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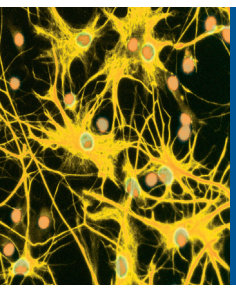

Breakthroughs and Challenges in the Pharmacologic Management of Common Chronic Pain Conditions

Presented by

U.S. Department of Health and Human Services

The Office on Women's Health

In cooperation with

American Academy of Pain Management

American Academy of Physical Medicine and Rehabilitation

American Headache Society

American Pain Society

American Society of Anesthesiologists

American Society of Clinical Oncology

American Society for Pain Management Nursing

Oncology Nursing Society

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U.S. Department of Health and Human Services
The Office on Women's Health

Dear Colleague:

I'm pleased to present this important educational program, which is a series of CME enduring materials developed from a scientific roundtable, *Breakthroughs and Challenges in the Pharmacologic Management of Common Chronic Pain Conditions*.

By best estimates, 75 million Americans are affected by chronic pain on an annual basis. The impact of pain is tremendous. It can interfere with daily activities, work, family activities, and things that we take for granted day in and day out. When we think about the numbers of people who live with chronic pain, for whom adequate treatment is not provided, not accessible, or somehow not available—we have a lot of challenges in this area.

The purpose of this educational initiative is to summarize the epidemiology and pathophysiology of chronic pain, describe the public health impact of chronic pain, discuss methods of pain assessment, familiarize clinicians with therapeutic options and their appropriate use in treating patients with chronic pain, and finally, to discuss the challenges surrounding pain management.

I must acknowledge Dr. Richard Payne and Dr. Christine Miaskowski, who have co-led with their expertise, leadership, and insight in developing the agenda and identifying the faculty for the roundtable. Our partner organizations are also critical in this effort, including the CME sponsor, Penn State College of Medicine.

We at the Office on Women's Health are proud to present this program, and believe it will contribute to the awareness and ability to assess and effectively manage chronic pain conditions.

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Breakthroughs and Challenges in the Pharmacologic Management of Common Chronic Pain Conditions

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Virus-mediated methods	Neuropathic pain
Antidepressants	Migraine
Anticonvulsants	Migraine
Some beta-blockers	Migraine (timolol and propranolol are approved for migraine)
Calcium channel blockers	Migraine
NSAIDs	Chronic pain
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Rofecoxib†	Lower back pain, osteoarthritis

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Target Audience

Primary care clinicians, neurologists, anesthesiologists, physical medicine and rehabilitation specialists, nurses, and other healthcare professionals who treat patients suffering from common chronic pain conditions.

Statement of Need

Chronic pain is a major public health problem in the United States, affecting at least 70 to 75 million Americans each year, with approximately 1 adult in 5 suffering from chronic pain. Some of the most common chronic pain conditions include daily headache, low back pain, osteoarthritis, cancer pain, postherpetic neuralgia (PHN), and diabetic neuropathy. Osteoarthritis affects at least 20 million Americans, at least 5 million Americans suffer from low back pain, 40 million Americans suffer from chronic headaches, and it is estimated that up to 200,000 Americans are affected by PHN. Back pain is the most common type of pain for which patients seek medical attention; it is the second most common cause of office visits, and the third most common reason for hospital admissions. Other chronic pain conditions, such as diabetic neuropathy and cancer pain, also have a significant impact. Patients with chronic pain often experience decreased physical and psychosocial function, depression, loss of sleep, and overall, diminished quality of life.

Chronic pain has a severe economic impact stemming from increased healthcare costs and lost workdays. Each year, more than $4 billion is spent on medications for treating chronic pain. Chronic back pain alone accounts for nearly 3 times as many lost workdays, 3 times as much disability as other disease states, and in 1 year, accounts for an estimated $16 billion in lost productivity, workers' compensation, and associated healthcare costs.

For some of the chronic pain conditions, guidelines exist. However, utilization of these guidelines in clinical practice is not consistent. There are several evidence-based guidelines for the treatment of various chronic pain conditions, including neuropathic pain, osteoarthritis, and cancer pain, and clinicians need to become familiar with the recommendations and learn how to apply them in their practice.

Poor pain assessment and diagnostic challenges are major barriers to appropriate treatment. Since pain is subjective, the best measure of its existence and severity is patient self-report, and there are many types of pain assessment scales available for clinicians to use. However, it is important not only to assess pain, but to evaluate the impact of pain on the patient's quality of life and ability to function. Measures of functional status can be used to evaluate the effectiveness of pain management. Additionally, the diagnosis and classification of various chronic pain conditions can be challenging to the clinician. For example, the differential diagnosis of headache is complicated by the many presentations and types of headache. In addition, race, ethnicity, and cultural background may affect how patients perceive pain, and need to be considered when assessing a patient.

Learning Objectives

After completing this program, participants should be able to:

- Summarize the epidemiology and public health impact of common chronic pain conditions, as well as current clinical practice guidelines and evidence regarding evaluation and treatment of patients with chronic pain
- Discuss the impact of ethnicity, gender, and age on the pathophysiology, assessment, drug metabolism, and management of various chronic pain conditions
- Explain the mechanisms of chronic pain
- Describe clinically useful methods to assess pain (eg, numeric rating scales, multidimensional assessment tools), barriers to pain assessment, and the use of assessment data to select pain management strategies and to evaluate patient outcomes
- Outline a stepwise approach for effective pain management based on the mechanisms of action, routes of analgesic administration, and comparative risks and benefits of commonly used therapies
- Describe recent advances in the management of chronic pain
- Differentiate between addiction, pseudoaddiction, physical dependence, and tolerance, and understand the clinical implications of each
- Outline best practices for the use of opioid analgesics with respect to patient selection, responsible prescribing, titration/rotation, adjunctive therapy, regulatory scrutiny, and risk/benefit evaluation
- Discuss challenges surrounding pain management in the primary care setting, the impact of managed care, and the importance of patient education to improve outcomes

Educational Method

Breakthroughs and Challenges in the Pharmacologic Management of Common Chronic Pain Conditions as published in this *CLINICIAN*® is based, in part, on the proceedings of a scientific roundtable held in Washington, DC.

Release date: October 2005

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Breakthroughs and Challenges in the Pharmacologic Management of Common Chronic Pain Conditions is a self-study educational monograph designed for physicians, nurses, and other healthcare professionals. Continuing medical education credit and/or nursing contact hours will be awarded to participants who successfully complete this activity. Participation should take approximately 2 hours. To complete this activity and receive credit, the participant should:

- Read and review the learning objectives and educational materials included in this monograph
- Complete the posttest and evaluation form online at www.hmc.psu.edu/ce/pain, or mail or fax them to:

  Enduring Materials Coordinator
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  P.O. Box 851
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Participants must receive a score of 80% or better to receive credit.

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Introduction

Chronic pain is an important medical condition that has a significant clinical and societal impact. Despite scientific advances in the diagnosis of chronic pain, large numbers of individuals remain inadequately treated. A multidisciplinary scientific roundtable was convened in Washington, DC to discuss chronic pain, including its epidemiology, pathogenesis, assessment, and treatment. This synopsis provides a summary of the meeting.

Epidemiology and Impact of Common Chronic Pain Conditions

National epidemiologic studies on chronic pain, although limited in number, indicate that the prevalence of chronic pain is high and that its impact is substantial and wide ranging.

Kroenke and Price analyzed data from 13,538 individuals interviewed in the Epidemiologic Catchment Area Program, a multicommunity mental health survey.[2] The lifetime prevalence rates for the 6 most common nonmenstrual symptoms cited by this national sample are shown in Table 1. The majority of these painful symptoms were considered to be major at some point, meaning they interfered with routine activities or led respondents to take medication or visit a physician.

Table 1

Lifetime Prevalence of Pain in Residents of Four Communities in the Epidemiologic Catchment Area Program

Symptom	Lifetime Prevalence (N=13,538)
Joint pain	37%
Back pain	32%
Headache	25%
Chest pain	25%
Arm or leg pain	24%
Abdominal pain	24%

Adapted with permission from Kroenke K, Price RK. *Arch Intern Med*. 1993;153:2476. © 1993 American Medical Association. All rights reserved.

In their study, Reyes-Gibby et al formulated pain prevalence estimates based on the Asset and Health Dynamics Among the Oldest Old (AHEAD) study, which involved 5807 individuals 70 years of age or older.[3] The overall prevalence of pain was 33%. Chronic medical conditions associated with pain reported in this study are listed in Table 2.

Disparities in Pain Assessment and Management

Important gender-, ethnic-, and age-related disparities exist with respect to the occurrence of pain as well as its treatment. For example, women compared to men are at higher risk for the development of pain, and experience pain of greater severity and of longer duration than do men.[4,5] In addition, women may be at increased risk for inadequate treatment of pain, and for pain-related disabilities.[6,7] However, women may respond better than men to a subset of opioid analgesics (kappa-opioids, including nalbuphine), although the exact mechanisms underlying these differences remain unclear.[8] Patients belonging to racial/ethnic minority groups are also at risk for undertreatment of pain.[9] One more correlate of a higher pain prevalence and inadequate pain treatment is advancing age. Indeed, studies in elderly nursing home residents have shown that greater than 71% have at least one pain complaint.[10,11] Older individuals are also less likely than younger persons to receive adequate analgesia.[12]

Table 2

Lifetime Prevalence of Pain in Elderly Individuals (≥70 years) With Common Medical Conditions

Chronic Condition	Prevalence of Pain (N=5807)
Arthritis	60%
Lung disease	44%
Stroke	41%
Heart disease	41%
Diabetes	39%
Hypertension	37%
Cancer	34%

Adapted with permission from the International Association for the Study of Pain®. Reyes-Gibby CC et al. *Pain*. 2002;95:75-82.

Impact of Chronic Pain

The impact of chronic pain on the individual and on broader society is substantial. People with chronic pain are far more likely than those without pain to perceive their health status to be poor, to experience severe activity limitations, and to report decreases in quality of life.[3,13,14] Pain is also associated with elevated rates of anxiety, depression, and suicidality.[13,15-18]

In terms of healthcare resource utilization, some 22% of individuals who are treated by primary care physicians report having persistent pain, and, in the 2001 National Ambulatory Medical Care Survey of the Centers for Disease Control and Prevention (CDC), medications used for relief of pain were the second leading therapeutic class of drugs mentioned during medical office visits (after cardiovascular drugs).[13,19]

Another important consequence of chronic pain is its negative impact on work outcomes. In analyses of data from the National Health Interview Survey (NHIS), back pain resulted in a total of 149 million lost workdays annually in the United States, including nearly 102 million workdays lost due to work-related back pain.[20] In another study, the annual cost of lost productivity due to common pain complaints was estimated at over $61 billion.[21]

Pathophysiology

The pathophysiology of pain is extremely complex. At its most basic level, nociceptive pain is a warning system—an adaptive mechanism with a protective function. Pain is a physiologic event that involves the entire nervous system, and is conventionally classified as *acute* or *chronic*. Acute pain occurs as a result of trauma to protect the organism from further damage, diminishes with healing, and disappears when healing is complete. Conversely, chronic pain has little or no protective purpose, persists despite healing after injury or disease, and ultimately interferes with normal activity.

