts:

- If a non-mainstream practice is used together with conventional medicine, it is considered complementary.
- If a non-mainstream practice is used in place of conventional medicine, it is considered alternative. True alternative medicine is uncommon. Most people who use

non-mainstream approaches use them along with conventional treatments. (NCCIH, 2016b)

Complementary therapies differ from Western medicine in at least four ways:

1. They are often not covered by health insurance providers.
2. There is limited, but growing, scientific evidence about their safety and effectiveness.
3. They view the patient as a whole (*holistically*).
4. They view the body as more than the sum of its parts.

Integrative Pain Management

Integrative healthcare brings conventional and complementary approaches together in a coordinated way. Researchers are currently exploring the potential benefits of integrative health in a variety of situations, including pain management for military personnel and veterans, relief of symptoms in cancer patients and survivors, and programs to promote healthy behaviors (NCCIH, 2016b).

Complementary and integrative medicine provide patient-centered care, addressing physical, emotional, mental, social, spiritual, and environmental influences that affect a person's health. They use the most appropriate interventions from an array of disciplines to heal illness and help people regain and maintain optimal health. Because integrative medicine is a "whole systems" approach that employs **multiple modalities**, as opposed to an isolated complementary therapy, studying outcomes is more challenging than evaluating an isolated pharmaceutic or botanic intervention (Abrams et al., 2013).

Integrative medicine is a popular approach to pain management, although for a large, structured healthcare organization, integrating diverse practices can be challenging. Healthcare organizations must balance supply and demand for services as well as combine the integrative medicine program into the established culture of a large hospital (Nate et al., 2015).

In an effort to capture data on patient-reported outcomes in integrative medicine, a number of leading clinics have collaborated to form the first practice-based research network in the field: the Bravewell Integrative Medicine Research Network (BraveNet). BraveNet's initial project involved 4182 patients seeking care at nine clinical sites. The data confirmed the high utilization of integrative medicine by chronic pain patients and led to a Study on Integrative Medicine Treatment Approaches for Pain (SIMTAP). In this study, researchers reported the impact of a six-month integrative approach on chronic pain and a number of other related patient-reported outcome measures (Abrams et al., 2013).

In the SIMTAP study, practitioners at each of the sites devised treatment plans for participating chronic pain patients. All BraveNet sites include integrative physicians, acupuncturists, mindfulness instructors, and yoga instructors; some also incorporate massage therapists, manual medicine therapists, fitness and movement specialists, dieticians and nutritionists, psychologists, healing touch therapists, and other energy practitioners. The results of this study suggest that the tailored, multimodal approach to treating chronic pain that combined conventional and complementary therapies improves quality of life and reduces pain, stress, and depressive symptoms (Abrams et al., 2013).

How complementary and integrative therapies affect the nervous system and other physiologic systems such as organs and tissues, remains understudied. Such studies are challenging for both the complementary and integrative health and the research communities. Nevertheless, recent advances in genomics, neuroscience, stem cells, systems biology, neuroimaging, and computational modeling offer excellent resources and opportunities for innovative studies of complementary health approaches (NCCIH, 2016a).

For the treatment of chronic pain among active-duty military personnel and veterans, the National Center on Complementary and Integrative Health (NCCIH), the U.S. Department of Veterans Affairs and other agencies are sponsoring research to see whether integrative approaches can help patients with chronic pain. NCCIH-funded studies are testing the effects of adding mindfulness meditation, self-hypnosis, or other complementary approaches to pain management programs for veterans. The goal is to help patients feel and function better and reduce their need for pain medicines that can have serious side effects (NCCIH, 2016b).

Some cancer treatment centers are using integrative healthcare programs such as acupuncture and meditation to help manage symptoms and side effects for patients who are receiving conventional cancer treatment. Although research on the potential value of these integrative programs is in its early stages, some NCCIH-funded studies have had promising results:

- Cancer patients who receive integrative therapies while in the hospital have less pain and anxiety.
- Massage therapy may lead to short-term improvements in pain and mood in patients with advanced cancer.
- Yoga may relieve the persistent fatigue that some women experience after breast cancer treatment. (NCCIH, 2016b)
- A growing body of evidence supports the efficacy and safety of non-drug and complementary health approaches to reduce pain and increase patients' coping ability and general well-being. Many of these techniques have the potential to reduce the

need for costly pain medications with harmful side effects. At a minimum, providers should have a basic understanding of the scientific evidence on complementary health approaches so that patients will not be reluctant to disclose their use.

- Non-drug interventions for pain management introduced early in the course of an illness are more likely to succeed because they can be learned and practiced by patients while they have sufficient strength and energy. Patients and their families should be given information about and encouraged to try several strategies, and to select one or more mind-body techniques for regular use.

Mind and Body Practices

Mind-body techniques(also called *cognitive/behavioral techniques*) focus on the interactions among the brain, mind, body, and behavior, with the intent of using the mind to affect physical function and promote health. The concept that the mind is important in the treatment of illness is integral to the healing approaches of traditional Chinese medicine (TCM) and Ayurvedic medicine,* which are both more than two thousand years old (NCCIH, 2016b).

*Ayurvedic medicine is a healing system from India emphasizing balance among body, mind, and spirit.

Mind-body techniques require that patients understand the information and instructions involved; therefore, these techniques are not appropriate for patients with significant cognitive impairment. Cognitive therapies require cooperation and practice and are thus contraindicated for use with patients who are uncooperative, unable, or unwilling to practice the necessary behaviors.

Mind and body practices include a large and diverse group of procedures and techniques administered or taught by a trained practitioner or teacher. The 2012 National Health Interview Survey showed that yoga, chiropractic and osteopathic manipulation, meditation, and massage therapy are among the most popular mind and body practices used by adults. The popularity of yoga has grown dramatically in recent years, with almost twice as many U.S. adults practicing yoga in 2012 as in 2002 (NCCIH, 2016b).

Other mind and body practices include acupuncture, relaxation techniques (eg, breathing exercises, guided imagery, progressive muscle relaxation), tai chi, qi gong, healing touch, hypnotherapy, and movement therapies (eg, Feldenkrais method, Alexander technique, Pilates, Rolfing Structural Integration, Trager psychophysical integration) (NCCIH, 2016b).

The amount of research on mind and body approaches varies widely depending on the practice. For example, researchers have done many studies on acupuncture, yoga, spinal manipulation, and meditation, but there have been fewer studies on some other practices (NCCIH, 2016b).

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Chiropractic Medicine

Chiropractic is a healthcare profession that focuses on the relationship between the body's structure—mainly the spine—and its functioning. Although practitioners may use a variety of treatment approaches, they primarily perform adjustments (manipulations) to the spine or other parts of the body with the goal of correcting alignment problems, alleviating pain, improving function, and supporting the body's natural ability to heal itself (NCCIH, 2012).

Chiropractic Treatment

A chiropractor demonstrating an adjustment on the patient's thoracic spine. Source: Michael Dorausch, Wikimedia Commons.

In the United States, chiropractic is often considered a complementary health approach. According to the 2007 National Health Interview Survey (NHIS), which included a comprehensive survey of the use of complementary health approaches by Americans, about 8% of adults and nearly 3% of children had received chiropractic or osteopathic manipulation in the past 12 months (NCCIH, 2012).

Massage Therapy

Massage is a centuries-old healing art, practiced in ancient China, Japan, India, the Arabic nations, Egypt, Greece, and Rome. Massage is sometimes considered a relaxation therapy because that is one of its major effects.

Massage therapy, one of the complementary and alternative treatments, is defined as a therapeutic manipulation using the hands or a mechanical device that includes numerous specific and general techniques often used in sequence, such as effleurage (stroking), petrissage (kneading), and percussion. It may be the earliest and most primitive tool used to improve pain. The most ancient references to the use of massage come from China (circa 2700 B.C.). Common types of massage therapy include Swedish massage, Shiatsu, Rolfing, reflexology, myofascial release, and craniosacral therapy

Massage Therapy

Photograph of a man massaging a woman's foot using baby oil as a lubricant. Attribution: Lubyanka, Wikimedia Commons.

(Kong et al., 2013).

In general, massage therapists press, rub, and otherwise manipulate the muscles and soft tissues of the body. They use massage not only to relieve pain but also to rehabilitate sports injuries; reduce stress, anxiety, and depression; increase relaxation; and aid general well-being.

Massage is effective in general pain management because it mechanically assists in venous and lymphatic flow, improves skin integrity and mobility, desensitizes tissue, and provides comfort and psychological support. Massage may be used to stretch muscles and is generally used in combination with other treatments.

Massage can also be helpful for older adults. Nurse researchers who reviewed 21 studies on massage in elders found that slow-stroke back massage and hand massage significantly increased relaxation across all care settings (Harris & Richards, 2010).

