Causes and Consequences of Inadequate Management of Acute Pain

Raymond Sinatra, MD, PHD

Department of Anesthesiology, Yale School of Medicine, Yale-New Haven Hospital, New Haven, Connecticut, USA

Reprint requests to: Raymond Sinatra, MD, PhD, Department of Anesthesiology, Yale School of Medicine, 20 York Street, Yale-New Haven Hospital, Tompkins Building, 3rd Floor, New Haven, Connecticut, USA. Tel: 203-785-2802; Fax: 203-785-6664; E-mail: rss9@email.med.yale.edu.

Abstract

Context. Intense acute pain afflicts millions of patients each year. Despite the recently increased focus on the importance of pain control, management of acute pain has remained suboptimal.

Objective. The objective of this study was to identify through a review of recent literature the barriers to effective treatment of acute pain and the potential consequences of inadequate pain management.

Design. A comprehensive literature review was conducted to identify articles relevant to the management of acute pain. Information regarding the underlying causes of inadequate pain management, as well as the sequelae associated with undermanaged pain was extracted and summarized.

Results. Studies indicate that treatment of acute pain remains suboptimal due to attitudes and educational barriers on the part of both physicians and patients, as well as the intrinsic limitations of available therapies. Inadequate management of acute pain negatively impacts numerous aspects of patient health, and may increase the risk of developing chronic pain. Although opioids are the preferred treatment for most moderate to severe acute pain, their side effects can impede their use, and thus, their clinical effectiveness. Analgesic regimens with an improved efficacy/tolerability balance have the potential to improve acute pain management, and thus reduce the incidence of chronic pain. Studies examining the use of multiple analgesics with different mechanisms of action suggest that multimodal therapies may offer an improved efficacy/tolerability balance over single agent regimens.

Conclusions. There exists a significant need for effective, well-tolerated analgesic therapies to limit the negative consequences of undermanaged acute pain. The use of multimodal therapy has demonstrated increasing promise and is supported by current practice guidelines.

Key Words. Acute Pain, Analgesia, Chronic Pain, Opioid

Introduction

Millions of patients each year suffer from acute pain as a result of trauma, illness, or surgery. Pain is the most common reason for admission to the emergency department (ED), comprising more than 40% of the over 100 million ED visits annually [1]. Furthermore, a large proportion of cases in the ED setting involve pain of moderate to severe intensity [2]. The prevalence of intense acute pain is similarly high among patients undergoing surgery; in the United States, over 73 million surgical procedures are performed annually, and most patients report experiencing a high degree of pain postoperatively [3].

Recent years have seen an increased awareness regarding the importance of pain management, with the congress declaring the 10-year period beginning in 2001 as the "Decade of Pain." Regardless, the management of acute pain remains inadequate across various treatment settings, with a substantial proportion of patients continuing to experience intense pain despite the availability of effective treatment. In a study of 71 patients presenting to the ED with acute pain, most reported moderate to severe pain, and nearly half reported that their pain had not been relieved at discharge from the ED [4]. A subsequent, larger study of 842 patients presenting to the ED with moderate to severe pain found that only 60% received analgesics, and 74% of patients continued to experience pain of moderate to severe intensity at discharge [5]. The results of these studies, conducted nearly a decade apart, highlight the lack of improvement in the management of acute pain in the ED setting despite the increased focus on pain by clinicians. Acute pain management in the postoperative setting is similarly suboptimal. A national survey of 250 patients who underwent surgery found that most patients (82%) experienced pain during the period immediately following surgery until 2 weeks after discharge, and of these, the majority (86%) classified their pain as being of moderate to extreme intensity [3]. The incidence and severity of acute postoperative pain in this study were

comparable with those reported by Warfield and colleagues nearly a decade earlier [6], illustrating the lack of progress in postsurgical pain management during this time, similar to the state of therapy in the ED setting.

Barriers to Pain Management

Numerous factors can contribute to inadequate pain management, including lack of sufficient physician training, lack of patient education about opioid use, as well as the side effects associated with certain analgesic therapy that contribute to noncompliance [3,7–14]. Opioids are generally considered the treatment of choice for moderate to severe pain and are recommended for patients who are unresponsive to other types of analgesic agents [15,16]. However, a relatively low proportion of patients suffering from moderate to severe pain actually receive opioids to control their pain. In one study of patients who reported to the ED with closed fractures, among patients 16 to 69 years of age with moderate to severe pain, only about 60% received opioid analgesia (Figure 1) [17]. The proportion receiving opioids was less than half among patients aged 70 years and older who had comparable pain [17]. A separate study of 160 patients reporting to the ED with a chief complaint related to pain found that as few as 15% of patients received an opioid analgesic despite a high degree of pain (mean pain numeric rating score = 6.13 out of 10) [11].

Even for the management of moderate to severe pain in the postsurgical setting, opioids tend to be underused/underdosed. A study by Orgill et al. showed that opioids
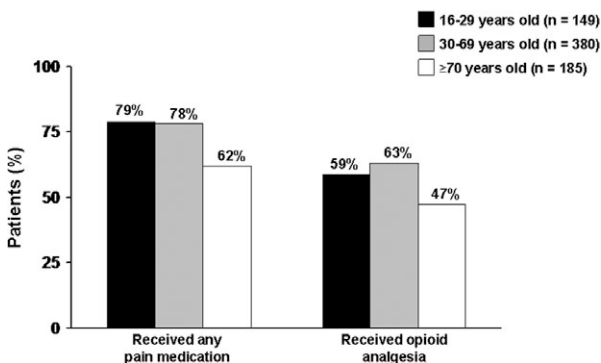

Figure 1 Use of analgesics in the emergency department (ED) among patients with documented moderate or severe pain due to extremity or clavicular fracture. The ED component of the National Center for Health Statistics/National Hospital Ambulatory Medical Care Survey for the years 1997 through 2000 was analyzed. Use of any analgesic and opioid analgesic medication in the ED among patients with extremity or clavicular fracture was determined [17].

were under-administered to patients with postsurgical pain following total laryngectomy or laryngopharyngectomy [18]. During intensive care, patients received significantly lower doses of morphine than those actually prescribed by their physicians, and remarkably, no patient received the recommended minimum daily dose of morphine for adequate management of moderate postsurgical pain despite the fact that this dose was prescribed in over two-thirds of hospital days (69%). Additionally, although a relatively large number of patients (35%) continued to experience pain due to inadequate analgesic therapy, only 22% had their opioid dose increased [18].