Pain can be categorized as *nociceptive* or *neuropathic*. Nociceptive pain begins as an impulse detected and transmitted by the peripheral nervous system to the spinal cord by receptors on either A-delta or C-fibers located in the skin. Impulses converge on the dorsal horn of the spinal cord. The pain signal is transmitted to the cerebral cortex, where it is perceived, localized, and interpreted.[22]

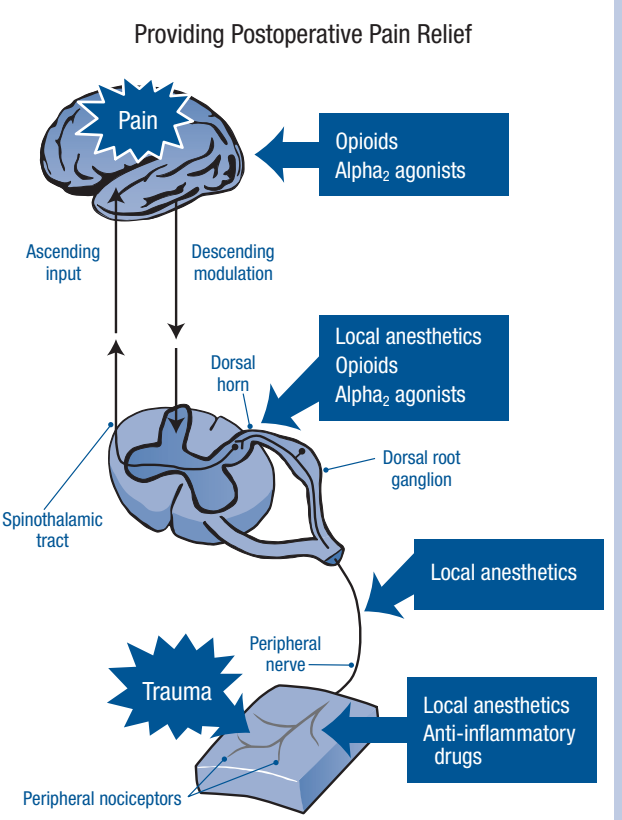
Nociceptive pain is either somatic or visceral. Somatic pain is well localized, constant, and described as sharp, aching, throbbing, or gnawing; visceral pain is usually described as cramping or squeezing in nature.[23] Examples of nociceptive pain include postoperative pain, pain associated with trauma, tumor invasion, inflammation, and chronic arthritis, which usually respond best to nonsteroidal anti-inflammatory drugs (NSAIDs) and/or opioids.[24]

The mechanisms of chronic neuropathic pain are not completely understood; yet it is a common pain problem in clinical practice. Neuropathic pain is produced by pathologic changes in the peripheral or central nervous systems and has no known biologic function. Neuropathic pain persists beyond the initial injury or damage, and develops into a chronic pain condition. In effect, chronic pain becomes the disease itself. Examples of neuropathic pain include postherpetic neuralgia (PHN), diabetic peripheral neuropathy (DPN), HIV-associated peripheral neuropathy, phantom limb syndrome, and complex regional pain syndrome. Patients with a neuropathic pain problem often complain of spontaneous and/or evoked pain. Spontaneous pain is usually described as paroxysmal, constant burning, cramping, or aching pain.[25] Components of evoked pain include hyperalgesia (a lowered threshold to noxious stimuli), allodynia (pain evoked by normally innocuous stimuli, such as light touch), and hyperpathia (an elevated threshold to noxious stimuli with an explosive response that outlasts the stimulus).

Understanding the mechanism(s) that may underlie a painful condition may have clinical relevance because it may help to guide the selection of more appropriate treatments. Different treatments act at different sites along the pain pathway and affect different targets (Figure 1). The fact that several mechanisms may coexist simultaneously supports the need and rationale for polypharmacy for many patients with chronic pain.

Figure 1

The Pain Pathways and Interventions That Can Modulate Activity at Each Point



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Assessment of Pain

The regular assessment of pain is the cornerstone of effective pain management because it guides clinicians in the selection and titration of pain treatments. Pain assessment is now mandated in institutions accredited by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). Accurate and reproducible pain assessments are critical to the determination of the effectiveness of the pain management plan, as well as to the evaluation of new analgesic modalities. To this end, the multidisciplinary Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) was formed. This initiative identified 5 core domains that represent important outcomes in clinical trials and in the management of patients with chronic pain: pain characteristics and intensity, physical function, emotional function, global improvement and satisfaction, and symptoms and side effects.[26] A comprehensive assessment of pain should include a detailed pain history, psychosocial assessment, physical examination and diagnostic tests, and ongoing reassessments (Table 3).

Pain Rating Scales

Three types of rating scales are often used in clinical practice to quantify pain intensity—verbal rating scales, visual analog scales, and numeric rating scales (Figure 2). All have good reliability and validity, but each has particular strengths and weaknesses. The strengths and weaknesses of each of these scales are listed in Table 4. In addition, specific scales are available to evaluate the impact of chronic pain on physical function (eg, interference items on the Brief Pain Inventory).

Table 3

Components of a Comprehensive Pain Assessment

Detailed Pain History	Psychosocial Assessment	Physical Examination and Diagnostic Tests	Ongoing Reassessments
• Onset and temporal pattern • Description • Location • Intensity/severity • Aggravating and relieving factors • Previous and current treatments and effectiveness (pharmacologic and nonpharmacologic) • Effects of pain on function	• Effects of the pain problem and/or the chronic illness on the patient and the family caregiver • Meaning of the pain to the patient and the family caregiver • Significant past experiences with pain • Changes in mood • Typical coping responses to stress or pain • Expectations regarding pain management • Concerns about using opioid analgesics • Economic impact of pain and its treatment • Evaluation of support systems	• Examine the site of the pain and evaluate common referral patterns • Perform pertinent portions of the neurological examination depending on the pain complaint • Perform appropriate diagnostic tests to facilitate the diagnosis of the cause of the pain (may need to give analgesics to facilitate the diagnostic workup)	• Use valid and reliable tools • Perform the reassessments at appropriate intervals • Document reassessment (pain intensity, extent to which pain interferes with function, pain relief is a distinct parameter from pain assessment, level of adherence with the pain management plan)

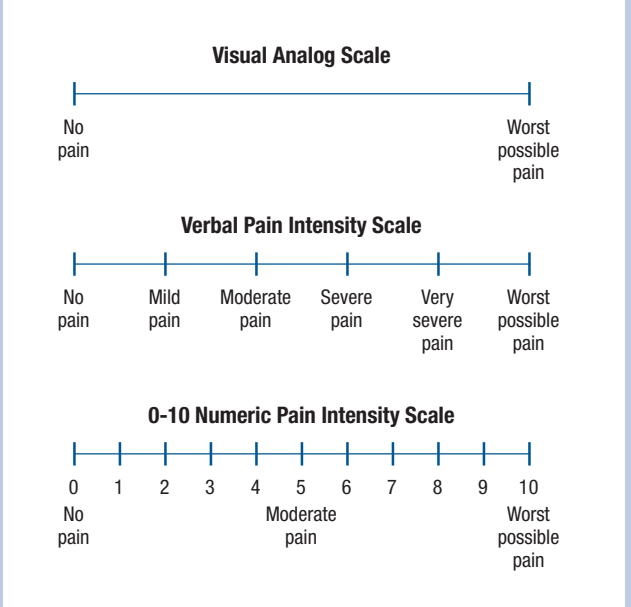
Adapted from Miaskowski C, Cleary J, Burney R, Coyne P, Grossman S, Janjan N, Finley R, Foster R, Ray J, Syrjala K, Weisman S, and Zahrbock C (2005). Guideline for the Management of Cancer Pain in Adults and Children, APS Clinical Practice Guidelines Series, No. 3. Glenview, IL: American Pain Society, with permission from American Pain Society.

Patient Education

Patient education and counseling are critical components of a pain treatment program. It is important that education is provided not only to the patient, but also to his or her family caregiver. Moreover, just as in other chronic medical conditions such as diabetes, education about pain and its treatment should be comprehensive, and therefore requires an adequate investment of time.

Figure 2

Categories of Pain-Assessment Scales



Adapted from McCaffery M, Pasero C. *Pain: Clinical Manual*. 2nd ed. St. Louis: Mosby, Inc. 1999:62-63, with permission from Elsevier.

Table 4

Strengths and Weaknesses of Three Types of Pain Rating Scales

Scale	Strengths	Weaknesses
Visual Analog Scales (VAS)	• Easy to administer • Many ("infinite") response categories • Good evidence for construct validity	• Extra step in scoring the paper-and-pencil version can take more time and adds an additional source of error
Verbal Rating Scales (VRS)	• Easy to administer • Easy to score • Good evidence for construct validity • Compliance with measurement task is high	• Can be difficult for persons with limited vocabulary • Relatively few response categories compared to the VAS or 101-point NRS • People are forced to choose 1 word, even if no word on the scale adequately describes their pain intensity
Numeric Rating Scales (NRS)	• Easy to administer • Many response categories if 101-point NRS is chosen • Easy to score	• Limited number of response categories if 11-point NRS is used • Compliance with measurement task is high

Adapted with permission from Jensen MP, Karoly P. Self-report scales and procedures for assessing pain in adults. In: Turk D, Melzack R, eds. *Handbook of Pain Assessment*. 2nd ed. New York, NY: The Guilford Press; 2001:25.

Examples of Patient Education Programs

Osteoarthritis

Patient education is an integral and cost-effective component of pain management for patients with osteoarthritis.[27] Osteoarthritis education should have 3 primary goals: helping patients understand the mechanisms underlying their pain; helping them understand what pain management options are available to them; and teaching them self-management skills. In terms of content, the program should include the following: basic information about joint anatomy and arthritis; self-help principles; tips for using joints wisely and conserving energy; pain management; exercise; relaxation; facts about patients' medications and their effects and side effects; psychologic aspects and problem solving; clinician-patient relations; good nutritional habits; methods of heat/cold application; and identification of unproven remedies.