Massage has proved effective in reducing pain, anxiety, and tension after cardiovascular surgery. In a study at Mayo Clinic, patients were randomized either to receive a massage or to have quiet relaxation time following surgery. Those who received massage therapy had significantly less pain, anxiety, and tension than the control group (Braun et al., 2012).

Burn victims suffer some of the most severe physical and psychological pain imaginable. Turkish researchers found that massage therapy reduced pain, itching, and anxiety levels in adolescents in the burn unit of a large university hospital. Massage therapy reduced all three symptoms from the first day of the study until the last (Parlak et al., 2010).

Researchers in Spain studied the effects of massage combined with myofascial release therapy* on patients diagnosed with fibromyalgia. Patients were randomized to receive either the massage-myofascial release therapy or a sham treatment during 20 weekly sessions. Immediately after treatment and 1 month later, the researchers found that anxiety levels, quality of sleep, pain, and quality of life were improved in the experimental group (Castro-Sánchez et al., 2011).

*Myofascial release therapy is a type of physiotherapy requiring special training that aims to release myofascial restrictions at the sites of certain painful points called trigger points.

A 2010 AHRQ evidence report—which summarized, critically appraised, and compared the evidence on clinical benefits, costs, and harms associated with use of complementary and integrative medicine and other therapies for the treatment of adults with low back, neck, and thoracic pain—found that massage was superior to placebo or no treatment in reducing pain and disability immediately post treatment only in subjects with acute/subacute but not in subjects with chronic low back pain (AHRQ, 2014).

Massage was:

- Significantly better than relaxation or physical therapy in reducing chronic nonspecific low back pain intensity but not range of motion, immediately after the treatment
- Better than no treatment in reducing immediate-term post treatment pain intensity in subjects with chronic or unknown duration of nonspecific pain
- Better than placebo in reducing neck pain intensity immediately after the treatment in subjects with acute/subacute or unknown duration of nonspecific pain
- Not different from placebo in improving well-being or range of motion in subjects with chronic pain (AHRQ, 2014)

Meditation

Meditation refers to a group of techniques rooted in ancient religious and spiritual traditions. It is used to increase calm, promote relaxation, improve psychological balance, cope with illness, or enhance overall health and well-being. People also use meditation for various health problems, including anxiety, pain, depression, stress, insomnia, and physical or emotional symptoms associated with chronic illness and their treatment.

Mindfulness meditation is one of the most studied and practiced forms of meditation in America. Pioneered at the University of Massachusetts Medical School's Stress Reduction Clinic in 1979 by Jon Kabat-Zinn, **mindfulness-based stress reduction (MBSR) meditation** has been shown to be effective in reducing depression and anxiety, both known to influence pain.

Monastic Practitioner of Meditation

Phra Ajan Jerapunyo, Abbot of Watkungtaphao meditating in Sirikit Dam, Thailand. Source: Wikimedia Commons.

Previous research has shown that mindfulness meditation helps relieve pain, but researchers have been unclear about how the practice induces pain relief—specifically, if meditation is associated with the release of naturally occurring opiates. Results from a new study, funded in part by the NCCIH, demonstrate that mindfulness meditation does not rely on the endogenous opioid activity to reduce pain, which is an important consideration for using meditation to treat chronic pain.

In this study, conducted by researchers at Wake Forest School of Medicine and Cincinnati Children's Hospital Medical Center, researchers recorded pain reports in 78 healthy adults during meditation or a non-meditation control in response to painful heat stimuli and intravenous administration of the opioid antagonist naloxone (a drug that blocks the transmission of opioid activity) or placebo saline. Participants were randomized to one of four treatment groups: (1) meditation plus naloxone; (2) control plus naloxone; (3) meditation plus saline; or (4) control plus saline. People in the control groups were instructed to "close your eyes and relax until the end of the experiment" (NCCIH, 2016c).

Researchers found that participants who meditated during saline administration had significantly lower pain intensity and unpleasantness ratings compared to those who did not meditate while receiving saline. Importantly, data from the meditation plus naloxone group showed that naloxone did not block meditation's pain-relieving effects. No significant differences in reductions of pain intensity or pain unpleasantness were seen between the meditation plus naloxone and the meditation plus saline groups. Participants who meditated during naloxone administration also had significantly greater reductions in pain intensity and unpleasantness than the control groups (NCCIH, 2016c).

These findings demonstrate that mindfulness meditation reduces pain independent of opioid neurotransmitter mechanisms. The researchers noted that because opioid and non-opioid mechanisms of pain relief interact synergistically, the results of this study suggest that combining mindfulness-based and pharmacologic/non-pharmacologic pain-relieving approaches that rely on opioid signaling may be particularly effective in treating pain (NCCIH, 2016c).

Hypnotherapy

> In hypnotherapy a patient attempts to enter into a trance-like state in order to cope better with complaints such as pain, anxiety, and stress by actively diverting their attention towards relaxing thoughts.
>
> Katja Boehm, Markus Horneber
> and the CAM-Cancer Consortium

Hypnotherapy involves the power of suggestion by a hypnotherapist or by the patients themselves. Hypnotic techniques have proven to be useful for different kind of pain—especially pain associated with burns, cancer, invasive medical procedures, headaches, musculoskeletal conditions, irritable bowel syndrome, and fibromyalgia (Ardigo et al., 2016). Hypnotherapy may help reduce pain, decrease anxiety, and improve immune function. It overlaps with guided imagery and visualization, creating an altered state of awareness. Hypnosis enhances the ability to focus attention to the exclusion of other stimuli. It may take seconds to minutes to achieve entrance to a hypnotic state.

The practice of self-hypnosis has been shown in studies to be an important element in the long-term control of chronic pain. Self-hypnosis can be taught to the patient as a tool to modify behavior regarding nociceptive perception. It allows patients to take an active part in their own pain management using personal resources and experiences (Ardigo et al., 2016).

Hypnosis is thought to be beneficial for:

- Decreasing perioperative pain
- Reducing analgesic and sedative requirements
- Decreasing post operative anxiety
- Improving patient satisfaction and mood (Ardigo et al., 2016)

Hypnosis usually requires a trained professional, but even then it may not work for all patients, perhaps because of the social stigma associated with its use. However, the efficacy of hypnosis in relieving pain has been shown in cancer patients (Boehm & Horneber, 2016), burned children (Bayat et al., 2010), in adults with chronic and acute pain, and in older hospitalized adults (Ardigo et al., 2016).

Biofeedback

Biofeedback-assisted relaxation uses an external device to help the patient learn to relax specific muscle groups. Applying biofeedback requires special equipment and clinical training. Relaxation techniques may prove beneficial by reducing muscular arousal and distracting the patient from painful sensations. These techniques also reduce anxiety and increase the patient's sense of control.

Biofeedback is a popular intervention alone or within cognitive-behavioral or multidisciplinary pain treatments. Biofeedback is a procedure in which patients' bodily responses, such as muscle tension, heart rate, or skin temperature, are monitored and reported to the patient through an auditory or visual modality. In electromyographic feedback (EMG-FB), one of the most common types of feedback, patients learn to control and to alleviate their muscle tension (Glombiewski et al., 2013).

Biofeedback is often called a "psychophysiologic intervention," although its mechanisms are more psychological than physiologic. The effectiveness of EMG biofeedback is mediated by cognitive changes, such as increases in self-efficacy and coping strategies induced through biofeedback training, rather than primarily by learned physiologic control (Glombiewski et al., 2013).

Electroencephalographic feedback (EEG-FB) is often referred to as "neurofeedback" or "EEG biofeedback." EEG-FB records and reports back EEG waves. Patients are able to learn to influence evoked potentials and event-related potentials, and slow cortical potentials and EEG frequencies (Glombiewski et al., 2013).

Biofeedback has been found to be beneficial in the rehabilitation of headache and, in some studies, of chronic back pain and several other pain disorders (eg, temporomandibular or TMJ disorders). Findings on low back pain, however, show little to no improvement. A meta-analysis of the efficacy of biofeedback in fibromyalgia found that EMG-BFB was effective for the short-term reduction of pain intensity in fibromyalgia patients (Glombiewski et al., 2013).

Music Therapy

Music therapy dates back to Aristotle and Plato. In 1944 in the United States, Michigan State University offered the first music-therapy degree program worldwide (Schmid & Ostermann, 2010). Sedating or soothing music is instrumental, rhythmic, and 60 to 80 beats per minute. In much of the research, musical pieces are selected from five types of music: synthesizer, harp, piano, orchestra, or slow jazz.

Two types of music interventions are distinguished: live music therapy and recorded music. In live music therapy a trained music therapist plays music and applies various therapeutic techniques to reach a therapeutic goal. One of these techniques is known as **music entrainment**, in which the music therapist first uses music to match the patient's physiologic and emotional states and then gradually changes the music to modify the patient's state. Recorded music, on the other hand, implies listening to prerecorded music selected by a music therapist or by patients themselves, provided they are old enough to do so (van der Heijden et al., 2015).