Physician perceptions regarding analgesic therapy and lack of physician training in areas ranging from the recognition of inadequate pain management to the application of various available treatment modalities are factors that can contribute to inadequate pain management. Medical school and postgraduate training programs have historically placed a low educational emphasis on pain management [7], which has contributed to many physicians' negative attitudes about opioids and a reluctance to prescribe them [7,8]. For example, in a survey of 386 Texas physicians, 31% reported reluctance to prescribe opioids for patients with chronic pain, based on the belief that these analgesics should not be used for pain associated with benign conditions; a similar number (30%) believed opioids should be restricted to the treatment of severe intractable pain [8]. A high proportion of physicians expressed fear of addiction as a reason against the use of opioid analgesics—approximately 28% believed that patients receiving opioids for pain relief were at significant risk for addiction, and an even greater proportion of physicians (39%) were concerned about addiction if a family member were to be prescribed morphine [8].

Surveys suggest there may be some confusion among physicians regarding the regulation of controlled substances, and many may have an exaggerated perception of legal liability and regulatory scrutiny [19]. A survey of 161 physicians showed that 40% feared legal investigation if they prescribed opioid analgesics for chronic pain [20]. In a larger survey exploring physicians' knowledge of Schedule II controlled substance regulations, 54% of respondents were prepared to reduce opioid drug dose, reduce number of opioid refills, or choose a less potent nonopioid treatment for acute or chronic pain due to fear of regulatory scrutiny [19].

Patient concerns about the abuse and addiction potential of opioid analgesics are another barrier to appropriate use of these agents [3,10,11]. A survey of 250 postoperative patients revealed that of those who would choose a nonopioid agent for pain management (72%), almost half made their choice based on fear of addiction [3]. A similar attitude was observed in a study of 340 patients with chronic pain taking prescription analgesics, in which the majority of patients (69%) rejected opioids because they were convinced these drugs were addictive or habit forming [21]. Half of the patients believed major opioids were too

strong for their pain, and 29% felt that opioids should be reserved only for patients with terminal illness, such as cancer [21].

In contrast to the negative attitudes expressed by physicians and patients toward opioid therapy, studies have shown that when opioid analgesics are administered under proper physician supervision, treatment is associated with very low rates of opioid misuse. In one such study of 801 adults treated for pain associated with degenerative arthritis, low back pain, migraine, neuropathy, or fibromyalgia in a primary care setting, the incidence of opioid use disorders was only 3.8% of patients [22]. Long-term use of controlled-release oxycodone in 227 patients suffering from chronic pain resulted in a similarly low incidence of opioid misuse (2.6%), with no evidence of de novo addiction [23]. The apparent discrepancy between perceptions about the abuse potential of opioids and the actual risk of abuse supports the urgent need for improved physician and patient education with respect to the appropriate use of opioid analgesics for pain management.

Opioid-Related Adverse Effects Represent a Major Barrier to Adequate Analgesia

The overall effectiveness of any therapy consists of a balance between its efficacy and its tolerability. Side effects associated with opioid therapy, such as nausea, vomiting, and constipation have a major impact on pain therapy and represent one of the most significant causes behind the widespread undertreatment of acute pain today [12–14]. These side effects occur in a large proportion of patients taking opioid therapy. In a systematic review that analyzed opioid-associated adverse events in postoperative patients from multiple randomized controlled trials, observational studies, and case reports, 31% of patients reported an adverse gastrointestinal event, most commonly nausea, vomiting, ileus, or constipation. Sedation and somnolence were the most commonly reported central nervous system effects (30.3%). Other common adverse events included pruritus (18.3%), urinary retention (17.5%), and respiratory events (2.8%) [14]. These side effects can be a contributing factor to patients' discontinuation of opioid therapy, as well as being a barrier to opioid dosing to maximal efficacy by clinicians. Many patients may choose to cope with pain rather than experience these opioid side effects. This attitude was observed in pre- and postoperative interviews of 50 patients undergoing abdominal surgery, in which patients were asked to choose from among several hypothetical treatments with different characteristics reflecting the balance between analgesia and side effects. Overall, the severity of side effects was considered a more important consideration for therapy than the degree of pain relief, suggesting that many patients were willing to "trade" analgesic efficacy for a reduction in side effect severity (Figure 2) [24]. Thus, despite being highly efficacious for the management of acute pain, the clinical utility of opioids may be severely limited by their side effect profile, empha-
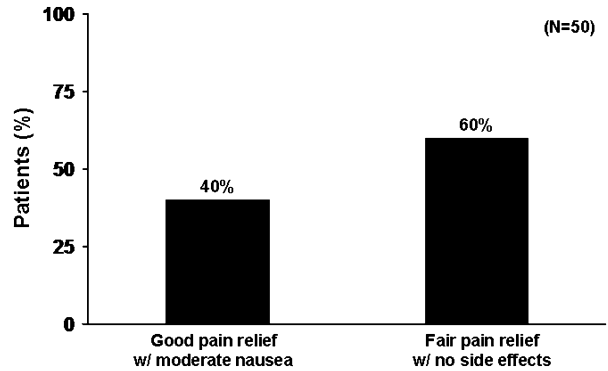

Figure 2 Hypothetical patient preferences for characteristics of analgesic therapy. Surgical patients (N = 60) were asked to choose from among several hypothetical treatments with different attributes pertaining to analgesic efficacy and side effects. The survey results revealed that patients were willing to compromise analgesia for a reduction in side effects [24].

sizing the need for analgesic regimens that improve tolerability while still maintaining analgesic efficacy.

