

Ethical Challenges in the Management of Chronic Nonmalignant Pain: Negotiating Through the Cloud of Doubt

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Abstract: After successful cancer pain initiatives, efforts have been recently made to liberalize the use of opioids for the treatment of chronic nonmalignant pain. However, the goals for this treatment and its place among other available treatments are still unclear. Cancer pain treatment is aimed at patient comfort and is validated by objective disease severity. For chronic nonmalignant pain, however, comfort alone is not an adequate treatment goal, and pain is not usually proportional to objective disease severity. Therefore, confusion about treatment goals and doubts about the reality of nonmalignant pain entangle therapeutic efforts. We present a case history to demonstrate that this lack of proportionality fosters fears about malingering, exaggeration, and psychogenic pain among providers. Doubt concerning the reality of patients' unrelieved chronic nonmalignant pain has allowed concerns about addiction to dominate discussions of treatment. We propose alternate patient-centered principles to guide efforts to relieve chronic nonmalignant pain, including accept all patient pain reports as valid but negotiate treatment goals early in care, avoid harming patients, and incorporate chronic opioids as one part of the treatment plan if they improve the patient's overall health-related quality of life. Although an outright ban on opioid use in chronic nonmalignant pain is no longer ethically acceptable, ensuring that opioids provide overall benefit to patients requires significant time and skill. Patients with chronic nonmalignant pain should be assessed and treated for concurrent psychiatric disorders, but those with disorders are entitled to equivalent efforts at pain relief. The essential question is not whether chronic nonmalignant pain is real or proportional to objective disease severity, but how it should be managed so that the patient's overall quality of life is optimized.

Perspective: *The management of chronic nonmalignant pain is moving from specialty settings into primary care. Primary care providers need an ethical framework within which to adopt the principles of palliative care to this population.*

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May I never see in the patient anything but a fellow creature in pain.

—Oath of Maimonides⁴⁹

Over the past two decades, untreated pain has been increasingly recognized as a public health concern by medical professionals³⁹ and the general public.¹⁰ The primary focus of this concern has been on the treatment of pain from cancer, and espe-

cially on pain management at the end of life. There are signs that this is changing. In December 2001, the American Medical Association (AMA), the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), and the National Commission on Quality Assurance (NCQA) began a 2-year initiative to "improve the quality and consistency of pain management," focusing on pain from back problems, arthritis, and cancer.³ In 2002, pain management was ranked as "the most challenging standard for behavioral health care organizations" by the JCAHO.⁴¹ There is increasing debate about the use of opioids to treat chronic nonmalignant pain (CNMP) in primary care settings,⁵³ but an ethical framework that would provide goals for this therapy and determine its place among other pain therapies has been lacking. This lack of ethical framework has seriously impeded the adaptation of palliative care to the problem of nonmalignant pain.

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Case History

A 66-year-old African-American woman was diagnosed 3 years ago with stage II breast cancer and was treated with mastectomy and chemotherapy. During this time, she had moderate axillary pain that was successfully treated with oxycodone. Her current medical problems include moderate obesity and well-controlled hypertension with no evidence of recurrent cancer. She has been seen in a general medicine clinic for reports of moderate to severe pain over the past year. Her pain is multifocal, including lower back pain, generalized joint pain, and dull pain in her right lower thorax. Physical examination and diagnostic studies, including a thoracic computed tomographic (CT) scan, are unremarkable. Pain reports are more than would be expected on the basis of objective findings.

The patient is a divorced woman with 4 adult children. A son who lives with her has a history of chronic depression. Her eldest daughter was recently diagnosed with breast cancer. The patient's pain has been unsuccessfully treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and physical therapy over the past 3 months. Her internist has tried a course of oxycodone every 4 to 6 hours as needed. She returns to the clinic today reporting that she needs to refill her prescription, which has reduced the pain from an "8" to a "5" on a scale of 1 to 10. The clinic nurse believes that the patient is not really having severe pain because she does not appear to be in acute distress. He thinks perhaps she is anxious about recurrence of her breast cancer given her daughter's recent diagnosis. The medicine resident is also reluctant to refill the oxycodone because there is no known cause for the pain. The previous resident attempted to refer the patient to the university pain clinic, but this request was denied by her insurance provider.

Case Discussion

Although the patient has a history of cancer, her current reports of pain exist without evidence of recurrent cancer or other objective disease. Her life includes important social and psychologic issues including her son's history of mental illness, her daughter's diagnosis of breast cancer, care rendered by professionals who doubt her report of pain, and third-party payers that have denied access to specialized pain services.