Research indicates that music therapy can be effective in reducing both chronic and acute pain in children and adults. A review of randomized clinical trials found that music therapy significantly reduced pain, anxiety, and distress in children undergoing orthopedic, cardiac, and day surgery procedures (van der Heijden et al., 2015). Music also reduced pain, anxiety, and muscle tension in children during burn dressing changes (Tan et al., 2010).

Effective music therapy requires a professional music therapist who can tailor the intervention to the individual patient. Music may accompany other mind-body techniques such as guided imagery, gentle massage, or bodywork. Home-based music programs are gaining importance for severely impaired or older adults who are unable to attend daycare centers where music is provided (Schmid & Ostermann, 2010).

Traditional Chinese Medicine

Traditional Chinese medicine (TCM) is a holistic medical system for diagnosis, prevention, and treatment of diseases. It has been an integral part of Asian cultures for thousands of years. TCM uses therapies such as acupuncture, massage, and herbal medicine and is characterized by its underpinning theoretical guide—the philosophy of yin-yang balance (Xu et al., 2013).

Traditional Chinese medicine views the body as a system of channels through which energy flows. The Chinese call this energy **qi** or **chi**. Disease or illness is caused when the energy gets blocked or stagnates and doesn't flow freely through the body. Herbs, acupuncture, qi gong, tai chi, and Chinese massage are mind-body techniques to help unblock the flow of chi through normal channels and thereby restore health. Practitioners of traditional Chinese medicine devise individualized treatment plans based on each patient's unique diagnosis rather than following a standard intervention based on the complaint (Abrams et al., 2013).

In a seminal randomized controlled trial of Chinese herbal medicine for treatment of irritable bowel syndrome, investigators compared a standard and an individualized Chinese herbal formulation to a placebo. Results showed that, compared with patients in the placebo group, patients in the two active treatment groups had improvements in bowel symptoms as rated by both the patients and their gastroenterologists at the end of the 16-week intervention. However, at follow-up 14 weeks after completion of the treatment, only the individualized herbal medicine treatment group maintained improvement (Abrams et al., 2013).

In China traditional medicine is one of the conservative treatments for lumbar disc herniation, and several studies have confirmed that it has certain effects on low back pain caused by lumbar disc herniation. Treatments include acupuncture, oral administration of Chinese medicine, external application of Chinese medicine, Chinese tuina (massage), and TCM-characteristic functional exercise. Clinically, these therapeutic methods are not used alone but in combination (Yuan et al., 2013).

In the treatment of pain due to lumbar disc herniation, different traditional Chinese medicine therapies have different advantages. Pain is the main symptom in the acute stage and acupuncture has good analgesic effect. Lumbar dysfunction is the main symptom in the remission stage and Chinese massage has good effect on improving dysfunction. Oral Chinese herbal formulae, external use of Chinese medicine, and Chinese herbal injection also showed good effect in relieving pain and improving dysfunction caused by lumbar disc herniation (Yuan et al., 2013).

Acupuncture

The term **acupuncture** describes a family of procedures involving the stimulation of anatomic points on the body using a variety of techniques. The acupuncture technique most often studied scientifically involves penetrating the skin with hair-thin metallic needles that are inserted a few millimeters into the skin.

According to *The Yellow Emperor's Inner Canon*, compiled between 206 B.C.E. and 220 C.E., there are meridians and collaterals in the human body comprising a network of channels through which chi and blood flow. Diseases, or pain, are caused by chi stagnation or blood stasis in the channels. Acupuncture treats this by inserting a fine needle into the skin at designated points (acupuncture points) (Zhang et al., 2013). An appropriate choice of the 361 classic acupuncture points is believed to restore balance in the body. Modern acupuncturists use not only traditional meridian acupuncture points, but also non-meridian or extra-meridian acupuncture points (AHRQ, 2010). Acupuncture promotes the circulation of chi and blood and harmonizes healthy and pathogenic chi in the channels (Zhang et al., 2013).

Acupuncture Sites

Source: NCCIH.

Acupuncture is not a single standardized intervention. In routine clinical practice, the same patient may receive acupuncture with different characteristics from different practitioners. These differences include specific characteristics of treatment—such as the number and frequency of sessions or the additional use of electrical stimulation—as well as the overall "style" of acupuncture. A distinction is often made between traditional Chinese acupuncture—in which diagnosis and treatment are based on a theoretical framework involving patterns of symptoms and concepts such as yin, yang, and the strength of chi—and westernized approaches, involving a neuro-anatomical basis for diagnosis and treatment (MacPherson et al., 2013).

Application of Acupuncture Needle

Researchers from the Acupuncture Trialists' Collaboration, a group that was established to synthesize data from high-quality randomized trials on acupuncture for chronic pain, conducted an analysis of individual patient data from 29 high-quality randomized controlled trials, including a total of 17,922 people. These trials investigated the use of acupuncture for back and neck pain, osteoarthritis, shoulder pain, or chronic headache (Vickers, 2012).

Basic acupuncture. Photo by Kyle Hunter, public domain.

For all pain types studied, the researchers found modest but statistically significant differences between acupuncture and simulated acupuncture approaches, and larger differences between acupuncture and no-acupuncture controls. (In traditional acupuncture, needles are inserted at specific points on the body. Simulated acupuncture includes a variety of approaches that mimic this procedure; some approaches do not pierce the skin or use specific points on the body.) The sizes of the effects were generally similar across all pain conditions studied (Vickers, 2012).

These findings suggest that the total effects of acupuncture, as experienced by patients in clinical practice, are clinically relevant. They also noted that their study provides the most robust evidence to date that acupuncture is more than just placebo and a reasonable referral option for patients with chronic pain (Vickers, 2012).

How acupuncture works to relieve pain and other symptoms is still incompletely understood, although functional MRI (fMRI) studies are beginning to provide some answers. Acupuncture seems to change the way the brain perceives and processes pain. Using fMRI in 18 volunteers, German researchers viewed pain centers in the brain while applying an electrical pain stimulus to subjects' ankles before and after acupuncture treatment. They reported that "activation of brain areas involved in pain perception was significantly reduced or modulated under acupuncture" (Theysohn et al., 2010).

Chinese Tuina (Massage)

Tuina is a form of bodywork or massage therapy that is generally used in conjunction with other types of traditional Chinese medicine. Among non-drug therapies, Chinese tuina is widely used in China for pain management. Tuina is thought to relieve pain by harmonizing the yin and yang of the organs. Tuina is considered gentle on the body and, as such, patients often prefer tuina over pharmaceutical drugs (Zhang et al., 2015).

Tuina involves a wide range of technical manipulations conducted by a practitioner's finger, hand, elbow, knee, or foot applied to muscle or soft tissue at specific body locations. It incorporates many of the principles of acupuncture, including the use of acupoints. For instance, tuina often uses manual techniques such as pushing, rubbing, kneading, or high-intensity, high-frequency patting to clear energy blocks along specific meridians associated with particular conditions (Yang et al., 2014).

According to traditional Chinese medicine, a state of health reflects an underlying state of balance in the chi and blood of the human body. Pain is usually caused by obstruction of chi and consequently of blood circulation in the affected body region. Pathogenic factors such as blood stasis, chi stagnation, phlegm, dampness, and others can be identified as causative factors in the blockage. The central therapeutic goal of tuina is to remove energetic blocks which lead to chi stagnation. This leads to increased circulation and reduction of localized edema, which helps to reduce associated pain (Yang et al., 2014).

The *A-Shi* point in acupuncture theory is the tender, local dermal or muscular area or site on the body surface which reproduces the specific pain being treated when it is gently pressed. Its location indicates the precise place where chi and blood are blocked. Manipulation at the *A-Shi* point is done with the intention of removing the energetic block there to promote the free movement of chi and improve blood circulation in the region. Studies have demonstrated that one mechanism by which this type of massage therapy appears to be clinically beneficial is by reducing inflammation and promoting mitochondrial biogenesis for repair of damaged skeletal muscle (Yang et al., 2014).

Cupping

Cupping therapy (CT) is a traditional Chinese medical treatment which has been practiced for thousands of years. The World Health Organization's defines cupping as a therapeutic method involving the application of suction by creating a vacuum. This is typically done using fire in a cup or jar on the dermis of the affected part of the body (Chi et al., 2016). Many Americans became aware of cupping when they noticed the characteristic marks on the bodies of the Olympic swim team.

Cupping Procedure Showing Resultant Markings

Cupping, as done by acupuncturists or other therapists, utilizes a glass or bamboo cup to create suction on the skin over a painful area or acupuncture point. It is mostly used in Asian and Middle Eastern countries and has been claimed to reduce pain as well as a host of other symptoms. There are two types of cupping. Dry cupping pulls the skin into the cup without drawing blood. In wet cupping the skin is lacerated so that blood is drawn into the cup (Kim et al., 2011).