Nerve Blockade

In addition to systemically-administered analgesics (i.e., oral and intravenous agents), localized techniques with proven efficacy and favorable safety profiles are also available for the management of acute pain, particularly in the postoperative setting. Nerve blockade is a technique whereby a local anesthetic such as lidocaine or bupivacaine is applied onto or near a nerve or nerve plexus to prevent afferent pain signal transmission by interfering with cation flux across the neuronal membrane [25–27]. Localized nerve block has been shown to provide effective pain control with a low incidence of side effects and a high degree of patient satisfaction in patients following major orthopedic surgery [28–30].

Incorporation of localized nerve block into a multidrug analgesic regimen could be a useful strategy for mitigating the impact of opioid-related adverse events on treatment effectiveness by allowing for a reduction in opioid consumption due to analgesic synergy attributable to complementary mechanisms of action. In fact, a number of clinical trials have already documented the benefit of these types of regimens, reporting equivalent or superior reductions in the level of acute pain with concomitant reductions in patient-controlled opioid consumption and/or opioid-related side effects including nausea, vomiting, sedation, and pruritus compared with opioid analgesic regimens that do not include nerve block [31–33].

Various practical barriers and potential complications may limit the clinical utility of nerve block techniques, particu-

larly in the primary care setting. Administering nerve blockade requires specialized training and a thorough knowledge of regional anesthetic techniques. Nerve blocks are typically performed by anesthesiologists [34], but can also be performed by physicians from other disciplines who receive special training [35]. However, utilization of nerve block may be viewed as too time consuming, which can limit acceptance of this technique within the overall pain management plan [36]. In contrast with this perception, set procedures can actually increase efficiency by reducing total procedure time and associated costs [36,37]. It should be noted that nerve block is not suitable for all patients, including those susceptible to bleeding (due to the potential for development of hematomas caused by catheter insertion that could cause nerve compartment compression), or patients with systemic disease or infection, as these conditions can alter serum pH and thus affect anesthetic absorption kinetics [25].

Inadequate Acute Pain Management Has Substantial Consequences for Patients

Unrelieved acute pain has consequences beyond the immediate perception of pain and can negatively impact patients' well-being on multiple levels [38]. The effects of acute pain on different aspects of patient quality of life have been explored in numerous studies in the postsurgical setting.

Reduced Quality of Life

Patients who had undergone radical prostatectomy, total hip replacement, or total knee replacement were assessed for pain, health-related quality of life, and physical and social function at 4 weeks post-hospital discharge using the Short Form (SF)-36 quality-of-life questionnaire and Treatment Outcomes of Pain Survey. Patients in each surgical group demonstrated worse mean scores compared with United States norms across several measures, including bodily pain, physical functioning, and social functioning. Acute pain also substantially impaired patients' sleep, sexual function, and ability to perform physical activities during the postoperative period [38].

Similar results were observed in a prospective cohort study of patients who underwent total hip or knee replacement surgery, in which a significant, inverse relationship was demonstrated between severity of acute postoperative pain and patients' health-related quality of life in the immediate postoperative period. Specifically, severity of pain was correlated with a decrease in both the physical ($R^2 = 0.1387$) and mental ($R^2 = 0.1299$) component of the SF-12 quality-of-life questionnaire ($P < 0.01$ for both) (Figure 3) [39].

Impaired Sleep

Unrelieved acute pain can have a significant impact on sleep, as observed in a study of 175 patients recovering from ambulatory surgery who experienced moderate to severe pain. Overall, during the first 24 hours after discharge, sleep was prevented or disrupted in 46% of the patients studied. A significant association was observed between impaired sleep on the night following surgery and drowsiness the following day. In patients who had difficulty falling asleep or were awakened because of pain, 71%
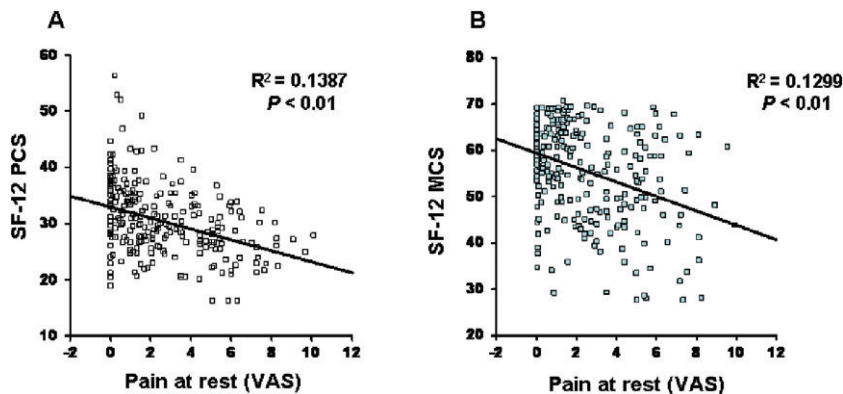

Figure 3 Association between acute postoperative pain and decreased quality of life (QOL) in the 2-week period following elective hip or knee replacement surgery: (A) physical and (B) mental components of Short Form (SF)-12 survey. Data were obtained during a 2-week recovery period from 37 patients undergoing total hip or knee replacement surgery. Pain was assessed on a visual analog scale (VAS) of 0–10. Physical and mental function was determined from the physical component scores (PCS) and mental component scores (MCS) from the SF-12 QOL questionnaire. The respective scores were correlated to the degree of postoperative pain intensity at rest. Decreases in PCS and MCS showed a significant correlation with increased pain at rest ($P < 0.01$) [39].

and 69%, respectively, reported drowsiness. In contrast, only 41% of patients without sleep disturbance reported drowsiness ($P = 0.004$). Activity level showed a strong negative correlation with drowsiness during the immediate postoperative period ($P < 0.0001$) [40].