Moral Privilege Accorded to Cancer Pain

Three decades after President Nixon declared a "War on Cancer," there have been many advances in cancer care, including increased attention to pain. Cancer pain is part of this malignant disease and is thus "malignant pain." It is viewed as progressive, urgent, and intensely threatening to personal dignity. These meanings of cancer pain imply that relieving it is a simple act of mercy. In recent years, there has been a moral crusade for aggressive treatment of cancer pain, with the World Health Organization (WHO) declaring undertreated cancer pain a top priority. Efforts to increase opioid availability have

been made by international, national, and state-based cancer pain initiatives. Pain relief is considered "basic and standard treatment" in the care of patients with incurable and terminal diseases.²⁴ The most difficult issue now facing physicians, according to a recent review, "is whether and how to prescribe opioid therapy for chronic pain that is not associated with terminal disease, including pain experienced by the increasing number of patients with cancer in remission."²⁵

The Ethical Challenge of CNMP

Pain intensity and associated distress in patients with nonmalignant pain is at least as high as in patients with cancer pain.⁸¹ A recent WHO survey of primary care patients in 15 countries reported that 22% of patients had pain for at least 6 months that required medical attention or medication or that interfered significantly with daily activities.³⁵ This is consistent with a previous meta-analysis²⁴ and subsequent surveys.¹⁶ The majority of these patients have pain that is not proportional to objective disease, such as back pain and headache.²³ Yet 13% of patients with headache and 18% of those with back pain in the United States report that they have been unable to work full time because of their pain.⁶³ In a 1999 nationwide telephone survey, 9% of Americans reported moderate to severe CNMP (≥ 5 on 10-point scale) with one third of them (3%) rating the pain as 10 (worst they could imagine). This pain had been present an average of 6 days per week for more than 5 years. About half of these thought their pain was "pretty much under control."¹⁸ The social burden of CNMP is large because, in contrast to cancer pain, it occurs in the midst of life.

Over the past decade, some providers have urged a response to this epidemic of CNMP parallel to that previously urged for cancer pain, focusing specifically on the broader use of opioid analgesics. They argue that selected patients with CNMP can have sustained analgesia and function better with these drugs, without development of an addictive disorder.⁵⁷ They claim that we have overestimated the possibility of addiction and underestimated the possibility of prolonged pain relief for these patients.⁵⁵ In response, many state medical boards instituted changes during the 1990s concerning the regulation of opioid analgesic prescriptions, modifying the characteristics of "addiction" and the legality of prolonged prescribing of opioids.³¹ Yet there is still widespread disagreement about the best approach to CNMP. Recent surveys of patients with CNMP document a 10-fold variation in opioid use, from 33% in one sample of veterans¹⁹ to 3.5% in a spinal pain sample.²⁶

Most of the debate about the use long-term opioids for CNMP has centered on the problem of iatrogenic addiction and the abuse of opioid medications. We believe that this focus has distorted the debate about the use of long-term opioids and hampered clinical care in a number of ways. First, to focus solely on the harms of opioid treatment does nothing to clarify the goals of CNMP treatment and how they might be different from those of cancer pain treatment. Pain relief in CNMP must

be balanced with the capacity for physical, psychologic, and social functioning over many years of treatment. The best evidence available indicates that long-term opioids provide about 30% pain relief and often do not improve physical function.⁷⁰ Perhaps in recognition of this complexity, Michigan physicians were much more likely to strive for "absolute and complete" pain relief in terminally ill or cancer patients than with CNMP patients.³² Second, the risks of iatrogenic addiction are not unique to the population with CNMP. Although definitive prevalence data are not available because of study of selected populations and variable definitions of addiction and abuse, it is estimated that 3% to 19% of patients with chronic pain may be abusing or addicted to opioids.^{28,48} This prevalence must be understood in light of the 10% to 16% rate of current substance abuse and addiction in medical outpatients and the general population.^{11,77} Iatrogenic addiction is a serious potential harm for some patients, but it must be weighed and understood in light of the potential benefits of chronic opioid treatment. Third, perhaps because of its roots in cancer pain initiatives, the effort to improve CNMP management has focused on increasing access to opioids. This effort has not been matched by an effort to increase access to other treatments proven effective for CNMP (especially low back pain) such as behavioral,⁷³ cognitive-behavioral,⁵¹ and multidisciplinary treatments.⁶² After rapid growth through the 1980s and 1990s, the number of inpatient or intensive outpatient chronic pain management programs accredited by the Commission on Accreditation of Rehabilitation Facilities (CARF) declined from 1999 to 2000 and has not changed since.¹⁷ Interest may be shifting to opioid therapy because it is perceived as cheaper and easier to implement than pain rehabilitation.⁷⁰ If patients with CNMP have a right to pain relief, this right should include all effective treatments and not just long-term use of opioids.