Cancer

With respect to cancer pain management, the overall goals of patient education are to address myths and misconceptions, reassure patients and family caregivers that cancer pain can be effectively relieved, and reassure patients and family caregivers that addiction and tolerance are not problems usually associated with effective cancer pain management. An effective cancer pain patient education program should include: causes of cancer pain; types and rationale for analgesic medications; instructions for getting the analgesic prescriptions filled; specific instructions on how to dose and titrate analgesic medications; how to manage side effects; storage and safe keeping of medications; who to call if pain is not relieved, increases in intensity, or if side effects occur; and when and how to use nonpharmacologic approaches for pain management.

Pain Management

Due to the complex nature and diverse causes of chronic pain, development of a satisfactory management program necessarily involves a collaboration between the clinician and patient. Specific goals should be set with the patient at the outset of any management program, including such objectives as reducing pain, restoring function, improving sleep, and returning to work or leisure activities. These goals often necessitate a multidisciplinary and/or multimodal approach—involving cognitive, pharmacotherapeutic, and physical/occupational interventions, tailoring pain management to the individual patient.

In all cases, a critical first step toward the goals of pain management is to establish or confirm the cause of the pain, followed by treatment of any medical conditions that underlie the painful condition. When beginning therapy for chronic pain, treatment should be initiated at the appropriate place on the pain continuum. While medications are critical elements of a comprehensive pain treatment plan, psychological and physical approaches to pain management, such as relaxation therapy, use of distraction and relaxation techniques, application of heat or cold, exercise, physical therapy, and cutaneous stimulation should also be considered and used concomitantly. These techniques are important to improve coping and function, and provide patients with a sense of control.

When initiating any therapy, treatment should be based on a comprehensive assessment of the patient and available therapies. Treatment choices can be considered on a risk continuum. Risks include, among others, invasiveness, drug adverse reactions, possibility for addiction, and drug-drug interactions. These risks may vary between patients, depending on such factors as age, cardiovascular condition, psychological well-being, physical fitness, and many other variables. In all cases, these risks must be weighed against the benefit of the therapy. This decision-making process must be based on clinical judgment, as much of the available information is not evidence-based. The rest of this monograph will focus on pharmacologic options for chronic pain management.

Optimizing Pain Management for Specific Chronic Pain Conditions

The optimal management of chronic pain can vary widely with the condition (eg, migraine vs cancer) and among specific epidemiologic groups (eg, the elderly vs younger individuals). Several common chronic pain conditions and their treatments are summarized below.

Low Back Pain

Low back pain (LBP) is the most common and costly of all chronic pain conditions in the United States.[28] Back pain affects up to 85% of individuals during their lifetimes, although the majority recover without long-term consequences.[29] The societal costs of LBP are substantial: it is the second most common reason for visits to U.S. physicians and is the third most common reason for surgical procedures.[30] The annual total cost of treatment (both direct and indirect costs) of LBP has been estimated at $100 billion.[30]

Besides the high prevalence and costs, LBP presents a challenge to clinicians as there are numerous treatment guidelines for the management of acute LBP, such as the Agency for Health Care Policy and Research (AHCPR) Guidelines for Assessment and Treatment of Acute LBP in Adults, the American College of Radiology (ACR) Appropriateness Criteria for Acute LBP-Radiculopathy, and the Institute for Clinical Systems Integration (ICSI) Healthcare Guidelines for Acute LBP. However, to date, no organization has reached consensus and developed evidence-based guidelines for the management of chronic LBP. In the absence of unbiased clinical practice guidelines, clinicians may select treatment strategies where efficacy has been established through published randomized controlled trials, consensus statements by reputable and unbiased professional associations, or other methodologies.[31] In selecting treatments for the management of LBP, the clinical challenge rests with the fact that there are only a limited number of well-controlled clinical trials that demonstrate efficacy. However, a large majority of the trials are weakened by poor study designs or significant methodologic flaws.[32-34]

The etiology of LBP is often complex and multifaceted. In some cases, LBP may be purely nociceptive—representing responses in neural pathways to tissue-damaging stimuli such as sports or exercise injuries, or internal disc disruption. Other causes of LBP, such as sciatica, can be purely neuropathic. However, the majority of the cases of chronic LBP are of mixed etiology, having both nociceptive and neuropathic characteristics.

Assessment of patients with LBP should include the medical history (including neurologic and psychosocial histories), physical examination (particularly the musculoskeletal and neurologic evaluations), and neuroanatomic imaging studies as appropriate.

Management approaches used to relieve LBP include physical/rehabilitative measures (eg, exercise, weight control, spinal manipulation, massage, transcutaneous electrical nerve stimulation [TENS], biofeedback), pharmacotherapy, and more invasive interventions that range from trigger-point injections to surgery. Physical measures such as exercise or increased physical activity have been found to be more effective than prolonged bed rest for treating acute LBP. In fact, one well-designed randomized controlled trial of patients limited for <3 months by LBP symptoms demonstrated that a program of gradually increased aerobic and back-strengthening exercise was superior to performing no exercise. Prolonged bed rest is associated with muscle atrophy, cardiopulmonary deconditioning, and bone mineral loss with hypercalcemia and hypercalciuria, and a potential risk of thromboembolism, among other side effects.[28] Available pharmacologic options currently used to relieve LBP include acetaminophen, NSAIDs, topical analgesics, muscle relaxants, opioids, corticosteroids, antidepressants, and/or anticonvulsants.

Emerging Therapies in LBP

In a prospective, multicenter, open-label, pilot safety and efficacy study, the lidocaine patch 5% as add-on therapy for LBP[35] was associated with significant reductions in pain intensity and significant pain relief in 60 patients as measured by the Brief Pain Inventory (BPI) ($P<.0001$). No serious or systemic adverse effects or drug-drug interactions were noted.[35] Opioids remain part of the emerging front in treating LBP. In a pooled sample of 2 double-blind, randomized, placebo-controlled studies of combined tramadol/acetaminophen versus placebo in 654 patients with chronic LBP, patients taking tramadol/acetaminophen scored significantly better than those taking placebo on the Pain Visual Analog (PVA) scale and on a pain relief rating scale (both $P<.001$).[36] A recent multicenter, randomized, placebo-controlled, double-blind study evaluating the analgesic effect of a long-acting opioid, oxymorphone extended release, found the drug to be generally safe and effective for controlling LBP.[37] Impact on function of another opioid, transdermal fentanyl, was studied for 9 weeks in 122 patients. Patient scores of pain intensity showed clinically significant improvement on both measures ($P<.001$).[38] Transdermal fentanyl compared favorably with oral morphine in pain relief and better than oral morphine on mean composite pain relief/constipation scores.[39] In addition, 3 studies of small numbers of patients show improvement in pain relief using botulinum toxin A, but no larger or long-term studies have been conducted.[40-43]

Migraine

Migraine is a chronic condition of enormous scope, affecting individuals across all socioeconomic backgrounds, with a lifetime prevalence of more than 90%.[44,45] Migraine affects more people than asthma and diabetes combined; nearly 28 million individuals in the U.S.—roughly 18% of women and 6% of men—suffer from this pain condition.[46] Despite new scientific knowledge in migraine, more than 50% of sufferers are undiagnosed, 39% of migraineurs do not seek professional treatment, and 21% of diagnosed sufferers discontinue care, citing inadequate results.[46-48] Migraine can be profoundly debilitating. The World Health Organization rated severe migraine as one of the most disabling chronic conditions.[44,49] Moreover, greater than 90% of sufferers report disability and nearly one third are severely disabled during an attack.[50] It reduces quality of life and the ability to perform everyday activities, and has a negative impact on spouses and family members.[46] The burden of migraine is staggering, with over 1 billion healthcare dollars spent annually, 112 million bedridden/missed work days per year, and an estimated cost to American employers for missed work days of $8 billion per year.[48,51] It has been estimated that U.S. employers lose more than $13 billion annually due to migraine-related absence or reduced productivity.[51]

Migraine typically consists of a one-sided, throbbing or pulsating pain of moderate to severe quality that is made worse by routine movement and is associated with photophobia, phonophobia, or nausea with or without vomiting, that lasts 4 to 72 hours.[44] While approximately 15% of patients experience an aura, or visual or sensory disturbances, many patients may experience a prodrome of a psychological, neurologic, autonomic, or somatic nature as well.[44,48]

The pathophysiology of migraine is a complex process. Central nervous system hyperexcitability, trigeminal brainstem activation, and neurogenic inflammation leading to meningeal vessel dilatation play major roles. Patients with migraine also experience cutaneous allodynia in which routine activities such as combing hair, shaving, or putting on eyeglasses can become painful, ranging from mild irritation to more severely painful; all as a result of central sensitization.[48]

The 3 tenets of effective management of migraine headache are to first, establish a proper diagnosis[46]; second, provide patient education[52]; and third, assure adequate treatment.[52] The first critical step in the migraine treatment process involves the proper identification and diagnosis of migraine. There may be a continuum in the pathophysiology of so-called "tension" headaches and migraines; nonetheless, the majority of patients who seek care for primary headache are experiencing migraine. However, these patients are frequently misdiagnosed by clinicians as having sinus or tension-type headache. Since migraine varies in frequency, severity, duration, and associated disability between patients and between attacks in the same patient, care should be stratified and tailored to individual patient needs, addressing headache severity, associated features, and headache-related disability.[48,52]

Criteria for a diagnosis of migraine established by the International Headache Society (IHS) are listed in Table 5.[44] Several screening tools, such as the ID Migraine Screener and the Migraine-Specific Quality of Life Questionnaire, version 2.1 (MSQ), are available to facilitate identification of patients with migraines when they present to a primary care clinician.[53]

Table 5

Diagnostic Criteria for Migraine

History of at least 5 attacks, lasting 4 to 72 hours, characterized by:

Any 2 of the following:	**plus**	**Any 1 of the following:**
Unilateral headache		Nausea or vomiting
Throbbing headache		Photophobia and phonophobia
Worsened by movement		
Moderate or severe in intensity		

Adapted from the Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgia, and facial pain. *Cephalalgia*. 1988;8:1-96 with permission from Blackwell Publishing.