Dihle and colleagues studied the relationship between pain intensity and sleep disturbance in 77 patients following joint replacement surgery. Sleep was most affected in patients with severe pain (numeric rating score 6 to 10) compared with those with mild pain (score 1 to 3) or moderate pain (score 4 to 5) on the third day after surgery ($P < 0.02$). Severe pain also significantly impaired a range of other functions, including walking ability, general activity, social relationships, and mood [41].

Impaired Physical Function

As previously described, unrelieved acute pain can severely impair patients' ability to perform the normal functions of everyday life. A prospective study of 411 patients admitted to the hospital for hip fracture demonstrated that more intense postoperative pain was associated with more impaired patient functionality. Compared with lower pain scores, higher pain scores at rest were associated with significant changes in numerous functional measures, which included decreased walking ability ($P < 0.001$), delayed time to ambulation ($P < 0.01$), greater potential for missed or shortened physiotherapy sessions ($P = 0.002$), and longer hospital stays ($P = 0.03$). Mobility remained significantly reduced up to 6 months postsurgery in patients with severe acute postoperative pain compared with those with less pain ($P = 0.02$) [42].

High Economic Costs of Unrelieved Pain

Pain is one of the most common reasons for postsurgical hospital readmission and may substantially increase the cost of hospital care. In a study of 20,817 patients who underwent same-day surgery, over one-third (38%) of the 313 patients who returned to the hospital for reasons directly related to their surgical procedure reported pain as the main reason for their readmission (Figure 4) [43]. The average cost per patient for readmission due to pain was $1,869 per visit [43]. Given that over 80% of patients experience postoperative pain despite the availability of effective analgesics, inadequate postsurgical pain relief will continue to add to the already high economic burden of treatment by extending recovery time and length of hospital stay [44].

Potential Physiological Consequences of Undermanaged Pain

There is increasing evidence of an association between the level of acute pain and risk for developing chronic pain. This progression, for which the mechanisms are poorly understood, has been observed in a variety of patient populations following surgical procedures [45–64], burn
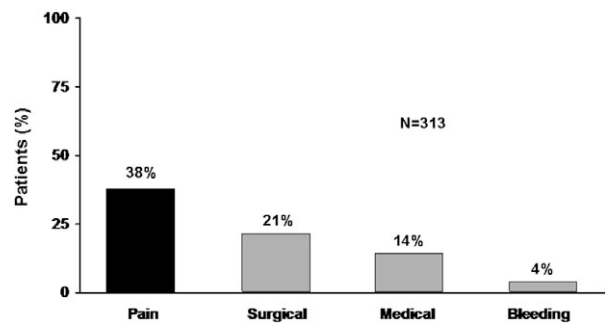

Figure 4 Primary reason for postoperative unanticipated hospital admissions or readmissions. Data were determined from a retrospective database study of 313 patients who were readmitted to the hospital with complications related to surgery within a 30-day period after discharge from same-day surgery. Pain was the most commonly reported reason for return to the hospital, occurring in 120 patients (38%) who had an unanticipated admission or readmission [43].

injury [65], acute herpes zoster [66–68], whiplash [69], childbirth [70], and in patients hospitalized for serious illnesses [71].

Up to one-half of patients reportedly suffer from chronic pain following common surgical procedures including lower limb amputation, coronary bypass surgery, breast surgery, and thoracotomy (Table 1) [72]. Clinically meaningful acute pain in the postoperative setting was a risk factor for the development of intense chronic pain in a study of 95 patients following breast surgery. A greater proportion of patients who ultimately developed chronic pain experienced acute postoperative pain (45%) compared with patients who did not develop chronic pain (27%; $P = 0.05$). Univariate analysis showed that severe acute postoperative pain was a significant risk factor for the development of chronic pain, although an independent contribution was not demonstrated in a logistic regression analysis [51]. Similar to breast surgery, post-surgical follow-up of 30 patients undergoing lateral thoracotomy reported that patients with greater levels of acute postoperative pain were more likely to develop long-term pain [50], and a retrospective review of 149 patients who had undergone posterolateral thoracotomy, considered to be one of the most painful surgical procedures, reported that a greater proportion of patients developing chronic postoperative pain reported acute postoperative pain compared with those who did not develop chronic pain (85% vs 62%; $P = 0.01$). Furthermore, the development of chronic pain was associated with a higher incidence of severe acute postoperative pain ($P = 0.0001$), constant acute pain ($P = 0.0004$), and presence of pain during the first postoperative week ($P = 0.0001$) [46].

Table 1 Estimated incidence of chronic postoperative pain and disability after selected surgical procedures[†] [72]

	% of Patients		
	Estimated Incidence of Chronic Pain	Estimated Chronic Severe (Disabling) Pain (>5 out of 10)	United States Surgical Volumes (1000s)
Amputation	30–50	5–10	159 (lower limb only)
Breast surgery (lumpectomy and mastectomy)	20–30	5–10	479
Thoracotomy	30–40	10	Unknown
Inguinal hernia repair	10	2–4	609
Coronary artery bypass	30–50	5–10	598
Caesarean section	10	4	220

[†] Gall bladder surgery not included, since preoperative diagnosis of pain specifically from gall bladder is difficult, and persistent postoperative pain could therefore be related to other intra-abdominal disorders.

The intensity of acute pain has also been shown to be a risk factor for the development of chronic pain in patients with acute herpes zoster [66–68]. A prospective study in patients with acute herpes zoster who were followed-up at 6 weeks and 3, 5, 8, and 12 months after the initial assessment reported that those who subsequently developed chronic, postherpetic neuralgia (PHN) had significantly greater pain intensity at the initial assessment than patients who did not develop chronic pain [66]. Similarly, baseline and follow-up data from nearly 1,000 patients with acute herpes zoster enrolled within 3 days of rash onset indicated an association between the intensity of acute zoster pain and subsequent development of PHN [67].