Current Modes of Clinical Triage for CNMP

Fears of iatrogenic addiction loom large, at least in part, because there are persistent widespread concerns about whether patients with CNMP are malingering, exaggerating, or otherwise manipulating their providers with reports of pain that cannot be validated or verified.^{27,44,45,52} Physicians resent being "fooled" or "taken advantage of" and will strive to prevent this, especially if they feel vulnerable to legal sanctions or lawsuits.⁶⁰ These concerns create doubts about when and to what extent patients with CNMP have the right to pain relief.⁵⁶

Real versus Unreal Pain

The most powerful predictor of inadequate cancer pain management in one large study was the discrepancy between the physician's and the patient's estimate of the severity of the patient's pain and its interference with daily activities. Nearly as powerful a predictor of inadequate management was physician belief that the pain was not caused by cancer.²⁰ Although actual prac-

tice is variable, the duty to relieve cancer pain has been considered ethically straightforward.⁶⁸ National Comprehensive Cancer Center practice guidelines dictate that if a cancer patient reports pain and requests more pain medication, he or she should receive it.³³

There is no corresponding ethical consensus about a duty of providers to offer relief for CNMP. CNMP has a highly variable association with disease and tissue damage, which throws its validity as a medical problem into question. The clinicopathologic method still dominant within medicine teaches that subjective pain is caused by objective lesions.⁶⁷ Physicians trained to plan medical therapy on the basis of a disease diagnosis find the inconsistent relationship of CNMP to tissue damage apparent on physical examination and diagnostic testing to be both confusing and frustrating.³⁶ Providers and patients rarely discuss openly whether pain is considered to be real or not, but it is clear that they both think in these terms about pain that is difficult to explain.⁸

The idea that "real pain" is associated with disease or damage is both clear and comfortable to providers and patients. But it implies its opposite, "unreal pain," which is neither clear nor comfortable. This murky concept of "unreal pain" can imply that pain reports arise from malingering or exaggeration. Indeed, it may be necessary for providers working in emergency departments to be on the alert for drug-seeking patients⁵⁹ and for those doing medicolegal evaluations to be on alert for patients seeking compensation.⁶ But studies from clinical settings where there is a continuing relationship between provider and patient indicate that malingering is quite rare. Evidence to date also indicates that malingering cannot be reliably identified by facial expression testing, questionnaire, sensory testing, or clinical examination.⁵⁶

The sorting of pain into "real" and "unreal" has appeal because it appears to provide a scientific basis for the ethical decision about which pains providers have a duty to relieve. Human society has always accommodated sick and injured members. Throughout history, this has included various ways to validate reports of sickness. But it is only in the modern period that this validation has consisted of the correlation of patient reports with findings of damage on objective medical tests.²⁵ Unfortunately, this principle of validation often fails for CNMP because objective tissue damage is neither necessary nor sufficient for chronic pain. In many of the most prevalent chronic pain syndromes, from chronic headaches to fibromyalgia, there are no reliable clinical test abnormalities.⁶⁹ Mild spinal abnormalities (such as bulging or degenerative vertebral discs) are as common in those without back pain as in those with back pain.⁴⁰ Other abnormalities, such as joint space narrowing in osteoarthritis, are often only loosely correlated with pain intensity.¹⁴ Lack of correlation between CNMP and objective tests does not prove that the pain is in any sense "unreal." It cannot, therefore, provide an ethical basis for lesser efforts at pain relief in these cases.

Somatogenic versus Psychogenic Pain

In most clinical settings where patients and providers have continuing relationships, CNMP without a validating test finding is usually not considered "unreal" but "psychogenic." Psychogenic pain is opposed to somatogenic pain, where a causal lesion in the body can be identified.⁷⁵ However, psychogenic pain is a confused concept. It can mean that the pain is imaginary or delusional or mislabeled psychosocial distress (ie, somatization). But it is unclear what imaginary pain could be. Delusional pain, even in schizophrenia, is very rare.⁷⁸ Pain relief in response to placebo does not identify pain as psychogenic.⁷² Labeling pain as psychogenic often functions as a stigmatizing prelude to sending the patient elsewhere for treatment.⁶⁴

The fundamental problem with dichotomizing pain as somatogenic or psychogenic is that clinical pain includes both elements. Both nociception and psychologic threat determine the intensity of clinical pain.⁶⁵ A recent neuroimaging study examining the correlates of social exclusion demonstrated that the brain bases of social pain (eg, anterior cingulate and right ventral prefrontal cortex) are similar to those of physical pain.²² Another study demonstrated that induced sadness was associated with significant deactivation of μ -opioid neurotransmission in the anterior cingulate and related limbic areas.⁸² These studies suggest that the boundary between physical and mental pain is not clear and distinct, especially from the patient's point of view. Confirming this is the fact that the somatization of psychologic distress into physical symptoms is pervasive in medical settings.⁴³

Whether psychogenic pain does not deserve treatment or whether customary pain treatments are inappropriate for psychogenic pain has not been clearly addressed. Rather, the possibility of invalid pain reports, whether "unreal" or "psychogenic," casts a cloud of doubt between the patient with CNMP and his provider. This notion of invalid pain allows providers to select some types of pain as less worthy of aggressive pain management. Patients are often left to address these invalid forms of CNMP on their own or through the use of alternative medicine.³⁷

Alternative Ethical Principles for CNMP Management

Because the physical and psychologic dimensions of CNMP are so intertwined, providers must be willing to address both the pain and the suffering of their patients. In 1992, the Agency for Health Care Policy and Research stated that "the ethical obligation to manage pain and relieve the patient's suffering is at the core of the health professional's commitment."³⁸ Yet clinicians clearly need some guidance about how to approach these often challenging, complicated patients. We offer below a few tentative guidelines and relate them to our case history.