A woman receiving fire cupping in Haikou, Hainan, China. Anna Frodesiak, Public domain.

Dry cupping creates a vacuum on the skin, with the ensuing negative pressure resulting in capillary rupture. The skin of the localized area becomes flushed and may show petechiae and ecchymosis or bruising, in which the duration is therapeutically beneficial. Cupping has multiple therapeutic functions which include (1) warming the channels to remove cold, (2) promoting chi and blood circulation, (3) relieving swelling, (4) accelerating healing, (5) adjusting body temperature, (6) treating fibromyalgia, (7) for stroke rehabilitation, hypertension, musculoskeletal pain, herpes zoster, (8) treatment of facial paralysis, acne, and cervical spondylosis, and (9) alleviating pain, including chronic neck, shoulder pain, and low back pain (Chi et al., 2016).

Movement-Based Therapies

Movement therapies can include, among others, tai chi, qi dong, yoga, Feldenkrais Method, and Pilates.

Qi Gong and Tai Chi

Tai chi and qi gong are centuries-old, related mind and body practices. They involve certain postures and gentle movements with mental focus, breathing, and relaxation. The movements can be adapted or practiced while walking, standing, or sitting. In contrast to qi gong, tai chi movements, if practiced quickly, can be a form of combat or self-defense (NCCIH, 2015).

Qi gong means, roughly, to cultivate or enhance the inherent functional (energetic) essence of the human being (Jahnke et al., 2010). Qi gong practice includes movement, body posture, mind exercises, concentration, relaxation, and breathing exercises. It is less demanding, both physically and cognitively, than tai chi. Researchers reported that 8 weeks of qi gong training significantly reduced pain for people with osteoarthritis of the knee compared with the control group (Selfe & Innes, 2009).

People Practicing Tai Chi

Tai chi involves slow movements emphasizing balanced postures, regular breathing, and concentration, integrating mind and body. The gentle, slow movements make it particularly useful for those with limited physical strength. Tai chi is used to help manage stress and anger; to improve strength, flexibility, and coordination; to improve lung function; to improve balance; and to reduce pain. Like qi gong, tai chi has been shown to relieve pain and improve function in people with osteoarthritis of the knee (Selfe & Innes, 2009).

Source: NCCIH, public domain.

For patients with painful knee osteoarthritis, tai chi was as helpful as physical therapy in reducing pain and improving physical functioning, according to a new study partly funded by the NCCIH. In this study, 204 patients age 40 or older who had knee pain and proven osteoarthritis of the knee were randomly assigned to standardized group tai chi training (two 1-hour sessions each week for 12 weeks) or standard one-on-one physical therapy (two 30-minute sessions per week for 6 weeks followed by 6 additional weeks of home-based exercises monitored by the research staff). Both groups were then encouraged to continue their tai chi practice or home exercises for a total of 52 weeks. Patients in the two groups had similar decreases in pain and improvements in physical functioning after 12 weeks, and the benefits of treatment were maintained for the full 52 weeks of the study. Patients in the tai chi group had more improvement in depression symptoms and quality of life than those in the physical therapy group (NCCIH, 2016d).

Yoga

Yoga is a mind and body practice with origins in ancient Indian philosophy. The various styles of yoga typically combine physical postures, breathing techniques, and meditation or relaxation. There are numerous schools of yoga. Hatha yoga, the most commonly practiced in the United States and Europe, emphasizes postures (asanas) and breathing exercises (pranayama). Some of the major styles of hatha yoga are Iyengar, Ashtanga, Vini, Kundalini, and Bikram (NCCIH, 2016e).

Yoga typically combines a series of stretching exercises, breathing techniques, and progressive deep relaxation.

A study involving ninety-five people aged 18 to 64 from six health centers in a low-income, predominantly minority area of Boston found that once- or twice-weekly yoga classes relieved pain, improved function, and reduced the need for pain medication in minority and low-income populations with chronic low back pain. The participants had moderate to severe chronic low back pain and significant related impairment. Most were non-white, unemployed or disabled, with annual household incomes of $40,000 or less. The program also included home practice, keeping a log, meditation, and information on yoga philosophy. Participants were allowed to continue with their usual back care (Saper et al., 2013).

Source: Photograph by Kennguru—own work, CC BY 3.0.

Researchers found statistically significant and clinically meaningful improvements in pain and back-related function in both the once per week and twice per week groups. The most benefit was experienced within the first 6 weeks, which may be of interest to clinicians who wonder how much yoga to recommend to patients. Adverse events, mostly musculoskeletal pain, were common; they generally resolved on their own and were not serious (Saper et al., 2013).

In another study, regular and long-term practice of yoga was shown to improve pain tolerance. Findings from the study also showed that yoga practitioners have more gray matter in multiple brain regions compared with individually matched people who did not practice yoga. The study involved 14 experienced yoga practitioners as well as 14 people who did not practice any mind-body techniques. Participants underwent a cold pain tolerance test by immersing a hand in cold water until they could no longer tolerate the pain. Researchers then asked participants about strategies they used to tolerate the pain. The researchers also conducted brain imaging scans to examine the structural differences in gray matter and white matter between the yoga practitioner group and the control group (Villemure et al., 2013).

Researchers found that yoga practitioners tolerated cold pain more than twice as long as the controls. They found no significant difference in total gray matter volume between groups, but yoga practitioners had greater gray matter volume in brain regions related to pain processing, pain regulation, and attention. Across participants, only the increased gray matter in the mid-insular cortex (a portion of the brain believed to play a role in autonomic integration) correlated with the higher pain tolerance (Villemure et al., 2013).

The volume of insular gray matter in yoga practitioners also positively correlated with the duration of yoga practice, suggesting that yoga experience contributed to these structural differences in the brain. In addition, yoga practitioners had increased white matter integrity within the left insula. Finally, the researchers observed that, to tolerate pain, yoga practitioners used cognitive strategies that are integral parts of yoga practice, such as observing the sensation without reacting, accepting the sensation, using the breath, and relaxation while most control participants did not (Villemure et al., 2013).

Other studies suggest that a carefully adapted set of yoga poses may reduce low-back pain and improve function. One NCCIH-funded study of 90 people with chronic low-back pain found that participants who practiced Iyengar yoga had significantly less disability, pain, and depression after 6 months (NCCIH, 2016e).

In a 2011 study, also funded by NCCIH, researchers compared yoga with conventional stretching exercises or a self-care book in 228 adults with chronic low-back pain. The results showed that both yoga and stretching were more effective than a self-care book for improving function and reducing symptoms due to chronic low-back pain (NCCIH, 2016e).

Conclusions from another 2011 study of 313 adults with chronic or recurring low-back pain suggested that 12 weekly yoga classes resulted in better function than usual medical care (NCCIH, 2016e).

Feldenkrais Method

The Feldenkrais Method (FM) is a type of exercise therapy that was developed over a period of decades in the last century by physician Moshe Feldenkrais. The basis of the approach was founded in the human potential for learning how to learn. Feldenkrais developed an experiential process, or set of processes, whereby an individual or a group could be guided through a series of movement- and sensation-based explorations (Hillier & Worley, 2015).

The purpose of the explorations is to learn to sense the difference between two or more movement options and discern which feels easier and is performed with less effort. This is compared with experiencing less favorable feedback such as pain, strain, or discomfort. Participants are encouraged to try many alternative movements to increase their awareness of distinctions and improvements. Thus the process of intention, action, gaining feedback, making decisions, and re-enacting with adaptations constitutes the learning framework in a somatic context (Hillier & Worley, 2015).

Because it promotes gentle movement within a comfortable range of motion, the Feldenkrais Method is particularly effective for older adults experiencing pain and stiffness from arthritis. It is taught in two parallel forms, Awareness Through Movement (conducted as a group exercise) and Functional Integration (one-on-one approach) (Webb et al., 2013).

Awareness Through Movement lessons are verbally guided explorations of movement that are about 30–60 minutes long. Each lesson explores movement related to a particular function such as walking, rolling, or sitting to enhance awareness of how movements are performed and invite the participant to investigate how they might expand their action and ability to function. The lessons address habitual patterns of movement and expand a person's self-image. By exploring novel movement sequences, attention is drawn to parts of the self which the person may not be aware of and may have excluded from their functioning. The method aims for a heightened self-awareness, an expansion of a person's repertoire of movement, and improved functioning where the whole body cooperates in movement and where maximum efficiency is achieved with minimum effort. Dr. Feldenkrais described the aim of the method as "a person who is organized to move with minimum effort and maximum efficiency, not through muscular effort, but through increased consciousness of how movement works" (Webb et al., 2013).