Second, effective management of migraine headache requires patient education. Patients need to understand their condition and how to avoid triggers, and individualized intervention strategies should be developed.[52]

Third, treatment of migraine focuses on 2 broad approaches: prophylactic therapy—aimed at preventing attacks; and acute treatment—aimed at treating attacks rapidly and consistently without recurrence.[52] Migraine is now seen as a chronic, potentially progressive disorder, with some sufferers evolving over time from episodic, infrequent headaches to more frequent, more severe headaches. Often a combination of nonpharmacologic and pharmacologic approaches are used together for migraine prophylaxis. Nonpharmacologic management approaches such as reassurance, sleep hygiene principles, and biofeedback are important in migraine prevention, as is avoidance of an individual's known triggers for attacks. Headache diaries are useful because they help clinicians track patterns of headaches and help guide therapeutic choices.[54] Due to the recurrence of migraines, preventive medications are now offered more commonly, especially in those patients who experience ≥4 headaches per month, even if on a short-term basis. Medications approved by the FDA for migraine prophylaxis include methysergide, propranolol, timolol, divalproex sodium, and topiramate (Table 6). Other non-FDA approved medications used for this purpose include antidepressants, other anticonvulsants, antihypertensive agents (beta-blockers, calcium channel blockers), some triptans, NSAIDs, and botulinum toxin.

While mild migraine may respond to NSAIDs, for those with moderate-to-severe migraine, prompt use of migraine-specific agents is critical, as it reduces disability and leads to higher rates of pain-free outcomes.[52] Triptans are the cornerstone of acute treatment of moderate-to-severe migraine as they act on serotonergic receptors to "turn off" migraine. The goal of treatment is to relieve pain and associated symptoms, with return to function. Triptans are extremely effective and well-tolerated medications. Seven FDA-approved triptans are currently available in different formulations (injectable, nasal spray, tablet, and oral disintegrating tablets): sumatriptan, zolmitriptan, rizatriptan, naratriptan, almotriptan, frovatriptan, and eletriptan.[52] This group of drugs represent highly effective abortive therapies that should be used as early as possible in the development of a migraine attack, unless the risk of overuse or premature use are present.[52]

Although triptans have generally supplanted ergot alkaloids as the treatment of choice for most patients with migraine, some patients appear to respond better to ergot-related medications, perhaps because of their broader receptor influence beyond serotonergic receptors alone. Dihydroergotamine, one formulation of ergot-related medications, is available in intravenous, intramuscular, subcutaneous, and nasal spray formulations and is believed to be effective in migraine, at least in part, because of its 5HT1D receptor-agonist properties.[52] The nasal spray has FDA approval for treatment of migraines.

Often, patients who experience frequent headaches overuse analgesics, which can produce a medication-induced "rebound headache," which reflects the medication-induced progression of frequency and refractoriness of the migraine disorder. Rebound headache is characterized by a pattern of predictable, escalating use of headache medications associated with an increasing frequency of headache and decreasing effectiveness of medications[44] and presents a serious challenge in the prophylactic management of headaches.[53] Commonly overused pain medications include opioids, ergots, butalbital-containing drugs, or triptans, as well as over-the-counter medications. The most important aspect in treating rebound headache is discontinuation of the medication,[52] which in severe cases may require hospitalizing patients to simultaneously treat existing and escalating pain while discontinuation of offending medication is underway.

Emerging Therapies in Migraine

A calcitonin gene-related peptide antagonist (CGRP), labeled BIBN4096 BS, a novel abortive therapy, has been found to be effective in stopping the release of the neuropeptide CGRP. CGRP is involved in the transmission of pain-producing stimuli from intracranial vessels to the central nervous system. A recent multicenter, double-blind trial demonstrated promising results in the treatment of acute migraines.[55]

Osteoarthritis

Osteoarthritis is a progressive, degenerative disease that involves the cartilage of weight-bearing joints. Osteoarthritis begins with some trauma-induced or idiopathic loss of integrity of the cartilage. A cascade of events occurs, characterized by a local inflammatory response of the tissues and, ultimately, mechanical and functional alterations.

Table 6

Commonly Used Prescription Migraine Medications

Acute/Abortive Treatment

FDA-Approved	Not FDA-Approved
• Triptans	• Steroids
– Almotriptan	• Antiemetics (for nausea)
– Eletriptan	• Opioids
– Frovatriptan	
– Naratriptan	
– Rizatriptan	
– Sumatriptan	
– Zolmitriptan	
• Dihydroergotamine (nasal spray)	
• NSAIDs	
• Butorphanol tartrate	

Prophylactic Treatment

FDA-Approved	Not FDA-Approved
• Valproate/Divalproex sodium	• Antidepressants
• Topiramate	• Other anticonvulsants
• Timolol	• Antihypertensive agents (other β-blockers, Ca-channel blockers)
• Propranolol	• NSAIDs
• Methysergide	• Botulinum toxin
	• Triptans (frovatriptan, naratriptan, sumatriptan)
	• Hormonal therapies

Prevalence rates vary, because there is neither clear-cut pathophysiology nor an objective diagnostic test for osteoarthritis other than x-ray. However, a 1998 study reported that approximately 4% of males and 7% to 9% of females over the age of 20 are affected. Among the subset of individuals over the age of 60, the prevalence rose to 17% in males and nearly 30% in females.[56]

Analgesic and anti-inflammatory medications are important in osteoarthritis pain management, but should be used concurrently with nonpharmacologic interventions.[57] Nonpharmacologic management approaches include patient education, moderate physical exercise, physical and occupational therapy, weight loss, and cognitive behavioral therapy. Pharmacologic options include acetaminophen, NSAIDs, joint injection with corticosteroids, and opioids. The choice of optimal therapy should be made using a risk-benefit analysis of the available pharmaceutical options in the patient's individual case. Acetaminophen is typically the medication of first choice for mild pain. For the person with moderate to severe pain and/or inflammation, an NSAID or an opioid analgesic may be required to effectively manage the pain. While a previous guideline recommended a cyclo-oxygenase 2 (COX-2) antagonist as first-line therapy for moderate to severe pain,[57] in 2004 the COX-2 inhibitor rofecoxib was voluntarily withdrawn from the market by Merck & Co., Inc. because of an excess risk of myocardial infarctions and strokes.[1] Increased concerns about COX-2 inhibitors and the potential for an elevated cardiovascular risk across the drug-class led the FDA to conduct a comprehensive review of pain medications.[58-60] Most recently, the FDA asked the manufacturer of valdecoxib to withdraw it from the market, concluding that the overall risk-versus-benefit profile of the drug is unfavorable.[61] New FDA recommendations regarding the use of COX-2 inhibitors and NSAIDs are discussed on page 12 (Older Patients).

Opioids should be used for the management of osteoarthritis when other medications and nonpharmacologic interventions produce inadequate pain relief and the patient's quality of life is affected by the pain.[57] This is frequently the case, because neither acetaminophen nor NSAIDs consistently provide suitable pain relief in the treatment of osteoarthritis, according to a preliminary study.[62]

In a double-blind, placebo-controlled study, Roth et al randomly assigned 133 patients with moderate to severe osteoarthritis pain to 14 days of double-blind treatment with either placebo or controlled-release oxycodone (10 mg or 20 mg every 12 hours).[63] Use of controlled-release oxycodone, 20 mg, was superior ($P<.05$) to placebo in reducing pain intensity and the interference of pain with mood, sleep, and enjoyment of life.

In an open-label trial, McIlwain et al studied an extended-release (ER) formulation of oxymorphone in the treatment of osteoarthritis pain.[64] A total of 153 patients with osteoarthritis were enrolled and received oxymorphone ER twice daily; the median daily dose of the medication was 40 mg. After 1 year, 92 patients withdrew from the study, mostly due to common opioid-related nonserious adverse events; the remaining 61 patients were evaluated for efficacy. More than 80% of these patients rated the medication as "excellent" to "good."

Patients with disabling arthritis should be referred for surgical care before contractures, severe deformity, advanced muscle wasting, and deconditioning occur.[57]

Emerging Therapies in Osteoarthritis

Emerging therapies in the pharmacologic management of osteoarthritis include the use of new combinations of older medications, such as ibuprofen plus hydrocodone[65] and acetaminophen plus tramadol.[66] Proposed to provide benefits in terms of joint restoration, hyaluronic acid injections[67] replace damaged joint fluid and generally need to be administered every 6 months.[68] Glucosamine and chondroitin have been proposed as an alternative treatment approach.[69] Trials using glucosamine for osteoarthritis have demonstrated substantial effects, but methodologic problems in these studies probably overestimate these results. Further studies are needed to determine the clinical utility of glucosamine.[70] With regard to topical applications, a pilot study suggests that the lidocaine patch 5% may be effective for the pain associated with osteoarthritis.[71]

Cancer Pain

Epidemiologic studies conducted over the past 3 decades indicate that approximately half of all individuals receiving active treatment for cancer experience moderate to severe pain. Among patients in the terminal stages of disease, some 80% to 90% experience such pain. Despite advances in understanding the pathophysiology and the broad availability of effective analgesics, cancer pain is frequently treated inadequately.[72] This undertreatment persists despite evidence-based cancer pain management guidelines published by the AHCPR in 1994 and by the National Comprehensive Cancer Care Network in 2001. A new guideline on the management of cancer pain was published by the APS in 2005.[73]

Cancer pain can have various causes: pain due to direct tumor involvement (most common); treatment-associated pain (eg, postsurgical pain, postchemotherapy oral mucositis or peripheral neuropathy, postradiation mucositis or esophagitis, plexopathies), or acute or chronic pain unrelated to cancer (eg, osteoarthritis, LBP). Indeed, a patient with cancer may experience several different types of pain that require assessment and treatment.

Assessment includes first determining the cause of the pain, and whether it is related to an oncologic emergency that requires an immediate intervention. Once a pain problem has been identified, assessments should be undertaken at each visit, ideally facilitated by the patient with the use of a pain diary. The clinician should elicit the presence of persistent pain and breakthrough pain, and the effect of pain on functioning. The degree of pain relief afforded by treatment should also be assessed (Table 7).