1. Believe the patient's report of pain, but negotiate about the treatment indicated.

Providers can replace suspicion about pain with nego-

tiation about treatment goals. No pain should be dismissed as unreal or unworthy of medical attention. However, providers need to learn how to listen to and validate patients' pain reports without acceding to inappropriate demands for tests or treatments. Disagreements between provider and patient about opioids produce emotional strain and a sense of personal defeat in providers. The result is that few providers deny the patient a desired prescription despite feeling caught in a dilemma.⁷ Providers may escalate opioid doses when treatment goals are not achieved rather than questioning the appropriateness of opioid treatment.⁵ More provider training is necessary, not just in saying no to inappropriate requests for opioids, but in alternative ways of validating patients' pain reports.

Treatment goals for CNMP need to be negotiated at the outset of care because cure is rarely possible. CNMP treatment often involves complex tradeoffs between comfort, vitality, physical functional capacity, and mental clarity. It is essential to make patients aware of these potential tradeoffs and engage them in shared decision making about them. Opioid contracts are a widely used strategy in CNMP management that could be adapted for this purpose.⁴⁶ Currently, these contracts are not often used for shared decision making. Fishman et al²⁹ studied contracts from 39 major academic pain centers. They found 125 statements, which they grouped into 12 categories. The most common categories (in $\geq 90\%$ of contracts) were terms of treatment, prohibited behavior by patients, and reasons for termination of care. Goals of care were among the least common categories, present in only 38% of contracts. Contracts are thus mostly used to put limits on patients rather than to empower or collaborate with patients. Truly collaborative treatment agreements focusing on goals for CNMP care could be a powerful tool for increasing patient participation and satisfaction with care. They have already shown value at coordinating care between pain specialist and primary care physician.³⁰ See Table 1 for guidelines on developing a patient care agreement.

Case History

After speaking to the patient about her treatment goals, the physician identifies walking to the park with her grandchildren as a top priority. Together they develop a treatment plan involving both time-contingent oxycodone and physical therapy to achieve this goal.

2. Initial and follow-up assessments in CNMP care should include all dimensions of health-related quality of life, not just pain intensity.

The responsibility of health care providers toward patients is not limited to diseases, injuries, and their associated symptoms but extends to include all aspects of health status as perceived by the patient.⁶⁶ The Institute of Medicine's recent report, *Crossing the Quality Chasm*, states that the experience of patients is "true north" for assessing the quality of health care.²¹ Yet this experience must include more than the symptom intensity reported in the provider's office. Multiple epidemiologic studies

Table 1. Guidelines for Negotiating a Patient Care Agreement for CNMP

1. Replace suspicion about pain with negotiation about treatment goals. Both provider and patient should collaborate in the formation of the care agreement.
2. Begin the negotiation with goals for treatment, emphasizing that cure or complete pain relief is rarely possible.
3. Solicit functional goals and symptom relief goals, prioritizing functions that are important to the patient. Pain, depression, and disability should all be addressed.
4. Assess for concurrent depression. Although depression is an understandable complication of chronic pain, it warrants additional treatment. All depressive symptoms count toward a diagnosis, even if the patient attributes them solely to pain.
5. Stress the need for a trusting collaborative care relationship with active and honest participation by all parties. Regular appointments with the provider responsible for pain management and adherence to prescribed medication are necessary.
6. Have provider and patient specify a set of minimum expectations which, if violated, would be reason for terminating the care relationship.
7. Agreements should address the overall plan of care, not just opioid use. Long-term opioids should not be the sole treatment in a plan of care.

have shown chronic pain, depression, and disability exist in a vicious cycle of reinforcement.^{34,54} A recent multidisciplinary task force has recommended that symptoms, function, and overall well-being must be assessed and addressed as outcomes for clinical trials.⁷¹ We believe these need to be monitored and targeted in clinical care as well.

Case History

In addition to problems with mobility, the patient reports that she has been sleeping poorly and not able to enjoy her favorite grandchild. The physician suggests that they include an antidepressant medication in her treatment plan.

3. Providers' first responsibility to patients with CNMP is to avoid harming them: *primum non nocere*.

Providers must avoid treatments that cause long-term harm to patients with CNMP, although patients may be desperate enough to demand these treatments. These duties are most clear concerning major and permanent adverse events.⁴² Ablative neurosurgical procedures,⁸⁰ repeated invasive procedures (eg, nerve blocks) with only transient benefit,⁴ and overuse of medications with net negative effects (eg, rebound headaches)⁷⁶ are examples of treatments that should be scrutinized for net long-term harm. It is not clear whether prolonged high-dose opioid therapy is either safe or effective. Prolonged opioid treatment may also result in hormonal changes and may alter immune function.⁵ Iatrogenic addiction to opioids is an important harm to avoid but rarely appears without a history of substance abuse.⁷⁹ Patients with such a history should have a pain management or psychiatric consultation before opioids are prescribed.