Likewise, data from subjects hospitalized for major burn injury (N = 333) reported that more severe pain during the week prior to hospital discharge was an independent predictor for the development of chronic pain [65]. In addition, a high level of patient-reported pain intensity was a predictive factor for the development of persistent neck pain following whiplash injury sustained from a motor vehicle accident [69]. Specifically, initial patient-rated pain was significantly associated with an increased risk of persistent neck pain 12 months after the trauma (hazard ratio = 2.3; 95% confidence interval = 1.6 to 3.5) [69]. Similarly, a prospective, longitudinal study of women (N = 1288) hospitalized for childbirth in which data was obtained within 36 hours postpartum, as well as 2 months later, reported that the severity of acute postpartum pain was an independent predictor of persistent postpartum pain and depression [70]. Specifically, women with severe acute postpartum pain had a 2.5-fold increased risk of persistent pain and a 3.0-fold increased risk of postpartum depression compared with those with mild postpartum pain [70].

Consistent with the aforementioned studies, a clinical trial designed to determine the predictive factors associated with chronic pain in patients hospitalized for serious illnesses reported that the level of hospital pain at enrollment was most strongly associated with increased levels of pain 2 and 6 months later [71]. Collectively, these data underscore the importance of prompt and effective management of acute pain for improving quality of life and minimizing patient morbidity, not only in the period immediately following the acute pain episode, but possibly throughout the remainder of the patient's life.

Effective Control of Acute Pain Improves Pain-Associated Sequelae

It is evident that unrelieved acute pain can have negative consequences for various aspects of patients' health and quality of life. Conversely, effective pain management has been shown to mitigate these same sequelae of acute pain.

Improved Sleep

Ilfeld and colleagues showed the benefit of effective pain management on sleep in a study of 30 patients undergoing lower extremity orthopedic surgery. Upon postoperative discharge, patients were administered oral opioid analgesia plus a portable infusion pump delivering either 0.2% ropivacaine solution or saline solution via catheter. Opioid plus ropivacaine therapy provided complete pain control on the first day postsurgery, while opioid therapy plus saline infusion was associated with significant pain (mean pain score of 4.0 on a scale of 1 to 10). Effective management of acute postoperative pain was associated with less insomnia ($P < 0.05$) and fewer awakenings per night ($P < 0.01$). Sleep disturbances were more than 10-fold lower for patients achieving complete pain control with opioid plus ropivacaine compared with the opioid-plus-saline control group [33].

Improved Function and Recovery

Effective management of acute postoperative pain can offer significant advantages to patients by improving their physical function and recovery, enabling them to return to work sooner. The duration of hospitalization and loss of work time was studied in a randomized, double-blind study of 100 patients having received morphine-containing epidural vehicle (n = 51) or control vehicle (n = 49) following lumbar microdiscectomy. Compared with the control group, patients administered morphine had significantly better postoperative pain control, experienced improved recovery as shown by greater angle of straight leg elevation ($P = 0.02$), shorter hospital stays ($P < 0.0001$), and reduced loss of postoperative work time ($P < 0.0001$). A substantially larger proportion of patients in the morphine group (63%) were able to return home as early as 24 hours postsurgery compared with the control group (4%) [73].

Reduced Risk for Development of Chronic Pain

Acute pain has been identified as a predictive factor for the development of chronic pain, and various data suggest that effective management of acute pain can reduce the risk for pain progression. Numerous clinical studies have demonstrated that effectively lowering the severity of acute pain was associated with a reduced risk for developing chronic/persistent pain months to years later in patients undergoing intracranial tumor resection [60], breast surgery for cancer [54,63,74], iliac crest bone harvesting surgery [56,58,59], orthopedic surgery [61], major abdominal surgery [75], and thoracotomy [55,76]. The use of intraoperative bupivacaine-induced nerve block plus postoperative administration of an opioid, NSAID and acetaminophen reduced acute postoperative pain at rest (24 hours postsurgery), and decreased the prevalence and severity of chronic pain 1 year after breast surgery compared with control patients who received the same postoperative analgesic regimen minus bupivacaine ($P < 0.01$) [54,74]. Similar findings were reported in a study of women (N = 29) undergoing breast surgery with axillary node dissection that randomly allocated patients to receive either a standard intraoperative and postoperative analgesic regimen (morphine, diclofenac, dextropropoxyphene hydrochloride, and acetaminophen) or a more aggressive analgesic regimen that included continuous paravertebral block for 48 hours plus acetaminophen and parecoxib (followed by celecoxib for up to 5 days). The latter, more aggressive analgesic regimen was associated with lower visual analog scale (VAS) pain scores on movement during the first five postoperative days compared with the standard analgesic regimen, as well as a lower incidence of chronic postsurgical pain (80% vs 0%, respectively; $P = 0.009$) [77]. An association between effective postoperative acute pain reduction and development of long-term pain was also observed in a placebo-controlled trial of 45 iliac crest bone graft donors. Significant acute postoperative pain relief during the first 24 hours after surgery was experienced in patients receiving local infusions of bupivacaine with or without morphine

(mean VAS scores = 1.8 and 2.0, respectively) compared with placebo (mean VAS score = 3.6; $P < 0.001$ vs both active treatment groups) [56]. At 12 weeks following surgery, none of the patients receiving bupivacaine plus morphine had chronic pain, while 13% of patients in the bupivacaine-only group and 33% in the placebo group developed chronic pain ($P < 0.05$ for placebo vs bupivacaine-plus-morphine group) [56].