Table 7

Persistent Pain versus Breakthrough Pain

Persistent pain:

- Constant pain that lasts for long periods of time
- Requires use of long-acting opioids

Breakthrough pain:

- Sudden flare-ups of pain that break through the persistent pain
  - Spontaneous
  - Incident-related
  - End-of-dose failure
- Requires use of short-acting opioids

Table 8

Commonly Used Nonopioid Analgesics for Acute and Cancer Pain

Medication	Average Adult Analgesic Dose (mg)*	Dose Interval (hrs)	Maximal Daily Dose (mg)	Comments
ACETAMINOPHEN	500-1000	4-6	4000	Rectal suppository available for children and adults. Sustained-release preparation available, >2 g/day may increase anticoagulation effects in patients receiving warfarin.†
SALICYLATES				
Acetylated				
Aspirin	500-1000	4-6	4000	Because of risk of Reye's syndrome, do not use in children under 12 with possible viral illness. Rectal suppository available for children and adults. Sustained-release preparation available.
Modified				
Diflunisal	1000 initial, 500 subsequent	8-12	1500	Dose in elderly 500-1000 mg/day. Does not yield salicylate.
Salts‡				
Choline magnesium trisalicylate	1000-1500	12	2000-3000	Unlike aspirin and NSAIDs, does not increase bleeding time.
NSAIDs				
Propionic Acids				
Ibuprofen	200-400	4-6	2400	
Naproxen	500 initial, 250 subsequent	6-8	1500	
Naproxen sodium	550 initial, 275 subsequent	6-8	1650	
Naproxen sodium OTC	220	8-12	—	
Fenoprofen	200	4-6	3200	
Ketoprofen	25-50	6-8	300	
Ketoprofen OTC	12.5-25	4-6	—	Sustained-release preparation available.
Oxaprozin	600	12-24	1200	
Indolacetic Acids				
Indomethacin	25	8-12	200	Not routinely used because of high incidence of GI and CNS side effects; rectal, IV, and sustained-release oral forms available for adults.
Sulindac	150	12	400	
Etodolac	300-400	8-12	1000	
Pyrrolacetic Acids				
Ketorolac	30-60 mg IM or 30 mg IV initial, 15 or 30 mg IV or IM subsequent	6	150 first day, 120 thereafter	Limit treatment to 5 days; may precipitate renal failure in dehydrated patients; average dose in elderly 10-15 mg IM/IV q6hr.
Tolmetin	200-600	8	1800	
Anthranilic Acids				
Mefenamic acid	500 initial, 250 subsequent	6	1500	In U.S., use is restricted to intervals of 1 week.
Phenylacetic Acids				
Diclofenac potassium	50	8	150	
Enolic Acids				
Meloxicam	7.5-15	24	15	
Piroxicam	20-40	24	40	
Naphthylalkanone				
Nabumetone	1000 initial 500-750 subsequent	8-12	2000	Fewer side effects.
COX 2 Selective§				
Celecoxib	200-400	12-24	400	

*All doses are oral unless otherwise specified.

†Maximum drug dose is lower in fasting patients and in patients regularly consuming alcohol.

‡Magnesium and sodium salicylate tablets also are commercially available, but are used less commonly today.

§Rofecoxib was voluntarily withdrawn from the market by Merck & Co., Inc., in 2004 because of an excess risk of myocardial infarctions and strokes.[1] Previously, rofecoxib was used as a first-line therapy for the treatment of osteoarthritis pain; however, the use of rofecoxib has been reconsidered based in part, on findings from a clinical trial that resulted in an increased risk of serious cardiovascular effects in patients taking the medication.[120] Most recently, the FDA asked the manufacturer of valdecoxib to withdraw it from the market, concluding that the overall risk-versus-benefit profile of the drug is unfavorable.[61]

GI = gastrointestinal; CNS = central nervous system; IM = intramuscular; IV = intravenous.

Adapted with permission from *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. 5th ed. Glenview, Ill: American Pain Society; 2003:4-7.

General principles of cancer pain management as recommended in the 2005 APS guidelines are as follows[73]:

1. Develop a systematic approach to cancer pain management.
2. Teach patients and family caregivers how to use effective strategies to achieve optimal pain control.
3. Provide patients with a prescription for analgesic medication and educate them to: fill the prescription, take the medication if an unexpected pain occurs, and then call their healthcare provider for an appointment to evaluate the problem.
4. Base the initial treatment of pain on the severity of pain the patient reports.
5. Once the patient's pain intensity and dose are stabilized, administer a long-acting opioid on an around-the-clock basis along with an immediate-release opioid to be used on an as-needed basis for breakthrough pain.
6. When the patient is started on an opioid analgesic, begin a bowel regimen to prevent constipation.
7. Adjust opioid doses to achieve pain relief with an acceptable level of side effects.
8. Provide patients and family caregivers with accurate and understandable information about effective cancer pain management: the use of analgesic medications; other methods of pain control; and how to communicate effectively with clinicians about unrelieved cancer pain.
9. Use cognitive and behavioral strategies as part of a multimodal approach to cancer pain management—not as a replacement for analgesic medications.

In addition to opioids, there is a role for the use of nonopioid analgesics and adjuvants in cancer pain management. The former include acetaminophen and NSAIDs and are used for mild pain or in combination with opioids. Table 8 lists commonly used nonopioid analgesics. Adjuvants include antidepressants, anticonvulsants (eg, gabapentin), topical agents such as the lidocaine patch 5%, and corticosteroids. These are generally used to treat neuropathic pain associated with cancer or its treatment.

Neuropathic Pain

Neuropathic pain is pain caused by a primary lesion or dysfunction in the peripheral and/or central nervous systems.[74] Examples of peripheral neuropathic pain include PHN, diabetic neuropathy, and HIV sensory neuropathy. Examples of central neuropathic pain include central poststroke pain, spinal cord injury pain, trigeminal neuralgia, and multiple sclerosis pain. Although few controlled studies on the prevalence of the various types of neuropathic pain have been conducted, estimates are shown in Table 9.

Goals in the clinical assessment of a patient with neuropathic pain are to establish the diagnosis of pain, identify the underlying causes of the pain, identify comorbid conditions including other medical problems, and evaluate relevant psychosocial factors and functional status. Important characteristics of the patient's pain to be elicited include its onset and duration, location/distribution, quality, intensity, aggravating/relieving factors, associated/secondary signs and symptoms, and treatment responses.[75,76]

As the number of published, randomized controlled trials involving neuropathic pain increase, an evidenced-based treatment approach will become increasingly possible.[77] However, the management of neuropathic pain continues to present a clinical challenge to clinicians as no single pain symptom points to the condition, and consensus is restricted to a single set of treatment guidelines published about the optimal therapeutic strategy for this pain state.[78,79] In light of the limited neuropathic pain data, conventional practice for clinicians may involve treatment approaches based on the available published, multicenter, randomized controlled trials that demonstrate efficacy and safety as well as recommendations from the Fourth International Conference on the Mechanisms and Treatment of Neuropathic Pain-Independent Expert Panel, published in 2003, that outline the diagnosis, assessment, and treatment of neuropathic pain.[31,77]

A recommended treatment approach for the management of the patient with neuropathic pain is summarized in Figure 3. Patient management encompasses establishing a diagnosis, treating any

Table 9

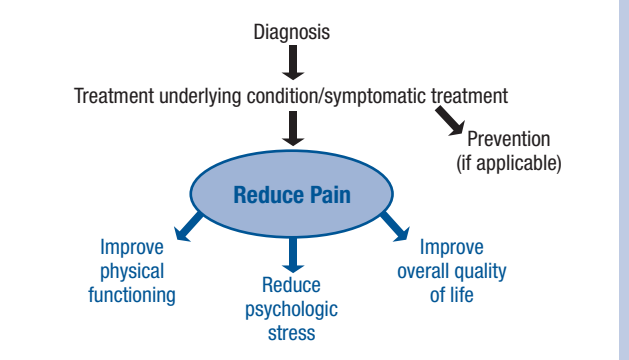
Estimated US Prevalence of Neuropathic Pain*

Condition	Number of Cases
Low-back pain associated	2,100,000
Painful diabetic neuropathy	600,000
Postherpetic neuralgia	500,000
Cancer associated	200,000
Spinal cord injury	120,000
Causalgia and reflex sympathetic dystrophy	100,000
Multiple sclerosis	50,000
Phantom pain	50,000
Poststroke	30,000
HIV associated	15,000
Trigeminal neuralgia (tic douloureux)	15,000
Total (excluding back pain)	**1,680,000**
Total (including back pain)	**3,780,000**

*Based on population of 270 million.
Adapted with permission from Bennett GJ. *Hosp Pract*. 1998;33:95-114.

Figure 3

Neuropathic Pain: Approach to Treatment



Turk DC. *Clin J Pain*. 2000;16:279-280.

underlying condition that may be causing the pain, providing symptomatic relief from pain and disability, and preventing recurrence. It is important for both clinicians and patients to have appropriate outcome expectations. Clinically meaningful goals can be achieved in a considerable proportion of patients. These include reducing pain, improving physical function, reducing psychological distress, and improving overall quality of life (QOL).

Nonpharmacologic strategies (eg, biofeedback, relaxation) may be useful in easing neuropathic pain and improving function when used as adjuncts to pharmacologic therapy. However, nonpharmacologic approaches are rarely sufficient on their own, especially in the case of chronic neuropathic pain. Pharmacotherapy is thus the primary intervention.

Among medications used for the treatment of neuropathic pain, those whose efficacy has been demonstrated consistently in randomized controlled trials are gabapentin,[77,80] lidocaine patch 5%,[81,82] tricyclic antidepressants,[77,83,84] tramadol,[77] and opioids.[77,85] Dosage recommendations for these agents are provided in Table 10.

In one of several well-controlled studies of gabapentin, Rowbotham et al conducted a randomized, double-blind, placebo-controlled clinical trial of this agent in the treatment of 229 patients with PHN.[80] Participants received 8 weeks of treatment with either gabapentin titrated to a maximum of 3600 mg/d, or a matching placebo. The proportion of patients treated with gabapentin who reported themselves improved on the Participants' Global

Table 10

First-Line Medications for Neuropathic Pain*

Recommendations from the Fourth International Conference on the Mechanisms and Treatment of Neuropathic Pain

Medication	Initial Dosage	Titration	Maximum Dosage	Duration of Adequate Trial	Most Common Adverse Effects
Gabapentin	100 to 300 mg every night or 100 to 300 mg tid	↑ by 100 to 300 mg tid every 1 to 7 days as tolerated	3600 mg/d (reduce if low CrCl)	3 to 8 weeks for titration plus 1 to 2 weeks at maximum tolerated dosage	• Somnolence • Dizziness • GI symptoms • Peripheral edema
Lidocaine patch 5%	≤3 patches daily for ≤12 hours	None needed	3 patches daily for ≤12 hours	2 weeks	• Mild skin reactions (erythema, rash) • Systemic absorption must be considered in patients receiving oral class 1 antiarrhythmic drugs
Opioids†	5 to 15 mg every 4 hours as needed	After 1 to 2 weeks, convert total daily dosage to long-acting opioid and continue short-acting medication as needed	No maximum with careful titration; consider pain-specialist evaluation at dosages >120 to 180 mg daily	4 to 6 weeks	• Constipation • Sedation • Nausea
Tramadol	50 mg once/twice daily	↑ by 50 to 100 mg daily in divided doses every 3 to 7 days as tolerated	400 mg daily	4 weeks	• Dizziness • Nausea • Constipation • Somnolence • Orthostatic hypotension
Nortriptyline or desipramine	10 to 25 mg every night	↑ by 10 to 25 mg daily every 3 to 7 days as tolerated	75 to 150 mg daily (continue titration with caution if blood level of drug + metabolite is <100 ng/mL)	6 to 8 weeks, with ≥1 to 2 weeks at maximum tolerated dosage	• Adverse cardiac events • Sedation • Anticholinergic effects • Orthostatic hypotension

*After these recommendations were published, pregabalin and duloxetine were approved by the FDA for treatment of painful diabetic neuropathy (pregabalin and duloxetine) and painful herpetic neuralgia (pregabalin); see text for more information.

