Complete Summary

GUIDELINE TITLE

Opioids in the management of chronic non-cancer pain: an update of American Society of the Interventional Pain Physicians' (ASIPP) guidelines.

BIBLIOGRAPHIC SOURCE(S)

Trescot AM, Helm S, Hansen H, Benyamin R, Glaser SE, Adlaka R, Patel S, Manchikanti L. Opioids in the management of chronic non-cancer pain: an update of American Society of the Interventional Pain Physicians' (ASIPP) guidelines. Pain Physician 2008 Mar-Apr;11(2S):S5-62. [350 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Trescot AM, Boswell MV, Atluri SL, Hansen NC, Deer TR, Abdi S, Jasper JF, Singh V, Jordan AE, Johnson BW, Cicala RS, Dunbar EE, Helm S II, Varley KG, Suchdev PK, Swicegood JR, Calodney AK, Ogoke BA, Minore WS, Manchikanti L. Opioid guidelines in the management of chronic non-cancer pain. Pain Phys 2006;9(1):1-39.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Chronic non-cancer pain

GUIDELINE CATEGORY

Counseling
Diagnosis
Evaluation
Management
Risk Assessment
Screening
Treatment

CLINICAL SPECIALTY

Anesthesiology
Internal Medicine
Neurology
Physical Medicine and Rehabilitation
Psychiatry
Psychology
Rheumatology

INTENDED USERS

Health Care Providers
Physicians
Substance Use Disorders Treatment Providers

GUIDELINE OBJECTIVE(S)

- To provide clear and concise guidelines to physicians, to improve patient access, and avoid diversion and abuse
- To provide guidance for the use of opioids for the treatment of chronic non-cancer pain, to bring consistency in opioid philosophy among the many diverse groups involved, to improve the treatment of chronic non-cancer pain, and to reduce the incidence of abuse and drug diversion

TARGET POPULATION

All patients suffering with chronic moderate to severe pain of non-cancer origin who may be eligible for appropriate, medically necessary opioid analgesic management*

***Note**: This management may include or be independent of interventional techniques.

INTERVENTIONS AND PRACTICES CONSIDERED

Use of Opioid Therapy for Management of Chronic Pain

1. Effectiveness of long-term opioids: morphine, transdermal fentanyl, oxycodone, hydrocodone, methadone, tramadol, oxymorphone
2. Adherence monitoring
    - Screening for opioid use (misuse and abuse)
    - Urine drug testing
        - Immunoassay drug testing

        - Gas chromatography/mass spectrometry, high performance liquid chromatography
    - Periodic review and monitoring
        - Medical and psychological diagnoses
        - Informed consent and treatment agreement
        - Appropriateness of therapy
        - Evaluation of progress toward treatment goals
        - Assessment of pain level and level of function
        - Prescription drug monitoring
        - Pill counts
        - Education

3. Evaluation
    - Pain, medical, and psychosocial history
4. Management
    - Physical, functional, and psychosocial assessment
    - Diagnostic testing
    - Diagnostic interventional techniques
    - Treatment plan
    - Therapeutic interventional techniques
    - 10-step process for chronic opioid therapy
    - Consultation and referral
    - Informed consent and controlled substance agreement
    - Documentation and medical records

MAJOR OUTCOMES CONSIDERED

- Effectiveness of opioids in the treatment of chronic pain
    - Symptom control
    - Quality of life
    - Emotional well-being
    - Functional status
- Rate of unemployment
- Adverse and comorbid effects of opioids in the treatment of chronic pain
- Sensitivity of drug testing assays for opioids
- Prevalence of controlled prescription drug abuse
- Prevalence of drug diversion
- Prevalence of drug interactions
- Cost of opioid use

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence

I	Evidence obtained from at least one properly randomized controlled trial.
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience descriptive studies and case reports or reports of expert committees.

Adapted from the Agency for Healthcare Research and Quality U.S. Preventive Services Task Force (USPSTF)

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A policy committee was convened and included a broad representation of academic and clinical practitioners, representing a variety of practices and geographic areas, all recognized as experts in opioid use and management of patients with chronic non-cancer pain. This committee formalized the essentials of

the guidelines. The elements of the guideline preparation process included literature searches, literature syntheses, systematic review, consensus evaluations, open forum presentations, formal endorsement by the American Society of Interventional Pain Physicians (ASIPP) Board of Directors and peer review.

