

[J Bone Joint Surg Am. 2009 Apr;91\(4\):919-27.](#)

## **Higher opioid doses predict poorer functional outcome in patients with chronic disabling occupational musculoskeletal disorders.**

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**BACKGROUND:** Opioids are frequently used for the postoperative treatment of chronic disabling occupational musculoskeletal disorders. In many such cases, long-term opioid use persists because of patient requests for ongoing pain relief. Little is known about the relationship between chronic opioid use and functional recovery in these patients. **METHODS:** A total of 1226 patients with a chronic disabling occupational musculoskeletal disorder were consecutively admitted into an interdisciplinary functional restoration program. They were divided into two groups: 630 patients who reported no opioid use at the time of admission (No group) and 596 patients who reported some opioid use at the time of admission (Yes group). The 516 patients for whom daily opioid doses could be determined were further divided into four subgroups: Low (<30 mg, n=267), Medium (31 to 60 mg, n=112), High (61 to 120 mg, n=78), and Very High (>120 mg, n=59). During the initial weeks of treatment, patients consented to be weaned from all opioid medications. In addition, the patients were assessed before and after rehabilitation with regard to self-reported measures of pain, function, and depression and were analyzed for change. One year after the termination of treatment, socioeconomic outcomes were assessed to measure work and financial status, healthcare utilization, and recurrent injury-associated pain. **RESULTS:** A higher post-injury opioid dose was associated with a greater risk of program noncompletion, which was anticipated because of the requirement that patients taper opioids. High opioid use was significantly related to important socioeconomic outcomes, such as lower rates of return to work and work retention as well as higher healthcare utilization ( $p \leq 0.05$  for all). Moreover, at one year after treatment, the group reporting the highest opioid use was 11.6 times as likely to be receiving Social Security Disability Income/Supplemental Security Income as compared with the group reporting no opioid use at the time of admission into the program. **CONCLUSIONS:** Chronic opioid use beginning after a work-related injury is a predictor of less successful outcomes for patients whose final treatment intervention is an interdisciplinary functional restoration program. Higher dose levels are associated with progressively greater indemnity and medical costs for ongoing disability. Physicians involved in the treatment of chronic disabling occupational musculoskeletal disorders should be aware of problems associated with permitting long-term opioid use in patients with a disabling occupational disorder.

[J Pain](#). 2009 Feb;10(2):147-59.

## **Research gaps on use of opioids for chronic noncancer pain: findings from a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline.**

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Chronic noncancer pain is common and use of opioids is increasing. Previously published guidelines on use of opioids for chronic noncancer pain have been based primarily on expert consensus due to lack of strong evidence. We conducted searches on Ovid MEDLINE and the Cochrane databases through July 2008 to identify studies that addressed one or more of 37 Key Questions that a multidisciplinary expert panel identified as important to be answered to generate evidence-based recommendations on the use of opioids for chronic noncancer pain. A total of 14 systematic reviews, 38 randomized trials not included in a previously published systematic review, and 13 other studies met inclusion criteria. Almost all of the randomized trials of opioids for chronic noncancer pain were short-term efficacy studies. Critical research gaps on use of opioids for chronic noncancer pain include: lack of effectiveness studies on long-term benefits and harms of opioids (including drug abuse, addiction, and diversion); insufficient evidence to draw strong conclusions about optimal approaches to risk stratification, monitoring, or initiation and titration of opioid therapy; and lack of evidence on the utility of informed consent and opioid management plans, the utility of opioid rotation, the benefits and harms specific to methadone or higher doses of opioids, and treatment of patients with chronic noncancer pain at higher risk for drug abuse or misuse. PERSPECTIVE: Currently, clinical decisions regarding the use of opioids for chronic noncancer pain need to be made based on weak evidence. Research funding priorities need to be set to address these critical research needs if the care of patients with chronic noncancer pain is to improve.

[Pain Physician](#). 2009 May-Jun;12(3):679-84.