Case History

The patient asks if she can have some prednisone for her back pain because this helped a friend of hers. The physician explains that without evidence of inflammation this is more likely to cause harm than benefit to her.

4. Chronic opioids may be indicated as part of a treatment plan for CNMP, but prescribers have a continuing obligation to make sure that there is overall benefit for the patient.

The American Pain Society (APS) and the American Academy of Pain Medicine (AAPM)¹ and the American Geriatrics Society² have endorsed the long-term use of opioids as part of the treatment plan for patients with CNMP. However, it is very important to know that opioids are not a cure for CNMP. On the basis of a weighted average of all the randomized trials of long-term opioids to date, the average pain reduction is 32%.⁷⁰ This partial pain relief must be weighed against opioid side effects and cost. For example, although oxycodone provided effective analgesia for patients with moderate to severe osteoarthritis pain, side effects were common and nearly 90% of patients discontinued therapy before 18 months.⁶¹ Concern has also been raised recently that long-term high-dose opioid use may be associated with not only pharmacologic tolerance but also opioid-induced abnormal pain sensitivity resulting from *N*-methyl-D-aspartate-receptor related changes.⁵⁰

Fear of opioids has prevented a dispassionate weighing by providers of potential harms and benefits to the patient.¹³ The APS/AAPM guidelines emphasize that "Review of treatment efficacy should occur periodically to assess the functional status of the patient, continued analgesia, opioid side effects, quality of life, and indications of medication misuse."⁶¹ A treatment trial of a month or two should give patient, provider, and family a sense of whether the patient's quality of life is improved. The goal for long-term opioid treatment should be an overall improvement in function and well-being, not just reduced pain intensity. "Attention should be given to the possibility of a decrease in global function or quality of life as a result of opioid use."⁶¹ Patients currently dependent on chronic opioids may overestimate the benefit and underestimate the burden of their medication compared with what they report after tapering off the medication.¹⁵ Providing assessment of overall benefit to the patient from multiple perspectives (ie, patient, provider and family) may counteract this tendency.

Although current or past substance abuse does increase the risk of opioid abuse in patients with CNMP, it does not negate the right to pain relief in cancer or human immunodeficiency virus or acquired immunodeficiency syndrome⁵⁸ and should not negate this right in CNMP.⁴⁷ It must be remembered that opioids may relieve

both physical and mental pain (including depression).⁹ Psychiatric disorders (including both substance abuse and mood disorders) may be especially common among patients who receive opioids rather than NSAIDs for chronic pain.¹² These psychiatric disorders should be assessed and treated before, or concurrent with, long-term opioid therapy. Patients at high risk for opioid abuse should not be denied treatment but need closer follow-up and full consideration of nonopioid pain and psychiatric treatments (eg, antidepressants and anticonvulsants). This level of care may require referral to a specialty care setting.

Case History

The physician asks the patient to keep track of her mood and her daily walking time for her next visit in a month. He also asks if her son or daughter can come with her so that they can be included in her treatment and the evaluation of its outcome.

Conclusions

A cloud of doubt hangs over the care of patients with CNMP, a cloud that has been largely banished from the

care of patients with cancer pain. The patient in our case history has reported both kinds of pain and received very different responses from health professionals. This difference is not based on the intensity of the pain or its degree of interference with her life, but on its association with a potentially lethal disease. We have argued that *whether pain is proportional to objective disease does not determine whether it is worthy of relief*. Providers have interpreted their duties concerning the relief of CNMP through the confused concepts of real versus unreal pain, or somatogenic versus psychogenic pain. Doubts about the reality of patients' pain have distorted decision making about CNMP care, bringing too much critical attention to the risks of treatment and not enough critical attention to the benefits of treatment. The core issue is not whether CNMP is real but how it should be managed so that the patient's overall quality of life is optimized.