Recommendations were provided based on methodological quality of supporting evidence, benefit versus risks and burdens, and implications (see "Rating Scheme for the Strength of the Recommendations" field below).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grade of Recommendation/Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
1A/strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B/strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/strong recommendation, low-quality or very low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A/weak recommendation, high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from	Weak recommendation, best action may differ depending on circumstances

Grade of Recommendation/Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
		observational studies	or patients' or societal values
2B/weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C/weak recommendation, low-quality or very low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Adapted from Guyatt et al. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians task force. *Chest* 2006; 129:174-181.

COST ANALYSIS

Health and Economic Impact

Chronic non-cancer pain is associated with significant economic, societal, and health impact. The cost of uncontrolled chronic pain is enormous, both to individuals and to society as it leads to a decline in the quality of life and disability. Estimates and patterns of direct healthcare expenditures among individuals with back pain in the United States reached $90.7 billion for the year 1998. On average, individuals with back pain generate healthcare expenditures about 60% higher than do individuals without back pain ($3,498 per year versus $2,178). It has been estimated that the cost of healthcare for patients with chronic pain might exceed the combined cost of treating patients with coronary artery disease, cancer, and AIDS. In the United States, it was estimated that the cost of treatment in the first year after failed back surgery for pain was

approximately $18,883 in 1997. Even further, annual healthcare cost incurred by chronic pain patients, excluding cost for surgical procedures, may range from $500 to as high as $35,400, with averages ranging from $12,900 to $18,883 annually.

The economic costs for chronic pain in general have been estimated to be over $86 billion per year. A cross-sectional study, based on survey data from 28,902 working adults in the USA was reported in 2003 with 13% of the workforce experiencing a loss of productivity during a 2 week period due to a common pain condition. In monetary terms, this loss of productivity was calculated to cost $61.3 billion, with $14.4 billion due to absenteeism and the rest due to the survey participants being at work, but with impaired productivity due to the pain.

In a recent survey of expenditures and health status among adults with back and neck problems, self-reported back and neck problems accounted for a large proportion of health care expenditures and spine-related expenditures have increased substantially from 1997 to 2005, without evidence of corresponding improvement in self-assessed health status. In this national estimate based on annual samples of survey respondents with and without self-reported spine problems from 1997 through 2005, a total of 23,045 respondents were sampled in 1997, including 3,139 who reported spine problems. In 2005, the sample included 22,258 respondents, including 3,187 who reported spine problems. This survey showed that in 1997, the adjusted medical cost for respondents with spine problems was $4,695 (95% CI, $4,181 to $5,209), compared with $2,731 (95% CI, $2,557 to $2,904) among those without spine problems in terms in inflation-adjusted dollars. Conversely, in 2005, the adjusted medical expenditures among respondents with spine problems was $6,096 (95% CI, $5670 to $6,522), compared with $3,516 (95% CI, $3,266 to $3,765) among those without spine problems. Consequently, total estimated expenditures among respondents with spine problems increased 65% after adjusting for inflation from 1997 to 2005, more rapidly than overall health expenditures. This is in contrast to the estimated proportion of persons with back or neck problems with self-reported physical function and limitations increasing from 20.7% (95% CI, 19.9% to 21.4%) to 24.7% (95% CI, 23.7% to 25.6%) from 1997 to 2005, which is an increase of 4%.

In one study evaluating the burden and determinants of neck pain in the general population and in workers after evaluating numerous studies, the 12-month prevalence of pain typically ranged between 30 and 50%, while, the 12-month prevalence of activity-limiting pain was 1.7% to 11.5% in the general population, in workers, the annual prevalence of neck pain varied from 27.1% to 47.8%, with between 11% and 14.1% of workers limiting their activities due to neck pain.

Economic Impact

The cost of opioid abuse is enormous ranging as high as $300 billion a year as per the estimates of the White House Budge Office. The White House Office of National Drug Control Policy, a component of the Executive Office of the President, established by the Anti-Drug Abuse Act of 1990, has been spending $12 to $13 billion each year.

A study by the Office of Management and Budget estimated drug abuse costs to the United States at $300 billion a year, including government anti-drug programs and the costs of crime, healthcare, accidents, and lost productivity. In the Aid to Family with Dependent Children (AFDC), Medicaid and food stamp programs, the incidence of drug abuse varies from 9.4% to 16.4%.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the quality of evidence (**I-III**) and recommendation grades (**1A-2C**) are provided at the end of the "Major Recommendations" field.

Clinical Effectiveness

Summary of Evidence

Based on the review of multiple systematic reviews and the available literature, the evidence for the effectiveness of long-term opioids in reducing pain and improving the functional status for 6 months or longer is variable. The evidence for transdermal fentanyl and sustained-release morphine is Level II-2 based on the quality of evidence criteria described by the U.S. Preventive Services Task Force as illustrated in Table 1 in the original guideline document. For oxycodone, the level of evidence is II-3, however, for hydrocodone and methadone, the level of evidence is III.