Video (3:33): Feldenkrais for Everyday Life

https://www.youtube.com/watch?v=uCM_C0Ly0Dc&index=4&list=PLx83c-HVFBfA5quYOUCc3F0z4ox3K054-

Single, randomized controlled studies of Feldenkrais exercises have reported statistically significant, positive benefits compared to control interventions and include the following improvements:

- Improved neck flexion and less perceived effort after a single Feldenkrais lesson for neck comfort
- Reduced prevalence of neck pain and disability in symptomatic women after Feldenkrais (individual and group sessions compared to conventional care or home exercises) and
- Reduced perceived effort in Feldenkrais group for people with upper torso/limb discomfort (Hillier and Worley, 2015)

The Moving with Ease program is a selection of Awareness Through Movement lessons from the Feldenkrais Method. Because the lessons are gentle and enjoyable, they may enable people with osteoarthritis to move more easily and better manage their pain. The self-exploratory nature of the classes provides an opportunity for participants to become aware of how they move, thus learning to minimize their functional limitations. The lessons become a form of self-management that addresses a significant aspect of the process of disablement in people with osteoarthritis (Webb et al., 2013).

In a small Australian study seeking to understand if participation in a Moving with Ease program improved mobility and decreased pain in participants with osteoarthritis, feedback was positive. When asked to describe what they had learned by participating in the program, comments included:

- "How exercise/movement is crucial to managing pain."
- "To exercise where it is comfortable, not to force it."
- "To walk with a more fluid, gentle motion."
- "I learnt to incorporate some of the exercises into my daily life."
- Participants were asked to comment on their experience of pain and, in particular, the pain associated with their osteoarthritis, after participating in the program. Ten of the fifteen participants said their pain level had improved, three were unsure and two said they had not noticed any difference. Comments included "The pain is continual, but I manage it better," "At the end of the session I was free from pain and felt energized," "I can experience less pain in the knees, which is where the osteoarthritis appears for my body," "The lessons…eased the pain in my lower back," "No pain in the knees when going up stairs," and "It is not a cure, however it is the best 'exercise' I have experienced for managing my osteoarthritis" (Webb et al., 2013).

Pilates Exercise

Pilates exercise is named after its founder, Joseph Pilates, who developed a series of exercises in the 1920s to encourage physical and mental conditioning. Core stability, strength, and flexibility are emphasized in Pilates exercise, as is control of movement, posture, and breathing. All of these aspects of Pilates exercise may benefit people with chronic low back pain, as exercises with similar features have been successful in reducing pain and improving functional ability (Wells et al., 2014).

Pilates teacher using verbal and tactile feedback to ensure proper form. Courtesy of Anne Kohler. Source: Wikimedia Commons.

Barriers to Effective Pain Management

> The [Institute of Medicine] committee [has] identified several important barriers to adequate pain care in the United States. These include the magnitude of the problem, provider attitudes and training, insurance coverage, cultural attitudes of patients, geographic barriers, and regulatory barriers.
>
> Institute of Medicine, 2011

Consider the following barriers to effective pain management.

Where are the tools and the time, and how am reimbursed? Those are the issues and barriers in pain management. Given the time constraints in an office setting, how can I improve my expertise and how can I be reimbursed? Regardless of the type of pain, it's fair to say that anyone who has chronic, prolonged pain is going to have psychological issues that must be addressed. Where you see a patient on the continuum of their pain is going to influence the provider and what sort of treatment modalities you offer.

We are being slammed with all these new position papers and regulations about abuse of opioids saying "Hey, you guys, this is all your fault and you should have been doing more"—even though the insurance companies aren't providing more reimbursement, nor is anyone providing practical tools to enhance provider training, skills, and all those things. For liability purpose the focus is going to shift onto the provider and that's going to make us reluctant to prescribe. The onus is on the prescriber not to prescribe. Treating pain properly and effectively is an order of magnitude more complicated than it used to be because of these issues and barriers.

Board Certified Family Nurse Practitioner, California

The complexity of our healthcare system creates significant barriers to effective pain management in all areas of medicine and across all age groups. The sheer magnitude and complexity of treating pain in a fragmented healthcare system that is struggling to contain costs means better education and training, better interdisciplinary communication and cooperation, and better reimbursement for proven treatment options are desperately needed.

According to the Institute of Medicine, treatment of pain is often disorganized, ineffective, and inaccessible. Many members of the public, people with pain themselves, and many health professionals are not adequately prepared to take preventive action, recognize warning signs, initiate timely and appropriate treatment, or seek specialty consultation when necessary with respect to pain (IOM, 2011).

Several factors influence treatment options, especially when pain is persistent or severe (PPSG, 2014b):

1. Knowledge, beliefs, and attitudes of healthcare professionals
2. Patient and family perceptions
3. Inadequate attention to pain in certain patient populations
4. Restrictive policies governing healthcare practice, as well as concerns about regulatory scrutiny when prescribing controlled substances

Costly, inappropriate, or inadequate procedures are sometimes carried out when other approaches—such as counseling, prevention, and self-management—might be more appropriate. There is still variability among clinicians in applying new and even existing knowledge about pain and its management. This is reflected in the documentation of inappropriate or indeed lack of treatment for cancer patients, HIV/AIDS patients, and neonates—and post operative pain, among others (Sessle, 2012).

To address these issues and barriers, the Institute of Medicine (IOM, 2011) has recommended:

- Providers should promote and enable self-management of pain.
- There should be easily accessible and cost-effective educational opportunities in pain assessment and treatment in primary care.
- Collaboration must be improved between pain specialists and primary care clinicians, including referral to pain centers when appropriate.

- Reimbursement policies must be revised to foster coordinated and evidence-based pain care.
- Providers must provide consistent and complete pain assessments.

> Education. Education. Education. Educate more physicians on proper diagnosis and proper pain management. Educate the person living with pain and their family on addiction versus physical dependency and proper storage of medication. Educate the public and press about the realities of pain medication and people living with pain.
>
> Person with Chronic Pain, IOM, 2011

The inadequate education of healthcare professionals is a major and persistent barrier to effective pain management. Despite the health professions' development of competencies in pain management, as well as the myriad guidelines and position articles on pain management issued by numerous professional bodies, core pain management competencies for pre-licensure, entry-level health professionals have not yet been established. The limited pain education that is currently provided may be ineffective because it focuses on traditional, impersonal topics such as anatomy and physiology that may have little direct relevance to the complex daily problems faced by patients, families, and clinicians (Fishman et al., 2013).

In most health professional programs, the topic of pain occupies only a minor component of the curriculum. In North America and Europe, for example, dental and medical students receive on average less than 20 hours of formal education about pain throughout their multi-year program. The Institute of Medicine has stated that pain education is critically important and that the federal government is in a position to contribute to improvements in patient and professional education about pain. The IOM recommends that the medical professionals (1) expand and redesign education programs, (2) improve curriculum and education for healthcare professionals, and (3) increase the number of health professionals with advanced expertise in pain care (IOM, 2011).

The American Academy of Pain Medicine has echoed the IOM recommendations by publishing a set of inter-professional core competencies for pain management, which are categorized within four domains. These domains address (1) the fundamental concepts and complexity of pain; (2) how pain is observed and assessed; (3) collaborative approaches to treatment options; and (4) application of competencies across the lifespan in the context of various settings, populations, and care team models (Fishman et al., 2013).

Undergraduate health science programs can play a role in improving our understanding of pain and its management. Currently, most undergraduate healthcare programs provide limited pain content, which does not ensure that graduates have the knowledge, skills, or clinical competence to provide quality pain care throughout the lifespan. Understanding the phenomenon of pain, its immediate and long-term consequences, and its effective management is lacking or is minimal in many health science curricula, including those for nursing. This lack of knowledge and effective translation into a usable form for practitioners raises the following question: Do graduates have sufficient knowledge and skills to be competent in giving appropriate pain management to their patients (Herr et al., 2015)?

Core competencies in pain management for pre-licensure health professional education have been established, which map well to the International Association for the Study of Pain's inter-professional pain curricula. These competencies delineate expectations for minimally acceptable skills for pain management for graduating health profession students, regardless of discipline. They provide a basis for preparing students to apply knowledge and skills successfully in a manner that supports inter-professional team contributions in providing quality pain care in the real world (Herr et al., 2015).

Concluding Remarks on Pain

Although international agreements have mandated that countries provide adequate pain medications to relieve the suffering of their people, pain remains one of the major unaddressed issues of modern society, particularly in poor countries. One of the great hopes of modern pain treatment, opioid analgesics, has led to an epidemic of overuse and diversion in some countries while at the same time being completely unavailable to those suffering from severe pain in other countries.

Pain management policies have been developed by a number of regulatory agencies, which provide voluntary and mandatory guidelines about pain management in healthcare organizations. A balanced multimodal approach to pain and its management is a key concept for healthcare organizations and clinicians.