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References

1. American Academy of Pain Medicine. The use of opioids for the treatment of chronic pain: a consensus statement from the American Academy of Pain Medicine and the American Pain Society. *Clin J Pain* 13:6-8, 1997
2. American Geriatrics Society. The management of chronic pain in older persons: AGS Panel of Chronic Pain in Older Persons. *J Am Geriatr Soc* 46:635-651, 1998
3. American Medical Association. AMA, JCAHO and NCQA to focus on measuring effectiveness of appropriate pain management. Joint Commission on Accreditation of Health-care Organizations Press Release; 17 Dec 2001
4. Ashburn MA, Staats PS. Management of chronic pain. *Lancet* 353:1865-1869, 1999
5. Ballantyne JC, Mao J. Opioid therapy for chronic pain. *N Engl J Med* 349:1943-1953, 2003
6. Bellamy R. Compensation neurosis: financial reward for illness as nocebo. *Clin Orthop* 336:94-106, 1997
7. Bendtsen P, Hensing G, Ebeling C, Schedin A. What are the qualities of dilemmas experienced when prescribing opioids in general practice? *Pain* 82:89-96, 1999
8. Blomquist K. Older people in persistent pain: nursing and paramedical staff perceptions and pain management. *J Adv Nurs* 41:575-584, 2003
9. Bodkin JA, Zornberg GL, Lukas SE, Cole JO. Buprenorphine treatment of refractory depression. *J Clin Psychopharmacol* 15:49-57, 1995
10. Bostrom M. Summary of the Mayday Fund Survey: public attitudes about pain and analgesics. *J Pain Symptom Manage* 13:166-168, 1997
11. Bradley KA, Bush KR, McDonnell MB, Malone T, Fihn SD. Screening for problem drinking: comparison of CAGE and AUDIT: Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol use disorders identification test. *J Gen Intern Med* 13:379-388, 1998
12. Breckenridge J, Clark JD. Patient characteristics associated with opioid vs nonsteroidal anti-inflammatory drug management of chronic low back pain. *J Pain* 4:344-350, 2003
13. Bruera E, Moyano J, Seifert L, Fainsinger RL, Hanson J, Suarez-Almazor M. The frequency of alcoholism among patients with pain due to terminal cancer. *J Pain Symptom Manage* 10:599-603, 1995
14. Bruyere O, Honore A, Rovati LC, Giacobelli G, Henrotin YE, Seidel L, Reginster JY. Radiologic features poorly predict clinical outcomes in knee osteoarthritis. *Scand J Rheumatol* 31:13-16, 2002
15. Buckley FP, Sizemore WA, Charlton JE. Medication management in patients with chronic non-malignant pain: a review of the use of a drug withdrawal protocol. *Pain* 26:153-165, 1986
16. Catala E, Reig E, Artes M, Aliaga L, Lopez JS, Segu JL. Prevalence of pain in the Spanish population: telephone survey in 5000 homes. *Eur J Pain* 6:133-140, 2002
17. Chapman SL. Chronic pain rehabilitation: lost in a sea of drugs and procedures? *Am Pain Soc Bull* 10:8-9, 2000
18. Chronic Pain in America. Roadblocks to Relief. [Nationwide telephone survey conducted for The American Pain Society, The American Academy of Pain Medicine and Janssen Pharmaceutica by Roper Starch Worldwide Inc.]. January 1999. Available at: www.ampainsoc.org/whatsnew/forward_road.htm. Accessed on March 18, 2003
19. Clark JD. Chronic pain prevalence and analgesic prescribing in a general medical population. *J Pain Symptom Manage* 23:131-137, 2002