Recommendation

Based on the review of multiple systematic reviews and the available literature, the recommendation is 2A — weak recommendation, high-quality evidence with benefits closely balanced with risks and burden; derived from randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies; with the implication that with a weak recommendation, best action may differ depending on circumstances or patients' or societal values.

Adherence Monitoring

Introduction

Important issues in opioid therapy in chronic pain revolve around appropriate use of prescription opioids. Patients that describe symptoms of pain, and lack of relief,

are one of the most common patient populations in the primary care community. Perceived interference of activities of daily living creates the perception of a need of drugs, and sometimes these patients are divulging signs and symptoms that may threaten the patient-physician relationship that is built on trust. The primary care physician is ill equipped to handle these patients, they rapidly lose control, and then they often are referred to the pain management physician as a "risk shift." These patients expect something to be done, and are often promised that the pain clinic will maintain the same level of care. It is the pain physician's responsibility to define their personal risk tolerance. Many times the primary care physician will not engage in opioid agreements and not fully explore non-narcotic medication alternatives. Adherence monitoring is crucial to avoid abuse of the drugs and at the same time to encourage appropriate use, and involves the initiation of drug screening, pill counts, and patient care agreements, with the motto of "trust but verify."

A high-risk practice, such as a pain management practice, will readily activate an adherence monitoring program, utilize advanced documentation, have a strong office policy, a threshold policy, and will define how many patients of this nature will be treated in the practice. If available, a second opinion from an addictionologist or psychologist may be advised, and a high-risk practice should understand that these charts should be readily available for the Board of Medical Examiners to review for legitimate need. Frequent functional assessments are mandatory. The risk environment is increased with Medicaid and disabled patients, patients with a previous history of substance abuse, and psychiatric disorders, particularly bipolar personalities, borderline personalities, history of alcohol abuse, and chaotic home environment. Boundary violations, which unfortunately do occur in this patient population, are never acceptable, and a difficult patient is best chaperoned at each visit.

The high-risk patient may have an abnormal pill count or drug screen. The patient that is discharged from a previous practice will have a documented historical reason, and records from this previous practice are recommended. High risk includes discharge from a previous practice, chaotic lifestyle, recent arrival to the area, poor response to multimodality approach to pain, sedentary lifestyle, cigarette smoker, and possibly obesity. Also patients that are litigating, disabled, and on Medicaid may also be at higher risk and may require more adherence monitoring. Patients should be expected to take a proactive role in their own healthcare. The risk/reward of the relationship is constantly reassessed. The patient should understand that pills kill, pain does not. The concept of legitimate medical need is reviewed with the patient, and function, adherence, compliance, and co-managing physicians are sometimes called upon.

Confusion surrounding a specific operational definition of opioid misuse among chronic pain patients has complicated the process of effectively assessing and predicting its occurrence. The typical elements of drug diversion involve theft, forgery, counterfeit prescriptions, fraud imposed against physician/pharmacy for other patients, and promoting pill mills.

There is a need for better tamper-proof opioids. As long as long-acting opioids can be easily converted into a rapidly absorbed form, there will be an effort to divert these medications for illicit use.

Screening for Opioid Abuse

The decision to use opioids for chronic pain patients, like all medical decisions, is based on a balance between risk and potential benefit. Screening for opioid misuse and abuse is an exercise to strengthen the patient-physician relationship. This should not be confrontational, and the patient has to understand that this is like any other lab test. A physician would respond to abnormal liver functions or anemia, just as a pain physician responds to a screening questionnaire, urine drug screen, or pill count.

Even though several investigators have described multiple screening instruments in detecting opioid abuse or misuse in chronic pain patients, there is no widely used screening instrument in the current practice. Most look at problematic behaviors such as focusing on opioids, escalation of opioid use, multiple phone calls and visits, lack of improvement with increased medications, multiple prescription problems (lost or stolen scripts), and opioids from multiple providers.

Urine Drug Testing (UDT)

Although drug testing may be performed by testing the urine, serum, or hair, urine is considered as the best biologic specimen for detecting the presence or absence of certain drugs due to specificity, sensitivity, ease of administration, and the cost. However, controversies exist regarding the clinical value of UDT, partly because most current methods were designed for, or adapted from, forensic or occupational deterrent- based testing for illicit drug use and are not necessarily optimized for clinical applications in chronic pain management. In chronic pain management, UDT should be used with an appropriate level of understanding (which can improve a physician's professional adherence, compliance, and co-managing physicians ability to manage therapeutic prescription drugs with controlled substance), and to diagnose substance abuse or appropriate intake of drugs, thereby leading to proper treatment. They should be random, well organized, and synchronized with a well-understood testing lab. The lab understands you, and you understand what they are testing. False-positives, negatives, and the scope of testing should also be understood.