Overall, considerable evidence supports the relationship between acute pain severity and risk for development of chronic pain. Additionally, the preponderance of evidence supports the potential for effective management of acute pain to improve long-term outcomes, including reducing the risk of chronic pain. However, in a few published studies, reduction of acute pain intensity did not affect incidence of chronic pain. In a study of 86 patients undergoing thoracotomy under standard general anesthesia, preoperative administration of ketamine improved immediate postoperative pain, but had no effect on the incidence of neuropathic pain 4 months after the procedure compared with saline controls [78]. However, it should be noted that the incremental effect of ketamine on acute pain in this study was transient, with the intergroup differences in VAS scores at 24 hours postsurgery disappearing by 48 hours [78]. Similarly, in women undergoing breast surgery for cancer, administration of gabapentin reduced pain at rest on postoperative day 3, and reduced pain upon movement on postoperative days 2–5, but had no effect on the incidence or intensity of pain 3 months postsurgery, except for a reduction in incidence of burning pain [79]. The lack of a correlation between acute pain control and incidence of chronic pain in this study may have been related to inconsistent differences in VAS scores during the acute period (i.e., treatment group VAS differences during the acute period noted during movement but not at rest) and/or potentially inadequate sample sizes [79]. Further investigation is warranted to clearly define the potential to reduce the risk of chronic pain through effective control of acute pain, and this remains an area of intense interest.

The Future of Pain Management

Multimodal Analgesia

While opioids remain the foundation of pain management for moderate to severe pain, the use of multiple analgesics with different mechanisms of action has shown increasing promise in clinical practice. A multimodal approach could provide significant benefits including reductions in pain intensity, opioid dose requirements, and opioid-related adverse events [33,55,56,58,60,63,73,74,80–94]. Several clinical studies have documented not only the ability of this approach to provide better pain relief with a reduced consumption of opioids and/or superior tolerability/side effect profile, but also the potential to lower the incidence of chronic pain development [54,56,60,61,63,74]. A shift in the pain treatment paradigm is supported by practice guidelines from the American Society of Anesthesiologists Task Force on Acute Pain Management, which recom-

mends use of multimodal analgesic therapy whenever possible for patients with acute postoperative pain [34].

Acute Pain Services

The practice of establishing a dedicated acute pain service may provide another means of improving the treatment of acute pain moving forward. Acute pain services can vary in structure, but at most major institutions, an anesthesiologist typically plays a pivotal role [95]. Most acute pain services are either anesthesiology-based or nurse-based with anesthesiologist supervision, whereby an anesthesiologist takes the lead in coordinating the efforts of all involved health care professional including other physicians, as well as nurses, pharmacists, and therapists in an attempt to minimize patient discomfort and treatment complications [95,96]. Acute pain services are designed to provide optimal pain management for every surgical patient, including children and outpatients, as well as regular review of institutional pain management policies and practices [95].

One of the primary components of an acute pain service is the availability of round-the-clock pain services for patients requiring analgesia or counseling [95]. Providing 24-hour pain services can be a costly and labor-intensive practice, but is critical to ensuring the comfort of the majority of patients. Regular pain assessments and documentation of pain scores is another important component of an acute pain service program as it increases the likelihood that patients' pain remains below an acceptable, predetermined threshold. Perhaps, the most important element of an acute pain service is cooperation among all involved health care professionals to develop protocols and achieve preset goals for postsurgical mobilization and discharge. Ongoing education for institutional staff regarding safe and cost-effective methods for providing analgesia, and patient education about the benefits and adverse events associated with various analgesic regimens are also important to helping maximize patient adherence with their analgesic regimen, thus increasing the likelihood that their pain will remain within an acceptable range. Finally, regularly scheduled review of cost-effectiveness and patient satisfaction are also important components of any acute pain service [97]. Regularly scheduled institutional reviews of acute pain service programs can improve cost-efficiency and identify areas of deficiency, as well as informing strategies to improve the quality of patient care [95]. The benefits of an acute pain service have been demonstrated in a number of studies including those reporting overall improvement in postoperative pain scores, patient satisfaction and sleep pattern after the establishment of an acute pain service [98–102].

Conclusion

Despite advances in analgesic therapy in this "Decade of Pain," substantial need still exists for better acute pain management, especially among patients with moderate to severe pain. Inadequate management of pain unquestionably continues to have an unacceptable negative impact on patients' overall quality of life and ability to function both physically and mentally. Failure to administer appropriate analgesic treatment may result in worsening of pain and more frequent hospital readmissions, adding to the already high economic burden associated with pain therapy. Moreover, the long-term consequences of under-treated acute pain should not be overlooked, since many patients with more severe acute postoperative pain may later suffer unnecessarily from chronic pain. Improved analgesic treatment that is well tolerated should provide more effective acute pain relief and is likely to benefit patients with respect to the various consequences associated with intense acute pain. Such measures are critical for facilitating early recovery and discharge, in addition to potentially reducing the risk for development of chronic pain. In this respect, a multimodal approach to analgesia and establishment of acute pain services may have an important role in the future of acute pain management.

References

1 Pletcher MJ, et al. Trends in opioid prescribing by race/ethnicity for patients seeking care in US emergency departments. JAMA 2008;299(1):70–8.

2 McCaig LF, Nawar EW. National Hospital Ambulatory Medical Care Survey: 2004 emergency department summary. Adv Data 2006;••(372):1–29.

3 Apfelbaum JL, et al. Postoperative pain experience: Results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg 2003;97(2):534–40. table of contents.

4 Guru V, Dubinsky I. The patient vs caregiver perception of acute pain in the emergency department. J Emerg Med 2000;18(1):7–12.

5 Todd KH, et al. Pain in the emergency department: Results of the pain and emergency medicine initiative (PEMI) multicenter study. J Pain 2007;8(6):460–6.

6 Warfield CA, Kahn CH. Acute pain management. Programs in U.S. hospitals and experiences and attitudes among U.S. adults. Anesthesiology 1995; 83(5):1090–4.

7 Rupp T, Delaney KA. Inadequate analgesia in emergency medicine. Ann Emerg Med 2004;43(4):494–503.

8 Weinstein SM, et al. Physicians' attitudes toward pain and the use of opioid analgesics: Results of a survey from the Texas Cancer Pain Initiative. South Med J 2000;93(5):479–87.

9 Juhl IU, et al. Postoperative pain relief, from the patients' and the nurses' point of view. Acta Anaesthesiol Scand 1993;37(4):404–9.

10 Stalnikowicz R, et al. Undertreatment of acute pain in the emergency department: A challenge. Int J Qual Health Care 2005;17(2):173–6.