20. Cleeland CS, Gonin R, Hatfield AK, Edmonson JH, Blum RH, Stewart JA, Pandya KJ. Pain and its treatment in outpatients with metastatic cancer. *N Engl J Med* 330:592-596, 1994
21. Committee on Quality of Health Care in America, Institute of Medicine. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC, National Academy Press, 2001.
22. Eisenberger NI, Lieberman MD, Williams KD. Does rejection hurt? An fMRI study of social exclusion. *Science* 302:290-292, 2003
23. Elliott AM, Smith BH, Penny KI, Smith WC, Chambers WA. The epidemiology of chronic pain in the community. *Lancet* 354:1248-1252, 1999
24. Emanuel EJ. Pain and symptom control: patient rights and physician responsibilities. *Hematol Oncol Clin North Am* 10:41-56, 1996
25. Fabrega H. *The Evolution of Sickness and Healing*. Berkeley CA: University California Press, 1998, pp 128-134
26. Fanciullo GJ, Ball PA, Girault G, Rose RJ, Hanscom B, Weinstein JN. An observational study on the prevalence and pattern of opioid use in 25,479 patients with spine and radicular pain. *Spine* 27:201-205, 2002
27. Fishbain DA, Cutler R, Rosomoff HL, Rosomoff RS. Chronic pain disability exaggeration/malingering and submaximal effort research. *Clin J Pain* 15:244-274, 1999
28. Fishbain DA, Rosomoff HL, Rosomoff RS. Drug abuse, dependence, and addiction in chronic pain patients. *Clin J Pain* 8:77-85, 1992
29. Fishman SM, Bandman TB, Edwards A, Borsook D. The opioid contract in the management of chronic pain. *J Pain Symptom Manage* 18:27-37, 1999
30. Fishman SM, Mahajan G, Jung SW, Wilsey BL. The trilateral opioid contract: bridging the pain clinic and the primary care physician through the opioid contract. *J Pain Symptom Manage* 24:335-344, 2002
31. Gilson AM, Joranson DE. Controlled substances and pain management: changes in knowledge and attitudes of state medical regulations. *J Pain Symptom Manage* 21:227-237, 2001
32. Green CR, Wheeler JRC, LaPorte F. Clinical decision making in pain management: contributions of physician and patient characteristics to variations in practice. *J Pain* 4:29-39, 2002
33. Benedetti C, Brock C, Cleeland C, Coyle N, Dube JE, Ferrell B, Hassenbusch S III, Janjan NA, Lema MJ, Levy MH, Loscalzo MJ, Lynch M, Muir C, Oakes L, O'Neill A, Payne R, Syrjab KL, Urba S, Weinstein SM, National Comprehensive Cancer Network. NCCN practice guidelines for cancer pain: version 2000. *Oncology* 11A:135-150, 2000
34. Gureje O, Simon GE, Von Korff M. A cross-national study of the course of persistent pain in primary care. *Pain* 92:195-200, 2001
35. Gureje O, Von Korff M, Simon GE, Gater R. Persistent pain and well-being: a World Health Organization study in primary care. *JAMA* 280:147-151, 1998
36. Hahn SR. Physical symptoms and physician-experienced difficulty in the physician-patient relationship. *Ann Intern Med* 134:897-904, 2001
37. Harris RE, Clauw DJ. The use of complementary medical therapies in the management of myofascial pain disorders. *Curr Pain Headache Rep* 6:370-374, 2002
38. Jansen LA. Deliberative decision making and the treatment of pain. *J Palliat Med* 4:23-30, 2001
39. Jacox A, Carr DB, Payne R. New clinical-practice guidelines for the management of pain in patients with cancer. *N Engl J Med* 330:651-655, 1994
40. Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic M, Malkasian D, Ross J. Magnetic resonance imaging of the lumbar spine in people without back pain. *N Engl J Med* 331:69-73, 1994
41. Joint Commission on Accreditation of Healthcare Organizations. Most challenging standards for BHC organizations. *BHC Accreditation News*. 2002; Issue 2. Available at <http://www.jcaho.org/accredited+organizations/behavioral+health+care/bhc+news/2002issue>. Accessed March 17, 2003
42. Kalso E, Edwards J, McQuay HJ, Moore RA. Five easy pieces on evidence based medicine (5): trading benefit against harm—pain relief vs adverse effects. *Eur J Pain* 6:409-412, 2002
43. Katon W, Sullivan M, Walker E. Medical symptoms without identified pathology: relationship to psychiatric disorders, childhood and adult trauma and personality traits. *Ann Intern Med* 134:917-925, 2001
44. Khostanteen I, Tunks ER, Goldsmith CH, Ennis J. Fibromyalgia: can one distinguish it from simulation? An observer-blind controlled study. *J Rheumatol* 27:2671-676, 2000
45. Klester PD, Duke AD. Is it malingering, or is it "real"? Eight signs that point to nonorganic back pain. *Postgrad Med* 106:77-80, 1999
46. Kirkpatrick AF, Derasari M, Kovacs PL, Lamb BD, Miller R, Reading A. A protocol-contract for opioid use in patients with chronic pain not due to malignancy. *J Clin Anesth* 10:435-443, 1998
47. Kirsh KL, Whitcomb LA, Donaghy K, Passik SD. Abuse and addiction issues in medically ill patients with pain: attempts at clarification of terms and empirical study. *Clin J Pain* 18 (4 Suppl):52-60, 2002
48. Kouyanou K, Pither CE, Wessely S. Medication misuse, abuse and dependence in chronic pain patients. *J Psychosom Res* 43:497-504, 1997
49. Maimonides M. Oath of Maimonides. Translated by Harry Friedenwald. *Bull Johns Hopkins Hosp* 28: 260-261, 1917
50. Mao J. Opioid-induced abnormal pain sensitivity: implications in clinical opioid therapy. *Pain* 100:213-217, 2002
51. McCracken LM, Turk DC. Behavioral and cognitive-behavioral treatment for chronic pain: outcomes, predictors of outcomes and treatment process. *Spine* 27:2564-2573, 2002
52. McGuire BE, Shores EA. Pain patient profile and the assessment of malingering pain. *J Clin Psychol* 57:401-409, 2001
53. Mitka M. Experts debate widening use of opioid drugs for chronic nonmalignant pain. *JAMA* 289:2347-2348, 2003
54. Ohayon MM, Schatzberg AF. Using chronic pain to predict depressive morbidity in the general population. *Arch Gen Psychiatry* 60:39-47, 2003
55. Pappagallo M, Heinberg LJ. Ethical issues in the man-