It is also critical to understand the metabolism of opioids, to avoid falsely accusing patients of abuse. For instance, codeine is metabolized to morphine, and hydrocodone to hydromorphone. However, it has only been recognized recently that morphine (in high doses) can be metabolized to hydromorphone. The hydromorphone is usually about 2% of the morphine dose (which can be determined by quantitative testing), and is usually seen in patients taking at least 100 to 200 mg morphine per day. In a retrospective case-control study, 66% of patients on morphine showed evidence of hydromorphone in the UDT; this was seen more commonly in females, despite the fact that the females were taking lower doses of morphine.

In principle, UDTs can detect the parent drug and/or its metabolite(s) and, therefore, demonstrate recent use of prescription medications and illegal substances. For most clinical applications, initial testing is done with class-specific immunoassay drug panels, which typically do not identify individual drugs within a class. However, this may, and perhaps should, be followed by a more specific technique such as a gas chromatography/mass spectrometry (GC/MS) to identify

or confirm the presence or absence of a specific drug and/or its metabolite(s). Numerous differences between various tests and even among the laboratories and manufacturers of various rapid drug screen tests include the number of drugs tested, cross-reactivity patterns, cut-off concentrations, and drug interferences. Clinicians should remember that the cut-off concentrations used for drugs in federally regulated testing, particularly opioids, are too high to be of value in clinical practice. Federally regulated testing includes 5 drugs or drug classes that are tested for in federal employees and federally regulated industries, including marijuana, cocaine, opiates, phencyclidine (PCP), and amphetamines/methamphetamines, with pre-determined cut-off levels with mandatory reconfirmation with the results by GC/MS, along with split sample in chain of custody requirements. In contrast, nonregulated testing is used for many purposes, including monitoring pain patients clinically.

In clinical practice, UDT is used for accurate record keeping, to identify use of undisclosed substances, to uncover diversion or trafficking, and to determine appropriate intake of prescribed substances. There are typically 2 types of UDT. These approaches used in proper combination can reduce cost, ensure accuracy, and improve efficiency. The 2 main types of UDT methods are:

1. Immunoassay drug testing, either laboratory based or by rapid drug testing ("site of service").
2. Laboratory-based specific drug identification with GC/MS, high-performance liquid chromatography (HPLC), etc.

Refer to the original guideline document for a discussion of drug-testing methods.

Table 18 (in the original guideline document) illustrates cut-off levels for various drugs detected by urine analysis. Ideally, a panel in chronic pain management settings for rapid drug screening should include not only opiates, but also oxycodone and methadone. In addition, the panel should include cocaine, marijuana, amphetamines and methamphetamines for illicit drugs, and benzodiazepines and barbiturates for other controlled substances. If a custom panel is not available, multiple tests may have to be performed as rapid drug screening.

Refer to the original guideline document for a list of common cross-reacting substances.

Since false-negatives and false-positives are possible, when questions arise, prior to taking any actions, a confirmatory test or no-threshold test must be performed in the laboratory.

Physicians may establish zero or low tolerance, but this should be discussed with the patient on the initial visit, and should be part of the written clinic policy. This may include referral to an addictionologist or psychologist, or may result in the refusal to prescribe opioids. However, it usually does not warrant dismissal of the patient. The practice limits for presence of cocaine and marijuana may range from only one positive screen (zero tolerance) to 3 positive screens and appropriate action later. Improper use of prescription drugs and doctor shopping should be dealt in the same manner.

Periodic Review and Monitoring

Periodic Review

Periodic reviews should assess the medical diagnoses, psychological diagnosis, informed consent, treatment agreement, appropriate opioid therapy with or without adjuvant medications or with or without interventional techniques, pre- and post-intervention assessment of pain level and function, and reassessment of pain score and level of function.

Regular assessment of the patient along with the periodic review of the diagnosis is extremely important. Routine assessment of the "4 As" (analgesia, activity, aberrant behavior, and adverse effects) will help to direct therapy and support the pharmacologic actions taken.

Further assessment should be performed by periodic monitoring, pill counts, and UDT (see below).

Periodic Monitoring

At reasonable intervals, depending on the specific circumstances of a given patient, the physician should review the course of treatment and any new information about the etiology of the pain. Continuation or modification of therapy should depend on the physician's evaluation of progress towards stated treatment goals, such as a reduction in a patient's pain scores and improved physical and/or psychosocial function (i.e., ability to work, utilization of healthcare resources, activities of daily living, and quality of social life). If treatment goals are not being achieved despite medication adjustments, the physician should reevaluate the appropriateness of continued treatment with the current medications. The physician should monitor patient compliance in medication usage and related treatment plans.