Analgesics are important component of pain management: non-opioid, opioid, and adjuvant medications are available for the treatment and management of pain. Safe use of analgesics is promoted by utilizing a multimodal approach, using more than one type of analgesic to treat an individual's pain. However, opioid analgesics carry a high potential for misuse, abuse, and diversion, even when prescribed for legitimate medical purposes, and clinicians must educate themselves about these issues and understand that opioid analgesics have the potential for misuse.

Consistent assessment and documentation of pain using an individualized approach is recommended by a number of organizations. Clinicians should be familiar with a variety of pain assessment tools and understand the necessity for regular assessment of pain based upon the needs of patient.

Many nonpharmacologic techniques are available for the treatment of pain. Physical and occupational therapy, chiropractic techniques, traditional Chinese medication, and complementary, alternative, and integrative practices are popular and well-tolerated. Although evidence-based studies are limited, there is increasing evidence that many of these techniques successfully decrease pain, and more research is underway.

The Institute of Medicine (2011) sums up the underlying principles related to effective management and treatment of pain, which provides a fitting conclusion to this course:

- Pain is a moral imperative.
- Chronic pain can be a disease in itself.
- Comprehensive treatment is critical.
- Interdisciplinary assessment and treatment may yield the best results.
- Prevention is important.
- Existing knowledge must be used more widely.
- Opioids present a conundrum.
- The clinician-patient relationship is of utmost importance.
- Public health and community-based approaches are invaluable.

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Post Test: Pain (190)

Use the answer sheet following the test to record your answers.

1. When morphine was first developed in 1805:

    a. It was unpopular because it caused constipation.
    b. It was used to treat opium addiction.
    c. It was soon shown to be ineffective for the treatment of pain.
    d. It was largely ignored.

2. Heroin was first marketed by the Bayer pharmaceutical company as:

    a. An effective asthma medication.
    b. A "reversal" drug for morphine overdoses.
    c. A less-addictive substitute for opium.
    d. A non-addictive morphine substitute.

3. Each year in the United States, the treatment and management of pain is estimated to cost:

    a. About 1 billion dollars.
    b. More than the budget of the Defense Department.
    c. About two-thirds of a trillion dollars.
    d. Less than the cost of injuries from car accidents.

4. Pain is often undertreated in which of the following groups?:

    a. Young and middle-aged men, pregnant women, and cancer patients.
    b. Nursing home residents, cancer patients, and ethnic minorities.
    c. Patients with arthritis, professional athletes, and white men.
    d. Patients newly diagnosed with HIV and middle-aged white women.

5. The Joint Commission's pain management standards state that:

    a. Pain and symptom management must be included in discharge planning.
    b. Because pain management is a specialty, most clinicians do not need to be competent in the assessment and management of pain.

c. Clinicians should understand that pain can and does interfere with optimal levels of function and rehabilitation.

d. Evidence-based clinical practice guidelines are not necessarily needed for good pain management.

6. Intractable pain treatment acts:

a. Should be added to statute in every state to ensure adequate management of intractable pain.

b. State that the use of opioids for pain management is not a part of legitimate professional practice.

c. Contain ambiguous and contradictory language and have been deleted from statute in several states.

d. Use the most recent evidence to restrict the use of opioid analgesics for management of severe pain.

7. The Central Principle of Balance, as it applies to pain policy, represents a government's responsibility to:

a. Remove opioid analgesics from the list of scheduled drugs, making it easier for patients to obtain pain medications.

b. Establish a system of drug controls that prevent abuse, trafficking, and diversion of narcotic drugs.

c. Restrict the supply of opioid analgesics (including for medical use) to prevent abuse, trafficking, and diversion.

d. Ensure that prescribers are prosecuted for failing to prescribe opioid analgesics needed for pain management.

8. Physiologically, pain occurs when:

a. Nociceptors come into contact with a painful or noxious stimulus.

b. Nociceptors in the brain send a painful stimulus to the periphery.

c. A sensory nerve impulse travels from the spinal cord to the extremities.

d. The thalamus signals the brain to send a noxious nerve signal to the spinal cord.

9. Neuroimaging studies in patients with chronic pain have found:

a. Anatomic, functional, and chemical changes in brain images.

b. No anatomic changes in the brain images of people with chronic low back pain.

c. Anatomic changes only in people with acute pain.

d. Functional and chemical changes in the brain images of matched, healthy control subjects.

10. Sensitization is:

a. Intense pain that lasts a relatively short time.

b. The increased responsiveness of nociceptive neurons to normal sensory input.

c. Pain from a stimulus that does not usually cause pain.

d. A type of intense, uncontrolled, peripheral pain.

11. Unrelieved or under-treated pain:

a. Is rarely an issue with HIV-infected women.

b. Decreases the risk of ileus.

c. Can produce weight gain and decreased respiratory response.

d. Can suppress immune function in cancer patients.

12. Acute pain is:

a. Usually resistant to treatments used to treat chronic pain.

b. Pain that comes on quickly but lasts a relatively short time.

c. Easily distinguished from chronic pain.

d. Generally not effectively treated with self-management techniques.

13. Chronic pain:

a. Usually responds to treatments and medications used in the treatment of acute pain.

b. Is caused by psychiatric disorders.

c. Rarely lasts more than 3 or 4 months.

d. Persists and is resistant to treatments and medications used in the treatment of acute pain.

14. Neuropathic pain:

a. Tends to be acutely painful but short lasting.

b. Is usually described as a localized, warm, throbbing sensation.

c. Should not be treated with anticonvulsants, gabapentin, or pregabalin.

d. Arises from damage to the brain, spinal cord, or peripheral nerves.

15. Persistent somatoform pain disorder (PSPD):

    a. Persists despite lack of any identifiable underlying physical cause.

    b. Generally produces hostility or aggression towards clinicians.

    c. Has been demonstrated to be "all in your head."

    d. Is identifiable with current technology.

16. Complex regional pain syndrome is characterized by:

    a. Acute pain in a specific region of the body that usually subsides by itself.

    b. A peripheral sensory nerve disorder that causes intense pain and is easily treated.

    c. Intractable pain in a very specific area of the body that is out of proportion to the trauma.

    d. Intractable pain that is out of proportion to the trauma or unrelenting pain that occurs subsequent to a nerve injury.

17. The self-management model of chronic pain management:

    a. Is not recommended by the Institute of Medicine or the American Pain Society.

    b. Is often the strategy of last resort for chronic pain patients.

    c. Is supported by strong evidence for efficacy.

    d. Possesses a relatively weak basis for efficacy in chronic pain care.

18. Primary care clinicians:

    a. Rarely see patients with intractable pain.

    b. Treat about half of chronic pain patients in the United States.

    c. Have more time to assess pain than pain management specialists.

    d. Generally do not prescribe pain medications.

19. Acute pain services:

    a. Typically comprise neurologists, internists, and rehab specialists.

    b. Are offered throughout hospitals in the United States.

    c. Provide consistent pain management for individual patients throughout the course of their hospital stay.

    d. Provide hospital-wide consensus regarding pain management protocols.

20. The most commonly performed procedures in interventional pain management are:

    a. Epidural injections.
    b. Conventional thermal radiofrequency.
    c. Disc replacement.
    d. Pain pumps.

21. Low back pain:

    a. Often begins with symptoms of nausea, vomiting, and sensitivity to light.
    b. Is generally not provoked by certain postures.
    c. Is the fifth most common reason for all physician visits.
    d. Can usually be reliably attributed to a specific disease or spinal deformity.

22. During the initial evaluation for low back pain:

    a. The clinician should avoid positions that provoke the patient’s pain.
    b. An MRI should be ordered prior to the physical examination.
    c. A specific disease or spinal abnormality should be identified.
    d. Various positions should be assessed in an attempt to provoke the patient’s pain.

23. Abortive therapy is:

    a. Treatment for chronic migraine.
    b. Treatment of a migraine attack once it has occurred.
    c. Talk therapy to give psychological support of migraine patients.
    d. Aversion therapy.

24. Post operative pain:

    a. Is not usually related to the presence of drains and tubes.
    b. Should be assessed in the morning just after the patient wakes up.
    c. Can be well-managed in the hospital where 90% of surgeries occur.
    d. Is influenced by multiple factors aside from the extent of the surgical trauma.

25. Pain associated with cancer:

    a. Tends to increase in severity as the cancer advances.
    b. Tends to localize to one or two sites.

c. Tends to decrease in severity as the cancer advances.

d. Tends to be well-treated throughout the world.

26. Breakthrough pain in patients with cancer:

a. Is unrelated to its etiology.

b. Can occur even when normal pain is relatively well-controlled.

c. Is not related to the stage of the disease.

d. Is a temporary flare of pain that occurs even when pain is well-controlled.

27. Best practice guidelines for chronic osteoarthritis focus on:

a. Surgical intervention: joint replacement and joint fusions.

b. Self-management: weight control, physical activity, and pharmacologic support for inflammation and pain.

c. Disease-modifying anti-rheumatic drugs.

d. Use of opioids to control breakthrough pain.