## **Opioid induced hyperalgesia: clinical implications for the pain practitioner.**

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Opioids have been and continue to be used for the treatment of chronic pain. Evidence supports the notion that opioids can be safely administered in patients with chronic pain without the development of addiction or chemical dependency. However, over the past several years, concerns have arisen with respect to administration of opioids for the treatment of chronic pain, particularly non-cancer pain. Many of these involve legal issues with respect to diversion and prescription opioid abuse. Amongst these, opioid induced hyperalgesia (OIH) is becoming more prevalent as the population receiving opioids for chronic pain increases. OIH is a recognized complication of opioid therapy. It is a pro-nociceptive process which is related to, but different from, tolerance. This focused review will elaborate on the neurobiological mechanisms of OIH as well as summarize the pre-clinical and clinical studies supporting the existence of OIH. In particular, the role of the excitatory neurotransmitter, N-methyl-D-aspartate appears to play a central, but not the only, role in OIH. Other mechanisms of OIH include the role of spinal dynorphins and descending facilitation from the rostral ventromedial medulla. The links between pain, tolerance, and OIH will be discussed with respect to their common neurobiology. Practical considerations for diagnosis and treatment for OIH will be discussed. It is crucial for the pain specialist to differentiate amongst clinically worsening pain, tolerance, and OIH since the treatment of these conditions differ. Tolerance is a necessary condition for OIH but the converse is not necessarily

true. Office-based detoxification, reduction of opioid dose, opioid rotation, and the use of specific NMDA receptor antagonists are all viable treatment options for OIH. The role of sublingual buprenorphine appears to be an attractive, simple option for the treatment of OIH and is particularly advantageous for a busy interventional pain practice.

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## **Opioid-induced hyperalgesia: pathophysiology and clinical implications.**

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**BACKGROUND:** Opioid-induced hyperalgesia (OIH) refers to a phenomenon whereby opioid administration results in a lowering of pain threshold, clinically manifest as apparent opioid tolerance, worsening pain despite accelerating opioid doses, and abnormal pain symptoms such as allodynia. **AIM:** The current review, while providing a clinically oriented updated overview on the pathophysiology of OIH, focuses predominantly on evidence-based clinical and management aspects of this important and often baffling phenomenon. **METHOD:** Online and manual search using key words such as opioid-induced hyperalgesia, opioid-induced abnormal pain sensitivity, opioid hyperalgesia, opioid-induced paradoxical pain, or opioid-induced abnormal pain, followed by full-text access and further crossreferencing. **RESULTS:** The underlying pathophysiology of this phenomenon, although still unclear, appears to be related to an opioid-induced imbalance between the internal antinociceptive and pronociceptive systems. Clinical differentiation of an apparent opioid tolerance state includes OIH. Once diagnosed or provisionally considered, treatment strategies could include opioid dose reduction, opioid rotation, use of agents with NMDA receptor antagonism, and a properly timed coxib. **CONCLUSION:** Despite initial skepticism and reservations, the phenomenon of OIH in humans is now accepted a clinical reality and a challenge faced by anesthesiologists, intensivists, pain specialists, and other workers in a diverse range of settings from perioperative care to palliative care medicine.

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### **Views and Reviews**

## **Excessive acute migraine medication use and migraine progression**

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Long considered a chronic disorder with a stable course, recent research demonstrates that, in a subgroup, migraine progresses to chronic migraine. Among the risk factors for migraine progression, acute symptomatic medication overuse (SMO) is regarded as one of the most important. Though SMO and chronic migraine are associated, several questions remain unanswered. First, the causal path is controversial (SMO as a cause or consequence). Second, it is unclear if specific classes of medication, as well as critical doses of exposures, are necessary. Herein we review this topic in the light of recent conducted research. Although several caveats exist and the data should be taken with caution, important findings are as follows: 1) Opiates are associated with migraine progression; critical dose of exposure is around 8 days per month, and the effect is more pronounced in men. 2) Barbiturates are also associated with migraine progression. Critical dose of exposure is around 5 days per month and the effect is more pronounced in women. 3) Triptans induced migraine progression in those with high frequency of migraine at baseline (10–14 days per month), but not overall. 4) Anti-inflammatory medications were protective in those with <10 days of headache at baseline, and, as triptans, induced migraine progression in those with high frequency of headaches. Accordingly, specific classes of medications are associated with migraine progression, and high frequency of headaches seems to be a risk factor for chronic migraine regardless of medication exposure.