Prescription Drug Monitoring

Prescription drug monitoring programs collect information to assist state law enforcement and regulatory agents in identifying and investigating illegal practices related to controlled substances. However, some of the existing prescription programs and the recently passed National All Schedules Prescription Electronic Reporting Act (NASPER) should also assist physicians and pharmacists in identifying controlled substance abuse. The purpose of NASPER is to ensure access to care, delegate the appropriate use of opioids to those in the most need, and identify potential abusers that misuse, divert, or doctor shop.

Periodic Education

Drug education for physicians, providers, and patients is crucial. While it appears that certain medications have revolutionized the treatment of chronic pain in the United States, physicians must balance the medical need with the possibility of abuse and diversion, as well as the necessity to comply with state and federal regulations. It is obvious that healthcare practitioners are not only expected to prescribe medications when there is medical need and document appropriately,

but they are also expected to prevent illegal diversion and identify drug abuse. Consequently, education is a critical component of any program to control the diversion of prescription drugs.

Pill Counts

Random pill counts, along with UDT and prescription monitoring, would greatly reduce controlled substance abuse. Pill counts are essential in patients with suspicion of abuse. However, these can also be performed randomly on high risk patients.

A pill count is performed by notifying the patient a day before or on the day of the appointment of the patient, requesting the patient to bring with them their unused pills. The inability to provide pills or providing a reduced number will indicate use beyond the prescription. Pill counts above the expected ranges would indicate inappropriate low intake (suggesting that the medications are being over-prescribed). Recently, it has been reported that some unsuspected elderly patients may be selling controlled substances to supplement their income.

Principles Of Opioid Use

Introduction

In interventional pain management, patients may receive not only opioid analgesics, but also other controlled or noncontrolled drugs. Further, patients may be receiving controlled substances as an adjunct to interventional techniques, as well as to manage comorbid psychiatric and psychological disorders. Thus, the effectiveness studies published thus far may not apply in the majority of interventional pain management patients. Indeed, in an interventional pain practice, controlled substances may be prescribed at lower doses, particularly opioid analgesics, in conjunction with interventional techniques. It has also been shown that interventional techniques reduce psychological distress and improve functional status. More likely than not, the requirement for opioids and adjuvant drugs may be reduced or at least become stable. Hence, interventional pain physicians probably should not compare patients in their settings undergoing interventional techniques with others receiving drug therapy as mainstay. Monotherapy, particularly with opioids, may be appropriate for only a small subgroup of those with chronic pain.

The concept of "universal precautions," first seen in medicine with the explosion of human immunodeficiency virus (HIV) and hepatitis tainted blood, was introduced to counter the misconception that a provider would be able to predict "by looking" who might have a communicable blood-borne disease. This led to the use of "precautions" (gloves, etc.) for all patients, regardless of their age or socieoeconomic class. A rational approach to the treatment of chronic pain with opioids has been described using a pain and addiction continuum and a substance use assessment in a pain patient leading to the implementation of "universal precautions" in pain medicine.

Recommendation

Based on the grading recommendations, the recommendation is 2A — weak recommendation, high-quality evidence: with benefits closely balanced with risks and burden; derived from RCTs without important limitations or overwhelming evidence from observational studies, with the implication that with a weak recommendation, best action may differ depending on circumstances or patients' or societal values.

Basic Philosophy

Principles for prescribing opioids must require a comprehensive evaluation (mandatory physical and optional psychological), appropriate documentation at regular intervals to assess the efficacy of therapy, with specific evaluation of the impact on functional status, degree of pain relief, identification and treatment of undesirable side effects, and monitoring for abuse behaviors. In addition, there must be adherence to a controlled substance agreement and with regulatory guidelines promulgated by various agencies. Figure 6 in the original guideline document shows an algorithmic approach to patient evaluation and management. The table below shows an algorithmic approach for chronic opioid therapy.