11 Tanabe P, Buschmann M. A prospective study of ED pain management practices and the patient's perspective. J Emerg Nurs 1999;25(3):171–7.

12 Moore RA, McQuay HJ. Prevalence of opioid adverse events in chronic non-malignant pain: Systematic review of randomised trials of oral opioids. Arthritis Res Ther 2005;7(5):R1046–51.

13 Eberhart LH, et al. Patient preferences for immediate postoperative recovery. Br J Anaesth 2002;89(5):760–1.

14 Wheeler M, et al. Adverse events associated with postoperative opioid analgesia: A systematic review. J Pain 2002;3(3):159–80.

15 Jovey RD, et al. Use of opioid analgesics for the treatment of chronic noncancer pain—A consensus statement and guidelines from the Canadian Pain Society, 2002. Pain Res Manage 2003;8(suppl A):3A–28A.

16 •• ••. 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 1997;13(1):6–8.

17 Brown JC, et al. Emergency department analgesia for fracture pain. Ann Emerg Med 2003;42(2):197–205.

18 Orgill R, Krempl GA, Medina JE. Acute pain management following laryngectomy. Arch Otolaryngol Head Neck Surg 2002;128(7):829–32.

19 Weissman DE, Joranson DE, Hopwood MB. Wisconsin physicians' knowledge and attitudes about opioid analgesic regulations. Wis Med J 1991;90(12):671–5.

20 Potter M, et al. Opioids for chronic nonmalignant pain. Attitudes and practices of primary care physicians in the UCSF/Stanford Collaborative Research Network. University of California, San Francisco. J Fam Pract 2001;50(2):145–51.

21 Moulin DE, et al. Chronic pain in Canada—Prevalence, treatment, impact and the role of opioid analgesia. Pain Res Manage 2002;7(4):179–84.

22 Fleming MF, et al. Substance use disorders in a primary care sample receiving daily opioid therapy. J Pain 2007;8(7):573–82.

23 Portenoy RK, et al. Long-term use of controlled-release oxycodone for noncancer pain: Results of a 3-year registry study. Clin J Pain 2007;23(4):287–99.

24 Gan TJ, et al. Patient preferences for acute pain treatment. Br J Anaesth 2004;92(5):681–8.

25 Turjanica MA. Postoperative continuous peripheral nerve blockade in the lower extremity total joint arthroplasty population. Medsurg Nurs 2007;16(3):151–4. quiz 155.

26 Scholz A, et al. Complex blockade of TTX-resistant Na+ currents by lidocaine and bupivacaine reduce firing frequency in DRG neurons. J Neurophysiol 1998;79(4):1746–54.

27 Komai H, McDowell TS. Local anesthetic inhibition of voltage-activated potassium currents in rat dorsal root ganglion neurons. Anesthesiology 2001;94(6):1089–95.

28 Borgeat A, et al. Patient-controlled interscalene analgesia with ropivacaine 0.2% versus patient-controlled intravenous analgesia after major shoulder surgery: Effects on diaphragmatic and respiratory function. Anesthesiology 2000;92(1):102–8.

29 Borgeat A, et al. Patient-controlled interscalene analgesia with ropivacaine after major shoulder surgery: PCIA vs PCA. Br J Anaesth 1998;81(4):603–5.

30 Borgeat A, et al. Patient-controlled analgesia after major shoulder surgery: Patient-controlled interscalene analgesia versus patient-controlled analgesia. Anesthesiology 1997;87(6):1343–7.

31 Klein SM, et al. Interscalene brachial plexus block with a continuous catheter insertion system and a disposable infusion pump. Anesth Analg 2000;91(6):1473–8.

32 Ilfeld BM, et al. Continuous interscalene brachial plexus block for postoperative pain control at home: A randomized, double-blinded, placebo-controlled study. Anesth Analg 2003;96(4):1089–95. table of contents.

33 Ilfeld BM, et al. Continuous popliteal sciatic nerve block for postoperative pain control at home: A randomized, double-blinded, placebo-controlled study. Anesthesiology 2002;97(4):959–65.

34 •• ••. Practice guidelines for acute pain management in the perioperative setting: An updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. Anesthesiology 2004;100(6):1573–81.

35 Stone MB, Wang R, Price DD. Ultrasound-guided supraclavicular brachial plexus nerve block vs procedural sedation for the treatment of upper extremity emergencies. Am J Emerg Med 2008;26(6):706–10.

36 Armstrong KP, Cherry RA. Brachial plexus anesthesia compared to general anesthesia when a block room is available. Can J Anaesth 2004;51(1):41–4.

37 Gonano C, et al. Comparison of economical aspects of interscalene brachial plexus blockade and general anaesthesia for arthroscopic shoulder surgery. Br J Anaesth 2009;103(3):428–33.

38 Strassels SA, McNicol E, Wagner AK, et al. Persistent postoperative pain, health-related quality of life, and functioning 1 month after hospital discharge. Acute Pain 2004;6:95–104.

39 Wu CL, et al. The effect of pain on health-related quality of life in the immediate postoperative period. Anesth Analg 2003;97(4):1078–85. table of contents.

40 Pavlin DJ, et al. A survey of pain and other symptoms that affect the recovery process after discharge from an ambulatory surgery unit. J Clin Anesth 2004; 16(3):200–6.

41 Dihle A, et al. The exploration of the establishment of cutpoints to categorize the severity of acute postoperative pain. Clin J Pain 2006;22(7):617–24.

42 Morrison RS, et al. The impact of post-operative pain on outcomes following hip fracture. Pain 2003; 103(3):303–11.

43 Coley KC, et al. Retrospective evaluation of unanticipated admissions and readmissions after same day surgery and associated costs. J Clin Anesth 2002; 14(5):349–53.

44 Shang AB, Gan TJ. Optimising postoperative pain management in the ambulatory patient. Drugs 2003; 63(9):855–67.

45 Romundstad L, et al. Chronic pain and sensory changes after augmentation mammoplasty: Long term effects of preincisional administration of methylprednisolone. Pain 2006;124(1–2):92–9.