28. In infants, poor or improper management of acute pain has been associated with:

a. Decreased metabolic rate during painful experiences.

b. Increased chance of pain in the abdominal area.

c. Improved ability of infants to self-manage pain.

d. Delayed wound healing and increased risk of infection.

29. The pathophysiologic profile of older adults significantly changes with age. Among the changes:

a. Decline in organ function, particularly renal and hepatic function.

b. Increases in body fat and water composition.

c. Increased ability to metabolize lipophilic and hydrophilic drugs.

d. An overall decrease in the ability to feel pain.

30. In older adults, polypharmacy has been associated with a higher risk of non-adherence to treatment. Adherence can be improved by:

a. Providing low-cost samples of drugs from the physician’s office.

b. Encouraging patients and caregivers to contact drugs companies to get lower-cost versions of the drugs.

c. Including patients and caregivers in decisions about starting, keeping, or changing a medication.

d. Providing frail elders with written instructions.

31. When managing pain at the end of life:

a. Patients and family members should be educated about dosing, compliance, addiction, tolerance, and side effects.

b. Involving the patient and family in establishing goals for palliative pain management is not recommended.

c. Consistent assessment of pain is not necessary because pain tends to stabilize at the end of life.

d. Opioid therapy should be avoided due to fear of causing addiction or hastening death.

32. At the end of life, cancer pain:

a. Usually decreases significantly.

b. Is often no longer an issue for most patients.

c. Stays about the same.

d. Can sharply increase.

33. In assessing pain, all healthcare professionals (within their scope of practice) are encouraged to:

a. Refer pain patients to a knowledgeable provider for a comprehensive, initial assessment.

b. Routinely assess all patients for pain.

c. Assure pain patients that there is no risk of addiction from opioid medications when taken as directed.

d. Inform patients with chemical dependency that opioids will not be a part of their treatment plan.

34. Pain questionnaires:

a. Are the best pain assessment tools for infants and children.

b. Typically use words to help patients distinguish among different kinds of pain.

c. Generally measure one aspect of pain.

d. Are effective for non-English speaking patients.

35. When assessing pain in children, keep in mind that:

a. A child’s ability to describe pain increases with age.

b. Behavioral measures of pain may be needed with older children and adolescents.

c. Physiologic measures of pain are rarely related to stress.

d. A child’s ability to describe pain is fairly constant throughout the developmental stages.

36. When assessing pain in infants and toddlers:

a. The McGill pain questionnaire is helpful.

b. A brief pain discrimination scale is useful.

c. Verbal responses should be used.

d. Pain-related behaviors must be relied on.

37. Assessing pain in cognitively impaired adults presents certain challenges because:

a. They rarely show changes in behavior as a result of pain.

b. Their pain cannot be reliably assessed using a behavior pain scale.

c. They tend to voice fewer pain complaints.

d. They do not feel pain as acutely as younger adults.

38. When assessing pain in a patient with severe dementia:

a. Lack of facial expression may be an indication of severe pain.

b. Positive vocalizations may mask pain.

c. Remember that pain significantly decreases in older patients with dementia.

d. Being unable to console, distract, or reassure a patient with dementia may indicate the presence of severe pain.

39. When chronic pain and depression are considered together:

a. No physiologic correlation has been found.

b. Reducing pain does not lead to a reduction of depressive symptoms.

c. Depression occurs in less than 10% of chronic pain patients.

d. Pain can be a symptom, a cause, or a consequence of depression.

40. NSAIDs are a group of analgesic medications with anti-inflammatory and antipyretic actions. However, some NSAIDs:

a. Have much weaker anti-inflammatory properties than acetaminophen.

b. Have few adverse effects even when taken in high doses.

c. Can decrease the risk of cardiovascular events in patients with known cardiovascular risk factors.

d. Can cause GI complications and increase the risk of heart attacks and stroke to varying degrees.

41. Acetaminophen has good fever-reducing and analgesic properties but must be used with caution due to:

a. Its ability to irritate the GI tract, particularly when taken in large amounts.

b. Serious risk of acetaminophen-related liver damage, particularly when taken in large amounts.

c. Serious and common risk of skin reactions, even when taken in small amounts.

d. The fact that such large amounts are required to reduce pain, the risk of stroke is greatly increased.

42. In older adults with pain:

a. NSAIDs have a good safety profile with no adverse effects.

b. Education and self-management strategies are rarely successful.

c. Acetaminophen is the first-line treatment for both acute and persistent pain, particular musculoskeletal pain.

d. Patients should be encouraged to wait until pain escalates before taking a pain medication.

43. The effectiveness of cannabis in decreasing pain is thought to be related to:

a. The role of the CB_2 cannabinoid receptor.

b. THC, which decreases neuro-inflammation.

c. The role of the CB_1 receptor.

d. The ability of cannabis to completely block pain signals.

44. Adjuvant drugs:

a. Are valuable during all phases of pain management to enhance analgesic efficacy.

b. Are not effective for treating concurrent symptoms.

c. Generally do not provide independent analgesia for specific types of pain.

d. Should not be used concurrently with opioid analgesics.

45. Opioid medications:

a. Do not have a narcotic effect if they are prescribed for medically needed pain management.

b. Have a narcotic effect, induce sedation, and are effective for the management of many types of pain.

c. Are contraindicated for pain management in cancer patients because of excessive side effects.

d. Provide adequate pain control in all patients with few unwanted side effects.

46. Balance between benefits and harm is a critical factor influencing the strength of clinical recommendations. Two practices that are particularly harmful are:

a. The use of opioids with acetaminophen and the use of opioids with alcohol.

b. Prescription drug monitoring programs (PDMPs) and urine drug testing.

c. When opioids are co-prescribed with benzodiazepines and the use of extended release/long-acting (ER/LA) opioid formulations.

d. The use of naloxone for opioid overdose and the risk of abusing heroin after opioids have been stopped.

47. Among the most successful state-based policies intended to reduce the abuse of prescription opioid medications is:

a. Allowing patients to shop for the best doctor.

b. Prescription drug monitoring programs.

c. Slowing regulatory action taken against healthcare providers who acted outside the limits of accepted medical practice.

d. Increasing law enforcement of illegal activities.

48. Addiction:

a. Does not occur when pain medications are prescribed by a medical professional.

b. Is easy for clinicians to recognize, especially in patients seeking treatment for chronic pain.

c. Is generally not affected by the social environment of the individual.

d. Is a chronic relapsing disease characterized by compulsive drug seeking and use despite the known, harmful consequences.

49. In treating pain patients with a history of substance abuse disorder (SUD):

a. Keep in mind that the overall prevalence of current SUDs in chronic pain patients is over 90%.

b. A single-question screening test is highly sensitive and specific for identifying drug use and drug use disorders.

c. Evidence-based clinical guidelines for managing pain while addressing SUDs are available but rarely used.

d. Few screening tools exist that can assist a clinician with determining the presence of or risk for substance abuse.

50. In pain patients who have a substance abuse disorder (SUD) in remission:

a. Opioids should never be used due to the risk of addiction relapse.

b. Use of opioids for pain management rarely leads to relapse of addiction.

c. Clinicians must continually assess the patient's relative risk for relapse and monitor for its emergence.

d. Assessment of the patient's relative risk for relapse is generally not needed.

51. Prescription drug abuse:

a. Is generally related to CNS stimulants such as amphetamine and methylphenidate rather than opioids.

b. Is the use of prescription medications in ways or amounts not intended by the prescribing clinician.

c. Is decreasing significantly in recent years due to enforcement of laws related to opioid use.

d. Is uncommon in pain patients because companies marketing prescription pain medications educate patients about the consequences of abuse.

52. Prescription opioid-related overdoses:

a. Are the leading cause of death for 35- to 54-year-olds.

b. Are unrelated to an increase in the availability of prescription pain medications.

c. Represent only a small fraction of the poisoning deaths in the United States.

d. Have decreased significantly in young adults.

53. Among adolescents and young adults:

a. Prescription and over-the-counter drugs were the drugs most abused.

b. Marijuana is by far the most abused drug in this age group.

c. The drug overdose epidemic is most severe in the Northeast.

d. Cocaine is abused at a higher rate than Vicodin.

54. Women display some gender difference rates in the nonmedical use of prescription drugs. These include:

a. Women may be much less likely than men to engage in "doctor shopping."

b. Women are more likely than men to be prescribed prescription painkillers, and in higher doses.

c. The number of women who have died from prescription painkiller overdoses has decreased significantly since 1999.

d. Men become dependent prescription painkillers more quickly than women.

55. Methadone differs from other opioid analgesics in that:

a. It rarely causes death from overdose because it does not act on the respiratory centers in the brainstem.

b. It has a long half-life, delayed onset, and narrow therapeutic window.

c. One dose generally relieves pain for 3 to 5 days.

d. It produces a much stronger euphoric rush than other drugs of abuse.