Table. Ten Step Process: An Algorithmic Approach for Long-Term Opioid Therapy in Chronic Pain

STEP I	**Comprehensive initial evaluation**
STEP II	**Establish diagnosis** • X-rays, magnetic resonance imaging (MRI), computed tomography (CT), neuro-physiological studies • Psychological evaluation • Precision diagnostic interventions
STEP III	**Establish medical necessity (lack of progress or as supplemental therapy)** • Physical diagnosis • Therapeutic interventional pain management • Physical modalities • Behavior therapy
STEP IV	**Assess risk-benefit ratio** • Treatment is beneficial
STEP V	**Establish treatment goals**
STEP VI	**Obtain informed consent and agreement**
STEP VII	**Initial dose adjustment phase (up to 8 to 12 weeks)**

	• Start low dose
	• Utilize opioids, nonsteroidal anti-inflammatory drugs (NSAIDs) and adjuvants
	• Discontinue due to
	  • Lack of analgesia
	  • Side effects
	  • Lack of functional improvement

STEP VIII	**Stable phase (stable - moderate doses)**
	
	• Monthly refills
	• Assess for four As
	  • Analgesia
	  • Activity
	  • Aberrant behavior
	  • Adverse effect
	• Manage side effects

STEP IX	**Adherence monitoring** • Prescription monitoring programs • Random drug screens • Pill counts

STEP X	**Outcomes**
	
	• Successful - continue
	  • Stable doses
	  • Analgesia, activity
	  • No abuse, side effects
	• Failed - discontinue
	  • Dose escalation
	  • No analgesia
	  • No activity
	  • Abuse
	  • Side effects
	  • Non-compliance

Evaluation

Appropriate history, physical examination, and medical decision-making based on the initial evaluation of a patient's presenting symptoms are essential. The guidelines of the Centers for Medicare and Medicaid Services (CMS) provide various criteria for 5 levels of evaluation and management services (E&M), with 3 crucial components: history, physical examination, and medical decision-making. Other components include counseling, coordination of care, nature of presenting problem, and time required for face-to-face evaluation. While there are numerous

techniques to evaluate a chronic pain patient, which vary from physician to physician, institution to institution, and textbook to textbook, following the guidelines established by CMS will assist a physician in performing a comprehensive and complete evaluation complying with regulations.

Some of the aspects specific in controlled substance abuse and chronic pain include evaluation of the effect of pain on physical and psychological function, such as activities of daily living.

Diagnostic and Therapeutic Injections

Diagnostic interventional techniques will assist in making the proper diagnosis by following an algorithmic approach. It has been shown that in approximately 70% to 85% of the patients with spinal pain an accurate diagnosis may not be provided in spite of the available history, physical examination, electromyographic (EMG) nerve conduction studies, and radiological evaluation. With precise diagnostic interventional techniques, the chances of correct diagnosis may be improved substantially, and proper treatment may be offered.

Therapeutic interventional techniques also may be used in a monotherapeutic way rather than using opioids for pain management and functional improvement. The effectiveness of various interventional techniques has been evaluated in systematic reviews.

A written treatment plan should document objectives that will be used to evaluate treatment success, including pain relief and improved physical and psychosocial function, and should indicate if additional diagnostic tests, consultations, or treatments are planned. After starting treatment, the physician should adjust with care the drug therapy to the individual medical needs of each patient. In the continuum of treatment, other modalities, including interventional techniques, rehabilitation, and psychological therapy may be necessary depending on the etiology of the pain and the extent to which pain is associated with physical, functional, and psychosocial impairment.

Consultation

Physicians should be willing to refer a patient as clinically indicated for additional evaluation to achieve treatment objectives. Special attention should be given to those patients who are at risk of misusing their medications and those whose living arrangements create a risk for medication misuse or diversion. The management of patients with a history of substance abuse or with a coexisting psychiatric disorder may require extra care, monitoring, documentation, and consultation with, or referral to, an addictionologist. The lack of well-trained psychologists and psychiatrists in many regions of the country may make this referral difficult to obtain. Likewise in many locations there are no clinically trained addiction specialists with whom to collaborate.

Informed Consent and Controlled Substance Agreement

At the initial visit, the physician should discuss the risks and benefits of the use of controlled substances with the patient or surrogate, including the risk of tolerance

and drug dependence. It is advisable to employ the use of a written agreement between physician and patient outlining patient responsibilities. Agreements are helpful, specifically if the patient is determined to be at high risk for medication abuse or has a history of substance abuse. Possible items of a controlled substance agreement between a physician and patient include:

1. One prescribing doctor and one designated pharmacy
2. Urine/serum drug screening when requested
3. No early refills and no medications can be called in.
4. If medications are lost or stolen, then a police report could be required before considering additional prescriptions.

The reasons for which opioid drug therapy may be discontinued, such as violation of a documented doctor/patient agreement, should be delineated. Additional items to be included in an agreement are listed in Table 20 of the original guideline document.