†Dosages given are for morphine sulfate.

CrCl = creatinine clearance; GI = gastrointestinal.

Adapted with permission from Dworkin RH et al. *Arch Neurol*. 2003;60:1528. © 2003 American Medical Association. All rights reserved.

Impression of Change at the end of treatment was significantly greater than the proportion of patients treated with placebo (Figure 4).

In their double-blind, crossover-design study, Meier et al compared the lidocaine patch 5% with a placebo patch in patients with PHN and other peripheral neuropathic pain syndromes (PNPS).[81] Patients reported the severity of their pain on a 100-mm visual analog scale (VAS) at baseline and at intervals for 12 hours following patch application. As shown in Figure 5a, the lidocaine patch 5% provided a highly significant (*P*<.001) reduction in VAS ongoing pain intensity at all time points investigated compared with pretreatment levels. Results for allodynia were similar (Figure 5b).

Emerging Therapies in Neuropathic Pain

New treatments for neuropathic pain include pregabalin, duloxetine, and the development of cellular minipumps, or immortalized, bioengineered cell lines that secrete various antinociceptive molecules to reverse neuropathic pain. With regard to emerging pharmacotherapies, pregabalin capsules recently received approval from the FDA for the medical management of neuropathic pain associated with DPN and PHN. The efficacy of pregabalin has been established in several double-blind, placebo-controlled trials. During these trials, pregabalin provided pain reduction in a significant portion of patients. Safety trials of pregabalin demonstrated adverse events that were mild to moderate with low treatment-related discontinuation rates. Pregabalin is expected to be classified as a controlled substance in a category with a lower potential for misuse or abuse compared with controlled substances in other categories. Therefore, product labeling may contain a black-box warning that outlines potential risks.[77,86-91]

Likewise, after 6-month priority review, duloxetine was deemed safe and effective by the FDA last year for the management of neuropathic pain associated with diabetes. The efficacy and safety of duloxetine was demonstrated in 2 randomized, 12-week, double-blind, placebo-controlled, fixed-dose trials in nondepressed patients with DPN. In both studies, duloxetine capsules significantly reduced 24-hour pain compared with placebo, and improvements were observed as early as the first week of treatment and were maintained for the duration of the trials. Duloxetine has been proven to relieve the stabbing, burning, and shooting pain associated with DPN; however, it does not alter the underlying nerve damage caused by this disorder.[92,93] Other emerging therapies such as virus-mediated methods, while at the early stages of evolution and use, may provide long-term relief of chronic neuropathic pain, without systemic side effects or surgical interventions.[94]

Figure 4

Subjects With PHN Reporting Improvement of Pain in Association With Gabapentin and With Placebo

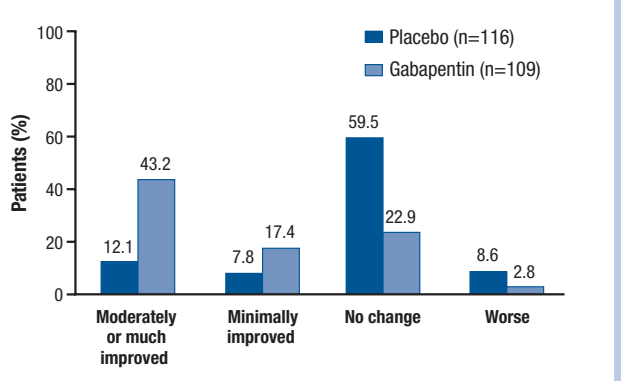


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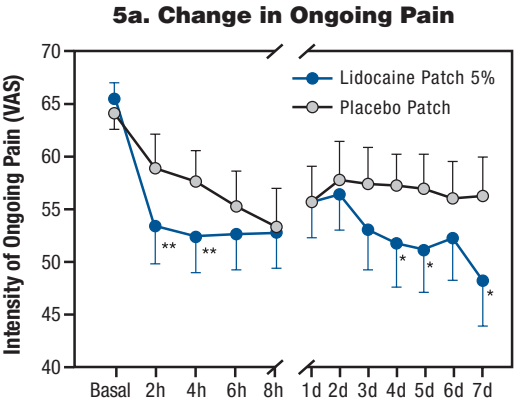
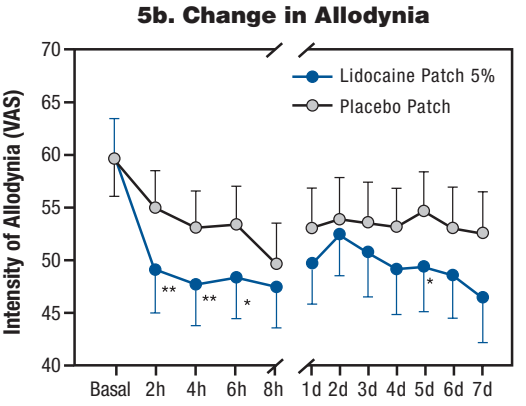
Figure 5a & 5b

Change of Basal Scores (VAS) in (5a) Ongoing Pain and (5b) Allodynia Throughout the First 8 h and 7-day Treatment Period After Patch Application; Mean (±SEM); Lidocaine Patch 5% vs Placebo Patch (N=40)





The decrease in ongoing pain intensity and allodynia was highly significant in the lidocaine group (*P*<.001) and significant in the placebo group (*P*<.05) compared with the pretreatment (basal) values at all time points of the assessment.

**P*<.05 and ***P*<.01

Reprinted with permission from International Association for the Study of Pain®. Meier T, Wasner G, Faust M, et al. Efficacy of lidocaine patch 5% in the treatment of focal peripheral neuropathic pain syndromes: a randomized, double-blind, placebo-controlled study. *Pain*. 2003;106:155.

Special Populations

Older Patients

A significant number of older Americans have untreated or undertreated chronic pain. Epidemiologic studies that involved community-dwelling older adults found prevalence rates of regular, untreated pain that ranged from 25% to 83%.[95-97] Similarly, up to 83% of the older in long-term care facilities were found to have chronic pain.[11,98] In other studies, substantial proportions of older patients with cancer and with hip fractures were found to receive no analgesics whatsoever.[12,99]

Persistent pain in older adults has been correlated with important sequelae, including sleep disturbance, malnutrition, physical function decline, falls, depression and anxiety, impaired cognition, impaired immune function, decline in social and recreational activities, decreased quality of life, and increased healthcare utilization and cost.[100,101] Table 11 summarizes the barriers to effective pain management in the older population.

The basic principles that can be used to guide the management of chronic pain in older persons include the following: clinicians should assess pain in all older adults during their initial presentation; any pain that an individual reports as having an impact on his or her physical function, psychosocial function, or other aspects of quality of life should be considered a significant problem; self-report of pain and its impact should be the gold standard of assessment, for those older persons who are able to do so. For those older persons who cannot self-report by virtue of cognitive impairment or other disabilities, alternative assessment strategies should be employed.[100]

Table 11

Barriers to Effective Pain Control in Older Adults

- Inadequate knowledge and skills regarding assessment and treatment
- Misbeliefs and fears regarding use of analgesics
- Fears related to side effects and adverse effects
- Fear of addiction and tolerance
- Multiple medical problems and sources of pain
- Multiple potential drug interactions
- Differences in pharmacokinetics
- Higher likelihood of cognitive and sensory impairment
- Underreporting and inadequate assessment of pain

All older adults with functional impairment or diminished quality of life due to chronic pain should be considered candidates for pharmacologic therapy.[100] The goal of such therapy is to provide the maximum in terms of therapeutic effects—decreasing pain and increasing function—while minimizing the risk of adverse effects, drug-drug interactions, and drug-disease interactions. The least invasive and least toxic interventions should be considered first.[100] This approach is particularly important in older individuals in whom drug pharmacokinetics might be altered and in whom comorbid medical conditions are common. Topical analgesics which exert their mechanism of action peripherally and do not result in clinically significant systemic blood levels may be particularly useful in the older, as are those systemic medications which possess the lowest risk of side effects or drug interactions.

When systemic medications are indicated, acetaminophen should be considered first for the treatment of mild to moderate pain of musculoskeletal origin.[100] For those older individuals who require NSAIDs, COX-2 selective agents or nonacetylated salicylates may be preferred over nonselective NSAIDs.[100] At the time that this publication was in development, the latest FDA recommendations involved "limited use" of COX-2 inhibitors. This limited use statement elucidates that COX-2 inhibitors may be most appropriate for patients with a history of gastrointestinal adverse events associated with nonselective NSAID use and patients not responding or intolerant to those agents. According to the FDA, for other patients, nonselective NSAIDs may be the appropriate first treatment. In the interim, the FDA recommends that physicians take into consideration the new safety information and make treatment decisions on an individual patient basis.[102]

Adjuvants such as anticonvulsant agents are important pharmacologic choices for older patients who have neuropathic pain conditions. Opioid therapy is recommended in those patients who report or who demonstrate behaviors suggestive of unrelieved pain with nonopioids, and who are experiencing moderate to severe pain with impaired function.

Improving Opioid Therapy

Opioids are widely used for the treatment of acute and chronic pain. However, while several controlled clinical trials have documented the efficacy and safety of opioids in these settings,[85,103] few studies have examined the compliance, safety, and long-term efficacy of opioid use for chronic pain therapy. One recent study of patients with intractable headaches who had daily scheduled opioids for at least 3 years found a relatively low percentage of patients with demonstrated efficacy and an unexpectedly high prevalence of misuse.[104] Therefore, caution must be used when prescribing opioids for chronic pain conditions.