56. More than 3 out of 4 people who misuse prescription painkillers:

a. Get them from a primary care physician or dentist.

b. Buy them from a drug dealer or stranger.

c. Use designer drugs, which are formulated to mimic the effects of controlled substances.

d. Use drugs prescribed to a friend or relative.

57. Providing naloxone kits to laypeople has been shown to decrease deaths due to overdose. In 2016:

a. Every state has a program that provides naloxone kits to people at risk of an overdose.

b. The AMA adopted a policy that encourages physicians to co-prescribe naloxone to patients at risk of an overdose.

c. CDC reported that naloxone is ineffective in reversing the effects of opioid overdose.

d. The AMA reported that providing opioid overdose training and naloxone kits to laypeople who might witness an opioid overdose does not reduce opioid overdose mortality.

58. Interdisciplinary pain rehabilitation programs:

a. Utilize practitioners from several different locations to treat chronic pain patients.

b. Have replaced physical therapy at many hospitals.

c. Have been shown to be no better than single-discipline treatments in the management of chronic pain.

d. Comprise clinicians from different disciplines working together to create a plan of care.

59. Therapeutic ultrasound, a technique commonly used by physical therapists in the treatment of pain, is thought to:

a. Have a negative effect on nerve conduction velocity.

b. Decrease collagen tissue extensibility.

c. Increase local blood flow and reduce muscle spasm.

d. Work better than opioids in the treatment of chronic pain.

60. Spinal and joint mobilization techniques:

a. Involve the application of gentle mechanical force and rhythmic oscillations to a painful joint.

b. Are contraindicated in patients using opioid pain medications.

c. Are recommended by the American College of Physicians prior to trying self-management of back pain.

d. Are usually performed by a physician or nurse practitioner.

61. Complementary and integrative medicine pain management programs:

a. Place the responsibility for pain management entirely upon the patient.

b. Are based on patient-centered care, which addresses the physical and emotional issues that affect a person’s health.

c. Do not use interventions that are based upon scientific disciplines.

d. Are generally very easily added to hospital-based pain management programs.

62. Complementary and integrative approaches for the treatment of pain:

a. Are used by only a small percentage of American adults.

b. Should be tried only after self-management and primary care has failed to address the pain complaint.

c. Should not be mixed with or used as an adjunct to conventional care.

d. Have the potential to reduce the need for costly pain medications with harmful side effects.

63. Massage therapy has been used for thousands of years for relaxation and to reduce pain. Recent studies have shown that it:

a. Provides only temporary comfort and psychological support to those in pain.

b. Can be used without concern in all conditions, including carotid disease and deep vein thrombosis.

c. Has no effect on acute or chronic low back pain.

d. Mechanically assists in venous and lymphatic flow.

64. Practicing mindfulness meditation appears to be associated with:

a. Decreased ability to deal with pain and stress.

b. Measurable changes in the brain regions involved in memory, learning, and emotion.

c. Feeling good but likely with no physiologic effects.

d. No impact on anxiety and depression.

65. According to classic acupuncture theory:

a. The power of suggestion can be used to reduce pain and induce a deep feeling of relaxation.

b. All disorders are reflected at specific points, either on the skin surface or just below it.

c. Acupuncture is a single standardized intervention.

d. Acupuncture cannot change the way the brain perceives and processes pain.

66. A number of studies showed that yoga practitioners:

a. Have an increased need for pain medication.

b. Tolerate cold pain more than twice as long as the controls.

c. May have less pain tolerance than those who do not practice yoga.

d. The practice has no effect on pain tolerance.

67. Pain management treatment options are influenced by:

a. Very lax regulatory scrutiny around prescribing controlled substances.

b. Patients who do not take the medications they are prescribed.

c. Providers who feel that patients are often faking the pain.

d. Inadequate attention to pain in certain patient populations.

68. One of the major factors contributing to the misunderstanding and limited knowledge of pain by many healthcare professionals is:

a. A desire to treat other chronic illnesses that may be more important than pain complaints.

b. Limited pain education that most clinicians receive in their undergraduate and postgraduate professional programs.

c. Not enough time during an appointment to adequately assess pain.

d. Inadequate resources to adequately address pain in most patients.

Answer Sheet (190)

Pain: Healthcare's Persistent Challenge

Name (Please print your name): _____

Date: _____

Passing score is 80%

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Course Evaluation: Pain (190)

Please use this scale for your course evaluation. Items with asterisks * are required.

- 1 = Strongly agree
- 2 = Agree
- 3 = Neutral
- 4 = Disagree
- 5 = Strongly disagree

* Upon completion of the course, I was able to:

a. Explain when morphine and heroin were first developed.

○1 ○2 ○3 ○4 ○5

b. Name three patient populations that experience undertreatment of pain.

○1 ○2 ○3 ○4 ○5

c. Define government's two major responsibilities under the Central Principle of Balance.

○1 ○2 ○3 ○4 ○5

d. Discuss the purpose of a prescription drug monitoring program.

○1 ○2 ○3 ○4 ○5

e. Explain three physiologic effects of unrelieved pain.

○1 ○2 ○3 ○4 ○5

f. Define acute pain, chronic pain, and complex regional pain syndrome.

○1 ○2 ○3 ○4 ○5

g. Compare and contrast two overall approaches to pain management.

○1 ○2 ○3 ○4 ○5

h. List five common pain conditions.

○1 ○2 ○3 ○4 ○5

i. Explain one over-reaching issue encountered in the treatment of pain in special populations.

○1 ○2 ○3 ○4 ○5

j. State three practices that all healthcare professionals are encouraged to use in the assessment of pain.

○1 ○2 ○3 ○4 ○5

k. Explain how depression and anxiety are related to chronic pain.

○1 ○2 ○3 ○4 ○5

l. Identify three commonly used pharmacologic components of non-opioid analgesic pain management.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

m. Define prescription drug abuse, tolerance, dependence, and addiction.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

n. List three patient populations that have experienced large increases in prescription opioid overdose deaths in recent years.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

o. Summarize three approaches to curbing prescription opioid abuse.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

p. Identify three non-pharmacologic treatments that have been shown to be effective in the treatment of pain.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

q. Describe three complementary or integrative approaches that have been shown to be effective in the treatment of pain.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

r. Discuss three barriers to the effective management of pain in the healthcare system.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

* The author(s) are knowledgeable about the subject matter.

1 2 3 4 5

* The author(s) cited evidence that supported the material presented.

1 2 3 4 5

* This course contained no discriminatory or prejudicial language.

Yes No

* The course was free of commercial bias and product promotion.

Yes No

* As a result of what you have learned, do you intend to make any changes in your practice?

Yes No

If you answered Yes above, what changes do you intend to make? If you answered No, please explain why.

* Do you intend to return to ATrain for your ongoing CE needs?

- Yes, within the next 30 days.
- Yes, during my next renewal cycle.
- Maybe, not sure.
- No, I only needed this one course.

* Would you recommend ATrain Education to a friend, co-worker, or colleague?

- Yes, definitely.
- Possibly.
- No, not at this time.

* What is your overall satsfaction with this learning activity?

1 2 3 4 5

* Navigating the ATrain Education website was:

- Easy.
- Somewhat easy.
- Not at all easy.

* How long did it take you to complete this course, posttest, and course evaluation?

- 60 minutes (or more) per contact hour
- 50-59 minutes per contact hour
- 40-49 minutes per contact hour
- 30-39 minutes per contact hour
- Less than 30 minutes per contact hour

I heard about ATrain Education from:

- Government or Department of Health website.
- State board or professional association.
- Searching the Internet.
- A friend.
- An advertisement.
- I am a returning customer.
- My employer.
- Other
- Social Media (FB, Twitter, LinkedIn, etc)

Please let us know your age group to help us meet your professional needs.

- ○ 18 to 30
- ○ 31 to 45
- ○ 46+

I completed this course on:

- ○ My own or a friend's computer.
- ○ A computer at work.
- ○ A library computer.
- ○ A tablet.
- ○ A cellphone.
- ○ A paper copy of the course.

Please enter your comments or suggestions here: _____

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Registration Form: Pain (190)

Please print and answer all of the following questions (* required).

* Name: _____

* Email: _____

* Address: _____

* City: _____ * State: _____ * Zip: _____

* Country: _____

* Phone: _____

* Professional Credentials/Designations:

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* License Number and State: _____

* Please email my certificate:

○ Yes ○ No

(If you request an email certificate we will not send a copy of the certificate by US Mail.)

Payment Options

You may pay by credit card or by check.
Fill out this section only if you are **paying by credit card.**
14.5 contact hours: $39

Credit card information

* Name: _____

Address (if different from above): _____

* City: _____ * State: _____ * Zip: _____

* Card type:

○ Visa ○ Master Card ○ American Express ○ Discover

* Card number: _____

* CVS#: _____

* Expiration date: _____