Documentation and Medical Records

The physician should keep accurate and complete medical records, which include all aspects of interventional pain management and medical care. These comprise, but are not limited to:

- The medical history and physical examination
- Diagnostic, therapeutic, and laboratory results
- Evaluations and consultations
- Treatment objectives
- Discussion of risks, benefits, and limitations of treatments
- Details of different treatments, medications, including date, type, dosage, and quantity prescribed
- Instructions to the patient
- Periodic reviews of outcomes, including documentation of functional status, preferably using validated tools

Records should remain current and be maintained in an accessible manner and readily accessible for review, not only for the physician and other members of the practice, but also for authorities.

To be in compliance with controlled substance laws and regulations required to prescribe, dispense, or administer controlled substances, the physician must have an active license in the state and comply with applicable federal and state regulations. Various boards have published regulations and recommendations for prescribing controlled substances. Physicians are advised to refer to these regulations for their respective state. Physicians should not prescribe scheduled drugs for themselves or immediate family except in emergency situations.

The following criteria should be considered carefully in providing controlled substances:

1. Complete initial evaluation, including history and physical examination
2. Psychological evaluation

3. Physiological and functional assessment, as necessary and feasible
4. Definition of indications and medical necessity:
    - Pain of moderate-to-severe degree
    - Suspected organic problem
    - Documentation of failure to respond to noncontrolled substances, adjuvant agents, physical therapy, and interventional techniques
    - For patients with interventional techniques as primary modality, controlled substance drugs may be used as a second line treatment.
    - For non-opioid controlled substances, appropriate documentation of psychological disorders should be maintained.
    - Continued opioid prescription requires monitoring of "the 4 As":
        - Analgesia
        - Activity
        - Aberrant behavior
        - Adverse effects

5. The use of the lowest possible dose to provide adequate analgesia with minimum side effects should be the goal of opioid therapy.
6. In general, do not combine opioids with sedative-hypnotics, benzodiazepines, or barbiturates for chronic, non-cancer pain unless there is a specific medical indication for the combination.
7. Adherence to the controlled substance agreement with patients understanding the risks and benefits of controlled substances and the policy and regulations of the practitioner, including controlled substances being prescribed by only one practitioner and being obtained from only one pharmacy.
8. Monitoring for drug abuse or diversion should be routine and, if confirmed, referral to rehabilitation centers may be made, along with termination of prescriptions of controlled substances.
9. Use caution when prescribing acetaminophen-containing opioids, especially given the ubiquitousness of acetaminophen in over-the-counter medications. Short-term use (<10 days) should be less than 4,000 mg/day, while chronic use should probably be limited to 2,500 mg/day.

While there are no universally accepted tools to assess opioid responsiveness, it is important to use a tool that monitors both function and pain relief.

Although opioids may be useful for the treatment of chronic pain, aberrant behavior and/or no improvement in function and pain after an adequate trial of opioids should trigger a consideration to discontinue the opioids, tapered over a several week period to avoid withdrawal symptoms. Evidence of diversion or illegal use warrants an immediate discontinuation of the medication. Clonidine orally (po) or transdermal 0.1 mg can be offered to counteract the majority of withdrawal symptoms.

KEY POINTS

1. These opioid guidelines for the treatment of chronic non-cancer pain were developed to improve the quality and appropriateness of care, improve patient access, improve patient quality of life, improve efficiency and effectiveness, and achieve cost containment by improving the cost-benefit ratio.
2. Opioids are extensively used in managing chronic pain.

3. There is significant evidence of opioid abuse in conjunction with or without illicit drugs.
4. Abuse terminology is variable. This document attempts to standardize and provide a common sense definition.
5. Opioid pharmacology is variable and essential to understand for proper management of patients.
6. Among the rules of opioid administration, comprehensive evaluation and diagnostic assessment is crucial, including diagnosis by interventional techniques.
7. Establishing goals of treatment and using a controlled substance agreement are essential in the practice of pain management with opioids.
8. Periodic review of the patient on opioids is essential, using appropriate adjustments, with routine assessment of analgesia, activity, aberrant behavior, and adverse effects.
9. Documentation, keeping accurate and complete medical records with all the essential elements to provide proper patient care and also meet regulatory and legal requirements, is essential.
10. The rationalization and importance of these guidelines lies in the fact that most available evidence documents a wide degree of variance in the prescribing patterns of opioids for chronic pain. The strength of available evidence in the use of opioids for chronic non-cancer pain is weak.

Definitions:

Quality of Evidence*

I	Evidence obtained from at least one properly randomized controlled trial.
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience descriptive studies and case reports or reports of expert committees.