- agement of chronic nonmalignant pain. *Semin Neurol* 17:203-211, 1997
56. Peter E, Watt-Watson J. Unrelieved pain: an ethical and epistemological analysis of distrust in patients. *Can J Nurs Res* 34:65-80, 2002
57. Portenoy RK. Current pharmacotherapy of chronic pain. *J Pain Symptom Manage* 19 (1 Suppl):16-20, 2000
58. Portenoy RK, Lesage P. Management of cancer pain. *Lancet* 353:1695-1700, 1999
59. Purcell TB. The somatic patient. *Emerg Med Clin North Am* 9:137-159, 1991
60. Rich BA. Moral conundrums in the courtroom: reflections on a decade in the culture of pain. *Camb Q Healthc Ethics* 11:180-190, 2002
61. Roth SH, Fleischmann RM, Burch FX, Dietz F, Bockow B, Rapoport RJ, Rutstein J, Lacouture PG. Around-the-clock, controlled-release oxycodone therapy for osteoarthritis-related pain: placebo-controlled trial and long-term evaluation. *Arch Intern Med* 160:853-860, 2000
62. Schonstein E, Kenny DT, Keating J, Koes BW. Work conditioning, work hardening and functional restoration for workers with back and neck pain. *Cochrane Database Syst Rev* 1:CD001822, 2003
63. Stang P, Von Korff M, Galer BS. Reduced labor force participation among primary care patients with headache. *J Gen Intern Med* 13:296-302, 1998
64. Sullivan MD. DSM-IV Pain disorder; a case against the diagnosis. *Int Rev Psychiatry* 12:91-98, 2000
65. Sullivan MD. Finding pain between minds and bodies. *Clin J Pain* 17:146-156, 2001
66. Sullivan MD. The new subjective medicine: taking the patient's point of view on health and health care. *Soc Sci Med* 56:1595-1604, 2003
67. Sullivan M. The problem of pain in the clinicopathological method. *Clin J Pain* 14:197-201, 1998
68. Swenson CJ. Ethical issues in pain management. *Semin Oncol Nurs* 18:135-142, 2002
69. Torpy DJ, Papanicolaou DA, Lotsikas AD, Wilder RL, Chrousos GP, Pillemer SR. Responses of the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis to interleukin-6: a pilot study in fibromyalgia. *Arthritis Rheum* 43:872-880, 2000
70. Turk DC. Clinical effectiveness and cost-effectiveness of treatments for patients with chronic pain. *Clin J Pain* 18:355-365, 2002
71. Turk DC, Dworkin RH, Allen RR, Bellamy N, Brandenburg N, Carr DB, Cleeland C, Dionne R, Farrar JT, Galer BS, Hewitt DJ, Jadao AR, Katz NP, Kramer LD, Manning DC, McCormick CG, McDermott MP, McGrath P, Quessy S, Rappaport BA, Robinson JP, Royal MA, Simon L, Stauffer JW, Stein W, Tolleit J, Witter J. Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. *Pain* 106:337-345, 2003
72. Turner JA, Deyo RA, Loeser JD, Von Korff M, Fordyce WE. The importance of placebo effects in pain treatment and research. *JAMA* 271:1609-1614, 1994
73. van Tulder MW, Ostelo R, Vlaeyen JW, Linton SJ, Morley SJ, Assendelft WJ. Behavioral treatment of chronic low back pain: a systematic review within the framework of the Cochrane Back Review Group. *Spine* 26:270-281, 2001
74. Verhaak PMF, Keressen JJ, Dekker J, Sorbi MJ, Bensing JM. Prevalence of chronic benign pain disorder among adults: a review of the literature. *Pain* 77:231-239, 1998
75. Wallis BJ, Lord SM, Bogduk N. Resolution of psychological distress of whiplash patients following treatment by radio frequency neurotomy: a randomised, double-blind, placebo-controlled trial. *Pain* 73:15-22, 1997
76. Warner JS. Prolonged recovery from rebound headaches. *Headache* 41:817-822, 2001
77. Warner LA, Kessler RC, Hughes M, Anthony JC, Nelson CB. Prevalence and correlates of drug use and dependence in the United States: results from the National Comorbidity Survey. *Arch Gen Psychiatry* 52:219-229, 1995
78. Watson GD, Chandarana PC, Merskey H. Relationships between pain and schizophrenia. *Br J Psychiatry* 138:33-36, 1981
79. Weaver M, Schnoll S. Abuse liability in opioid therapy for pain treatment in patients with an addiction history. *Clin J Pain* 18 (4 Suppl):61-69, 2002
80. Whitworth LA, Feler CA. Application of spinal ablative techniques for the treatment of benign chronic painful conditions: history, methods and outcomes. *Spine* 27:2607-2612, 2002
81. Zaza C, Reyno L, Moulin DE. The multidimensional pain inventory profiles in patients with chronic cancer-related pain: an examination of generalizability. *Pain* 87:75-82, 2000
82. Zubieta J, Ketter TA, Bueller JA, Xu Y, Kilbourn MR, Young EA, Koeppe RA. Regulation of human affective responses by anterior cingulate and limbic μ -opioid neurotransmission. *Arch Gen Psychiatry* 60:1145-1153, 2003