Table 12

Sources of Guideline Documents Relating to the Clinical Use of Opioids

American Academy of Pain Medicine	www.painmed.org
American Pain Society	www.ampainsoc.org
Federation of State Medical Boards	www.fsmb.org
Joint Commission on the Accreditation of Healthcare Organizations	www.jcaho.org
National Comprehensive Cancer Network	www.nccn.org
Pain & Policy Studies Group, University of Wisconsin (State regulations)	www.medsch.wisc.edu/painpolicy
U.S. Drug Enforcement Agency	www.usdoj.gov/dea
World Health Organization	www.who.int/en

Table 13a

Oral Opioid Analgesics Commonly Used for Moderate Pain

Medication	Starting Dose (mg)* Adults	Comments	Precautions and Contraindications
Morphine-Like Agonist (Mu Agonists)			
Codeine	30-60	~10% of people lack the enzyme needed to make codeine active. Codeine may cause more nausea and constipation per unit of analgesia than other mu agonist opioids.	Many preparations of codeine and the other opioids in this table are combinations with nonopioid analgesics.†
Oxycodone	5		Same as for codeine.
Meperidine	50	Shorter acting; biotransformed to normeperidine, a toxic metabolite.	Normeperidine accumulates with repetitive dosing, causing CNS excitation; avoid in patients with impaired renal function or who are receiving monoamine oxidase inhibitors; avoid any chronic use. Do not use for more than 1-2 days.
Propoxyphene	65-130	Weak analgesic; many preparations include nonnarcotic analgesics; biotransformed to potentially toxic metabolite (norpropoxyphene).	Propoxyphene and metabolite accumulate with repetitive dosing, overdose complicated by convulsions. Not recommended for use in older adults or patients with renal impairment.
Hydrocodone	5-10		Most preparations are combined with nonopioid analgesics.
Weak Mu Agonist-Monoamine Reuptake Inhibitor			
Tramadol	50-100	Unique mechanism; analgesia appears to result from synergy of the 2 mechanisms. Maximum dose 400 mg/day.	Lowers seizure threshold.
Mixed Agonist-Antagonist (Kappa Agonists)			
Pentazocine	50	Formulated in combination with acetaminophen, aspirin, and ibuprofen. Some preparations include naloxone to discourage parenteral abuse.	May cause psychotomimetic effects, may precipitate withdrawal in narcotic-dependent patients.

*Starting doses are approximately equianalgesic to aspirin 650 mg (adults). The optimal dose for each patient is determined by titration.

†The total dose of combinations with acetaminophen are limited by the maximal dose of that drug, 4 g/day in adults (8-12 tablets of the most common preparation).

Adapted with permission from *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. 5th ed. Glenview, Ill: American Pain Society; 2003:14.

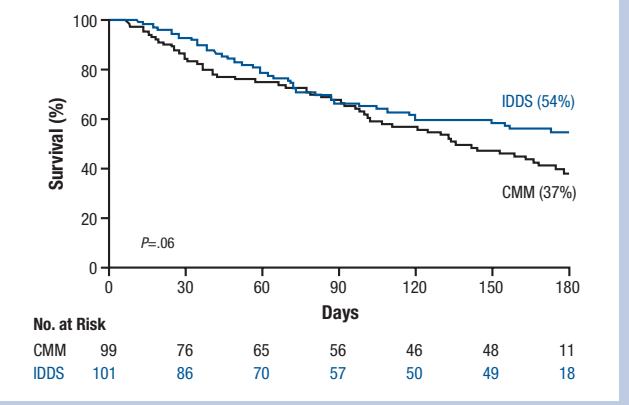
In the last several years, new evidence-based clinical practice guidelines have been published to promote the safe and effective use of opioids in patients with chronic pain. Sources for several of these guidelines are listed in Table 12.

While opioid analgesics remain an important option for many types of moderate to severe acute and chronic pain, clinicians and patients must understand both the clinical risks and benefits of this class of drugs. Neuropathic pain, a type of pain which had previously been regarded as poorly responsive to opioids, may in some instances also respond to opioids. Tables 13a & 13b (page 14) list commonly used oral opioids for moderate and severe pain, respectively.

A few intriguing studies have been published suggesting that aggressive pain management utilizing opioids may increase the survival time of cancer patients experiencing severe pain.[105,106] For example, Smith et al randomly assigned 202 patients with refractory cancer pain to treatment with comprehensive medical management (CMM) according to AHCPR cancer pain guidelines, or to CMM plus an implantable intrathecal drug delivery system (IDDS). At the end of 6 months, patients who received the IDDS demonstrated improved survival, with 54% remaining alive compared with 37% of patients receiving CMM alone (*P*=.06) (Figure 6).[106]

Figure 6

Kaplan-Meier Curve of Overall Survival in Patients With Refractory Cancer Pain Treated With Comprehensive Medical Management (CMM) or With CMM Plus an Implantable Intrathecal Drug Delivery System (IDDS)



Adapted with permission from Smith TJ, et al. *J Clin Oncol*. 2002;20:4048.
© 2002 American Society of Clinical Oncology.

Table 13b

Opioid Analgesics Commonly Used for Severe Pain

Medication	Starting Oral Dose Adults (mg)	Comments	Precautions and Contraindications
Morphine-Like Agonists (Mu Agonists)			
Morphine	15-30	Standard of comparison for opioid analgesics. Sustained-release preparations release drug over 8-12 hours. Other formulations last 12-24 hours. Generic sustained-release morphine preparations are now available.	For all opioids, caution in patients with impaired ventilation, bronchial asthma, increased intracranial pressure, liver failure.
Hydromorphone	4-8	Slightly shorter duration than morphine.	
Oxycodone	10-20		
Methadone	5-10	Good oral potency, long plasma half-life (24-36 hours).	Accumulates with repeated dosing, requiring decreases in dose size and frequency, especially on days 2-5. Use with caution in older adults.
Levorphanol	2-4	Long plasma half-life (12-16 hours, but may be as long as 90-120 hours after 1 week of dosing).	Accumulates on days 2-3. Use with caution in older adults.
Oxymorphone	—	5 mg rectal suppository – 5 mg morphine parenteral.	Like parenteral morphine.
Meperidine	Not recommended	Slightly shorter acting than morphine, accumulates with repetitive dosing, causing CNS excitation.*	Use with caution. Normeperidine (toxic metabolite) accumulates with repetitive dosing, causing CNS exitation and a high risk of seizure. Avoid in patients with renal impairment and patients on monoamine oxidase inhibitors.*
Mixed Agonist-Antagonists (Kappa Agonists)			
Nalbuphine	—	Not available orally, not scheduled under Controlled Substances Act.	Incidence of psychotomimetic effects lower than with pentazocine; may precipitate withdrawal in opioid-dependent patients.
Butorphanol	—	Like nalbuphine. Also available in nasal spray.	Like nalbuphine.
Pentazocine	—		
Partial Agonist			
Buprenorphine	—	Lower abuse liability than morphine; does not produce psychotomimetic effects. Sublingual tablets now available both plain and with naloxone for opioid-dependent patient management by specially certified physicians. These tablets are not approved as analgesics.	May precipitate withdrawal in narcotic-dependent patients; not readily reversed by naloxone; avoid in labor.

*Irritating to tissues with repeated IM injection.

Adapted with permission from *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. 5th ed. Glenview, Ill: American Pain Society; 2003:16-17.

The use of methadone for the treatment of chronic pain has been increasing. Methadone also has a long, albeit variable, half-life, which ranges from approximately 17 hours to 128 hours.[107] However, this and the other apparent advantages of methadone must be weighed against some important potential consequences, including concerns of accumulation with profound sedation,[108] electrocardiographic abnormalities (QTc interval prolongation), and cases of torsade de pointes.[109,110]

Principles of Opioid Prescribing for Chronic Pain

The adverse effects associated with the use of opioid analgesics may include side effects (such as nausea, vomiting, constipation, mental clouding/sedation and pruritus), other potentially negative pharmacologic effects (such as hypogonadism and its consequences),[111-116] and the risk of misuse, abuse, addiction, and diversion (Table 14). The monitoring and management of side effects should be viewed as an essential component of opioid pharmacotherapy. Side effect management, like the effort to optimize analgesia, requires a comprehensive assessment, treatment of underlying causes if possible, careful individualization of the dose, focused symptomatic therapy (such as the administration of a laxative for constipation or a psychostimulant for sedation), and consideration of new strategies if treatment-limiting toxicity compromises outcomes. New strategies include a trial of a different opioid (opioid titration) and coadministration of any of numerous analgesic therapies that may allow opioid dose reduction. The potential risks of misuse, abuse, addiction, and diversion also mandate a detailed assessment, including a substance use history and other factors that suggest the level of risk in the individual therapy. The risk of abuse or addiction is likely

Table 14

Approaches to Management of Opioid-Induced Side Effects

Side Effect	Precautions and Contraindications	Prevention and Management
Sedation	Elderly Concurrent sedating medications	General approach* plus: • Eliminate other nonessential medications with sedating effects • Consider use of mild stimulants during the day (eg, caffeine) • Consider use of psychostimulant (eg, methylphenidate) for persistent sedation, although exercise caution in combining psychoactive drugs in the elderly
Confusion Mental clouding	Elderly Preexisting CNS conditions	General approach plus: • Eliminate other nonessential medications with CNS effects • Consider use of neuroleptics for persistent delirium
Respiratory depression	Opioid-naïve patients taking large opioid doses Head injury, lung disorder	General approach plus: • Monitor sedation level and respiratory status regularly, especially during first 24 hours of treatment in opioid-naïve patients • Stop opioid until respiratory depression resolves and reinstitute opioid at 75% of the previous dosage • Stop opioid and administer naloxone** for minimally responsive or unresponsive patients • Use spirometry and oxygen, as needed
Pruritus (itching)		General approach plus: • Consider administering diphenhydramine or hydroxyzine • Consider naloxone infusion titrated to the desired effect if other treatments fail
Nausea and vomiting	Concomitant conditions or treatments producing nausea and vomiting	General approach plus: • If nausea is due to stimulation of chemoreceptor trigger zone (central mechanisms), consider adding ondansetron, prochlorperazine, or hydroxyzine • If nausea is due to slowed gastric mobility, consider adding metroclopramide • For chronic nausea, consider metroclopramide and/or other antiemetics
Constipation	Advanced age Immobility Abdominal problems or concurrent constipating medications	General approach plus: • Implement appropriate dietary changes • Assess regularly and use stool softeners and mild peristaltic stimulants for all patients on ATC opioids (prevention) • If no BM in a 48-hour period, add 1 or 2 additional agents (eg, lactulose, milk of magnesia, senna) • If no BM in a 72-hour period, assess for (and treat) fecal impaction • If not impacted, try additional method (eg, enema, mineral oil, magnesium citrate) • If impacted, use glycerine suppository or oil retention enema (as needed) to facilitate manual disimpaction, with appropriate analgesia

*The general approach to managing side effects includes changing the dosage or route of administration, trying a different agent in the same class, or adding an agent that counteracts the effect.

**For comatose patients, place endotracheal tube prior to administering naloxone. In addition, titrate naloxone carefully to avoid profound withdrawal, seizures, and severe pain.

ATC = around-the-clock administration; BM = bowel movement; CNS = central nervous system.