Adapted from the Agency for Healthcare Research and Quality U.S. Preventive Services Task Force (USPSTF)

Grade of Recommendations

Grade of Recommendation/Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
1A/strong recommendation,	Benefits	Randomized	Strong

Grade of Recommendation/Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
high-quality evidence	clearly outweigh risk and burdens, or vice versa	controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies	recommendation, can apply to most patients in most circumstances without reservation
1B/strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/strong recommendation, low-quality or very low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A/weak recommendation, high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B/weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from	Weak recommendation, best action may differ depending on circumstances or patients' or societal values

Grade of Recommendation/Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
		observational studies	
2C/weak recommendation, low-quality or very low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Adapted from Guyatt et al. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians task force. *Chest* 2006; 129:174-181.

CLINICAL ALGORITHM(S)

A clinical algorithm is provided in the original guideline document for evaluation and management of chronic pain.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

The perceived benefits of these guidelines include:

- Increased physician awareness about the current issues involving opioids and non-cancer pain
- Improved patient access
- Reduced level of opioid abuse
- Improved ability to manage patient expectations
- Reduced diversion
- Improved understanding by law enforcement about proper prescribing patterns
- Improved cooperation among patients, providers, and regulatory agencies

- Improved understanding by patients regarding their rights as well as their responsibilities when taking opioid medications

POTENTIAL HARMS

- The most significant consequences of long-term opioid therapy include, but are not limited to, tolerance, physical and psychological dependence, abuse, and diversion. See sections 3.4 to 3.8 in the original guideline document for discussions of nonmedical use of prescription drugs, substance abuse in chronic pain, and drug diversion.
- Commonly known side effects of opioids include constipation, pruritus, respiratory depression, nausea, vomiting, delayed gastric emptying, sexual dysfunction, muscle rigidity and myoclonus, sleep disturbance (morphine has been shown to reduce REM sleep via inhibition of acetylcholine release in the reticular activating formation, pyrexia, diminished psychomotor performance (which appears to be more of a problem with acute rather than chronic use), cognitive impairment, dizziness and sedation, all reflecting the effects of opioids at multiple organ systems.
- Implications and side effects of long-term opioid therapy include opioid-induced immunologic effects, hormonal changes, hyperalgesia, sedation, sleep disturbances, psychomotor disturbances, constipation, bladder dysfunction, and cardiac effects. Sections 4.2 to 4.5 of the original guideline document discuss adverse effects and drug interactions of opioids in detail.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines do not constitute inflexible treatment recommendations. These guidelines are not intended to address all possible clinical situations where opioids might be used for non-cancer pain in clinical practice. It is expected that a provider will establish a plan of care on a case-by-case basis, taking into account an individual patient's medical condition, personal needs, and preferences, as well as the physician's experience. Based on an individual patient's needs treatment different from that outlined here could be warranted. These guidelines do not represent a "standard of care."
- The focus of these guidelines is the effective management of chronic non-cancer pain, as well as the multiple issues involved in opioid administration. It is recognized that management of chronic non-cancer pain takes place in a wide context of healthcare involving multiple specialists and multiple techniques. Consequently, the decision to implement a particular management approach should be based on a comprehensive assessment of the patient's overall health status, disease state, patient preference, and physician training and skill.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Trescot AM, Helm S, Hansen H, Benyamin R, Glaser SE, Adlaka R, Patel S, Manchikanti L. Opioids in the management of chronic non-cancer pain: an update of American Society of the Interventional Pain Physicians' (ASIPP) guidelines. Pain Physician 2008 Mar-Apr;11(2S):S5-62. [350 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 (revised 2008)

GUIDELINE DEVELOPER(S)

American Society of Interventional Pain Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American Society of Interventional Pain Physicians

GUIDELINE COMMITTEE

Not stated

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Internal funding provided by the American Society of Interventional Pain Physicians was limited to travel and lodging expenses of the authors.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Trescot AM, Boswell MV, Atluri SL, Hansen NC, Deer TR, Abdi S, Jasper JF, Singh V, Jordan AE, Johnson BW, Cicala RS, Dunbar EE, Helm S II, Varley KG, Suchdev PK, Swicegood JR, Calodney AK, Ogoke BA, Minore WS, Manchikanti L. Opioid guidelines in the management of chronic non-cancer pain. Pain Phys 2006;9(1):1-39.

GUIDELINE AVAILABILITY

Electronic copies: Not available at this time.

Print copies: Available from the American Society of Interventional Pain Physicians, 2831 Lone Oak Road, Paducah, KY 42003; Phone: (270) 554-9412; Fax: (270) 554-8987; email: asipp@asipp.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Sample controlled substance agreement. Table 20 of the guideline document, available from the American Society of Interventional Pain Physicians Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 8, 2006. The information was verified by the guideline developer on May 19, 2006. This summary was updated by ECRI Institute on July 9, 2008. The updated information was verified by the guideline developer on July 22, 2008.

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Date Modified: 10/20/2008