Pain: Current Understanding of Assessment, Management, and Treatments: National Pharmaceutical Council, Inc. and Joint Commission on Accreditation of Healthcare Organizations; 2001. © Joint Commission on Accreditation of Healthcare Organizations, 2004. Reprinted with permission.

to be relatively high in those with a prior history of substance abuse, a family history of substance abuse, or some other major type of psychopathology.

Validated scales that assess the risk of abuse-related outcomes are available and could be brought into the clinical setting. Based on the assessment, clinicians should clarify who should not be treated, who should be treated with the help of consultants, and who should be referred. If the clinician is comfortable treating, an effort must be made to structure the opioid regimen in a way that reflects the degree of perceived risk. In some cases, the use of an opioid agreement that defines obligations and consequences of various behaviors is appropriate.[117] Other elements may include a

complete record review prior to therapy, routine urine drug screens, frequent visits, small prescriptions, required consultations, and a variety of related strategies that increase the ability to monitor the therapy and assist the patient in adhering to instructions. Clinicians should also document the treatment plan and its outcomes. The outcomes followed over time should include analgesia, side effects, functional outcomes, and adherence to the therapy. Opioid treatment should be discontinued if recognizable benefits are not achieved or if the risks or adverse events exceed acceptable levels.

Challenges of Chronic Pain Management in Primary Care Settings

The high prevalence of chronic pain in the United States coupled with the relatively small number of trained pain specialists necessitates that primary care clinicians manage the majority of chronic pain conditions. The American Pain Society conducted a consumer survey that found that nearly half of all respondents were seeing a primary care clinician for their severe pain, and 68% of those had never been referred to a specialized pain clinic or program.[118] One of the more challenging issues faced by primary care physicians is the decision of when to refer a patient to a pain specialist. Interviews with 56 primary care physicians indicate that many find the management of chronic pain to be particularly challenging. First, time constraints imposed by contemporary medical practice limit the ability of providers to adequately manage patients with chronic pain, especially given that pain is typically just one of several chronic conditions that require management in a given patient. Moreover, primary care clinicians reported that patients with chronic pain frequently have unrealistic expectations regarding outcomes—a fact that may foster an adversarial relationship between the clinician and the patient. Adding to the problem is a perception that even when referrals are made to pain specialists, patients still have pain when they return to primary care, and due to inadequate training in pain management, the clinician may not have a full understanding of the treatments that have been provided or recommended.

Accordingly, it has been suggested that primary care clinicians may benefit from greater proficiency in managing this population of patients. They may benefit by forming collaborative relationships with pain specialists, to whom they may then refer more complex cases, and with whom they may provide interdisciplinary care.

Clinicians can locate educational resources related to pain management through several national organizations:

- American Academy of Hospice and Palliative Medicine (http://www.aahpm.org/)
- American Academy of Neurology (http://www.aan.com/professionals/)
- American Academy of Pain Management (http://www.aapainmanage.org/)
- American Academy of Pain Medicine (http://www.painmed.org)
- American Academy of Physical Medicine and Rehabilitation (http://www.aapmr.org/)
- American Headache Society (http://www.ahsnet.org/)
- American Osteopathic Association (http://www.do-online.osteotech.org)
- American Pain Foundation (http://www.painfoundation.org/)
- American Pain Society (http://www.ampainsoc.org/)
- American Society of Anesthesiologists (http://www.asahq.org/)
- American Society of Clinical Oncology (http://www.asco.org)
- American Society of Pain Management Nurses (http://www.aspmn.org/)
- National Pain Foundation (http://www.painconnection.org/)
- Oncology Nursing Society (http://www.ons.org/)

Challenges of Pain Management in Managed Care Settings

In managed healthcare organizations (MCOs), despite the JCAHO mandate regarding the assessment and treatment of pain, many members may not receive adequate services due to:

- A lack of consensus regarding outcome measures
- A lack of robust and generalizable outcome studies
- Underappreciation of the utility/value of new, effective treatments
- Consideration of drug-acquisition costs without factoring in the costs of treating side effects associated with some medications (eg, tricyclic antidepressants, older anticonvulsants, nonselective NSAIDs)

Correcting deficiencies in MCO pain management should begin with implementation of the American Pain Society Position Statement on Pain Assessment and Treatment in the Managed Care Environment.[119] This guideline stresses education and credentialing of providers, recognition of the unique nature of chronic pain, and the need for case coordination and communication with patients' disability carriers, employers, and other relevant stakeholders.

Other specific actions that MCOs may implement include developing a protocol for baseline and ongoing assessment of patients' pain, pain-related disability, and responses to treatment; establishing a lexicon to foster common understanding of pain terminology and, thus, effective communication within the organization; providing feedback mechanisms for patients, especially those with chronic pain, as well as tools for assessing the information received in the context of improving care when necessary; and designing a multimodal, stepped-care program that, in most cases, will be spearheaded by patients' primary care providers in coordination with specialists as necessary.

Summary and Conclusions

Chronic pain is a major public health problem, from the standpoint of patients, society, and frequently clinicians who provide care. Patient education and assessment are cornerstones in the management of chronic pain. Treatment should be tailored to the nature and intensity of pain reported by the patient, beginning with the least invasive approach that is appropriate and then progressing to more invasive approaches as necessary. For many patients with chronic pain, an approach of rational polypharmacy (utilizing medications with complementary mechanisms of action) will optimize the management of the patient's pain and functionality.

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Breakthroughs and Challenges in the Pharmacologic Management of Common Chronic Pain Conditions

Posttest, Program Evaluation, and CME Credit Request

PENNSTATE
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Instructions: To receive CME credit, complete the posttest and evaluation. Participants must receive a score of 80% or better to receive credit.

Posttest

1. In the AHEAD study, the prevalence of pain among individuals 70 years of age or older was found to be:
a. 10%
b. 27%
c. 33%
d. 64%

2. Which one of the following statements is true?
a. Compared with men, women are at higher risk for the development of pain, and experience pain of greater severity and longer duration.
b. Compared with women, men are at higher risk for the development of pain, and experience pain of greater severity and longer duration.
c. Men are at higher risk for the development of pain, but women experience pain of greater severity and longer duration.
d. There are no substantial differences between women and men with respect to the experience of pain.

3. Chronic pain is defined as prolonged acute pain.
a. True
b. False

4. An effective cancer pain patient education program may include information about all of the following except:
a. The types and rationale for analgesic medications
b. Instructions on changing the route of delivery of opioid analgesics
c. Instructions for getting the analgesic prescriptions filled
d. Specific instructions on how to dose and titrate analgesic medications
e. How to manage side effects

5. Which of the following domains is not/are not relevant to the assessment of patients with chronic pain?
a. Physical function
b. Emotional function
c. Global improvement and satisfaction
d. Medication side effects
e. All of the above are relevant

6. The majority of cases of low back pain are of mixed etiology.
a. True
b. False

7. Which of the following is considered a first-line abortive therapy for the treatment of moderate to severe migraine?
a. An NSAID
b. A triptan
c. An opioid
d. All of the above

8. Osteoarthritis begins with trauma-induced or idiopathic loss of integrity of the cartilage.
a. True
b. False

9. Which of the following has/have been shown in controlled clinical trials to be effective in the treatment of neuropathic pain?
a. Gabapentin
b. Lidocaine patch 5%
c. Ibuprofen
d. Acetaminophen
e. a and b
f. All of the above

10. Which of the following is true regarding elderly patients?
a. All those with pain should be considered candidates for pharmacologic therapy.
b. All those with functional impairment or diminished quality of life due to persistent pain should be considered candidates for pharmacologic therapy.
c. Only those with severe pain should be considered candidates for pharmacologic therapy.
d. Pharmacologic therapy should be avoided in the management of the elderly.

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I verify that I have completed this CME activity _____ (signature)

Actual time spent on the activity (up to 2 hours) _____

For nursing contact hours provide RN license # _____

Posttest Answers

Please record your posttest answers: 1. ___ 2. ___ 3. ___ 4. ___ 5. ___ 6. ___ 7. ___ 8. ___ 9. ___ 10. ___

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Evaluation of this activity is integral to the CME process. CME certificate requests cannot be processed without the evaluation form.

Materials must be received by October 31, 2006. After this date, the activity will no longer be designated for credit. A CME certificate will be mailed within 6-8 weeks. It is recommended that participants keep a copy of their completed materials until they receive their certificate. For questions, please call Penn State Continuing Education at (717) 531-6483 or e-mail ContinuingEd@hmc.psu.edu. Please reference activity code I3244-06-R.

Please fill in the circles completely using a dark pen or pencil.

Overall Evaluation

1. Extent to which you are satisfied with the overall quality of the educational activity
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**

2. To what extent did the activity present scientifically rigorous, unbiased, and balanced information?
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**

3. To what extent was the monograph free of commercial bias?
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**

4. To what extent did this educational activity change your knowledge/attitudes?
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**

5. To what extent did this educational activity change your skills?
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**

6. To what extent will you make a change in your practice as a result of your participation in this educational activity?
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**

7. Which of the following best describes the impact of this activity on your performance? (choose one)
❍ This activity will not change my behavior because my current practice is consistent with what was taught
❍ This activity will not change my behavior because I do not agree with the information presented
❍ I need more information before I can change my practice behavior
❍ I will immediately implement the information in my practice

8. Extent to which educational objectives were achieved
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**

To receive nursing contact hours, evaluate each objective below

- Summarize the epidemiology and public health impact of common chronic pain conditions, as well as current clinical practice guidelines and evidence regarding evaluation and treatment of patients with chronic pain
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**
- Discuss the impact of ethnicity, gender, and age on the pathophysiology, assessment, drug metabolism, and management of various chronic pain conditions
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**
- Explain the mechanism of chronic pain
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**
- Describe clinically useful methods to assess pain (eg, numeric rating scales, multidimensional assessment tools), barriers to pain assessment, and the use of assessment data to select pain management strategies and to evaluate patient outcomes
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**
- Outline a stepwise approach to pain management based on the mechanisms of action, routes of analgesic administration, and comparative risks and benefits of commonly used therapies
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**
- Describe recent advances in the management of chronic pain
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**
- Differentiate between addiction, pseudoaddiction, physical dependence, and tolerance, and understand the clinical implications of each
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**
- Outline best practices for the use of opioid analgesics with respect to patient selection, responsible prescribing, titration/rotation, adjunctive therapy, regulatory scrutiny, and risk/benefit evaluation
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**
- Discuss challenges surrounding pain management in the primary care setting, the impact of managed care, and the importance of patient education to improve outcomes
❍ **Very High** ❍ **High** ❍ **Moderate** ❍ **Low** ❍ **Very Low**

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