46 Pluijms WA, et al. Chronic post-thoracotomy pain: A retrospective study. Acta Anaesthesiol Scand 2006; 50(7):804–8.

47 Steegers MA, et al. The role of angina pectoris in chronic pain after coronary artery bypass graft surgery. J Pain 2007;8(8):667–73.

48 Fassoulaki A, et al. Acute postoperative pain predicts chronic pain and long-term analgesic requirements after breast surgery for cancer. Acta Anaesthesiol Belg 2008;59(4):241–8.

49 Nikolajsen L, et al. Chronic pain following Caesarean section. Acta Anaesthesiol Scand 2004;48(1):111–6.

50 Katz J, et al. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. Clin J Pain 1996;12(1):50–5.

51 Poleshuck EL, et al. Risk factors for chronic pain following breast cancer surgery: A prospective study. J Pain 2006;7(9):626–34.

52 Yarnitsky D, et al. Prediction of chronic postoperative pain: Pre-operative DNIC testing identifies patients at risk. Pain 2008;138(1):22–8.

53 Hanley MA, et al. Preamputation pain and acute pain predict chronic pain after lower extremity amputation. J Pain 2007;8(2):102–9.

54 Kairaluoma PM, et al. Preincisional paravertebral block reduces the prevalence of chronic pain after breast surgery. Anesth Analg 2006;103(3):703–8.

55 Senturk M, et al. The effects of three different analgesia techniques on long-term postthoracotomy pain. Anesth Analg 2002;94(1):11–5. table of contents.

56 Gundes H, et al. Short- and long-term effects of regional application of morphine and bupivacaine on the iliac crest donor site. Acta Orthop Belg 2000;66(4):341–4.

57 Tasmuth T, et al. Treatment-related factors predisposing to chronic pain in patients with breast cancer—a multivariate approach. Acta Oncolo 1997; 36(6):625–30.

58 Singh K, et al. A prospective, randomized, double-blind study evaluating the efficacy of postoperative continuous local anesthetic infusion at the iliac crest bone graft site after spinal arthrodesis. Spine (Philadelphia, Pa: 1976) 2005;30(22):2477–83.

59 Singh K, et al. A prospective, randomized, double-blind study of the efficacy of postoperative continuous local anesthetic infusion at the iliac crest bone graft site after posterior spinal arthrodesis: A minimum of 4-year follow-up. Spine (Philadelphia, Pa: 1976) 2007;32(25):2790–6.

60 Batoz H, et al. The analgesic properties of scalp infiltrations with ropivacaine after intracranial tumoral resection. Anesth Analg 2009;109(1):240–4.

61 Morrison RS, et al. A novel interdisciplinary analgesic program reduces pain and improves function in older adults after orthopedic surgery. J Am Geriatr Soc 2009;57(1):1–10.

62 Shahin AY, Osman AM. Parietal peritoneal closure and persistent postcesarean pain. Int J Gynaecol Obstet 2009;104(2):135–9.

63 Fassoulaki A, et al. Multimodal analgesia with gabapentin and local anesthetics prevents acute and chronic pain after breast surgery for cancer. Anesth Analg 2005;101(5):1427–32.

64 Callesen T, Bech K, Kehlet H. Prospective study of chronic pain after groin hernia repair. Br J Surg 1999;86(12):1528–31.

65 Smith MT, et al. Sleep onset insomnia symptoms during hospitalization for major burn injury predict chronic pain. Pain 2008;138(3):497–506.

66 Dworkin RH, et al. A high-risk method for studying psychosocial antecedents of chronic pain: The prospective investigation of herpes zoster. J Abnorm Psychol 1992;101(1):200–5.

67 Jung BF, et al. Risk factors for postherpetic neuralgia in patients with herpes zoster. Neurology 2004;62(9):1545–51.

68 Harrison RA, et al. A mixed model for factors predictive of pain in AIDS patients with herpes zoster. J Pain Symptom Manage 1999;17(6):410–7.

69 Atherton K, et al. Predictors of persistent neck pain after whiplash injury. Emerg Med J 2006;23(3):195–201.

70 Eisenach JC, et al. Severity of acute pain after childbirth, but not type of delivery, predicts persistent pain and postpartum depression. Pain 2008;140(1):87–94.

71 Desbiens NA, et al. Pain during hospitalization is associated with continued pain six months later in survivors of serious illness. The SUPPORT Investigators. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. Am J Med 1997;102(3):269–76.

72 Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: Risk factors and prevention. Lancet 2006;367(9522):1618–25.

73 Mastronardi L, et al. Efficacy of the morphine-Adcon-L compound in the management of post-operative pain after lumbar microdiscectomy. Neurosurgery 2002;50(3):518–24. discussion 524–5.

74 Kairaluoma PM, et al. Single-injection paravertebral block before general anesthesia enhances analgesia after breast cancer surgery with and without associated lymph node biopsy. Anesth Analg 2004;99(6):1837–43. table of contents.

75 Lavand'homme P, De Kock M. The use of intraoperative epidural or spinal analgesia modulates postoperative hyperalgesia and reduces residual pain after major abdominal surgery. Acta Anaesthesiol Belg 2006;57(4):373–9.

76 Obata H, et al. Epidural block with mepivacaine before surgery reduces long-term post-thoracotomy pain. Can J Anaesth 1999;46(12):1127–32.

77 Iohom G, et al. The associations between severity of early postoperative pain, chronic postsurgical pain and plasma concentration of stable nitric oxide products after breast surgery. Anesth Analg 2006;103(4):995–1000.

78 Duale C, et al. Perioperative ketamine does not prevent chronic pain after thoracotomy. Eur J Pain 2009;13(5):497–505.

79 Fassoulaki A, et al. The analgesic effect of gabapentin and mexiletine after breast surgery for cancer. Anesth Analg 2002;95(4):985–91. table of contents.

80 Katz J, et al. Postoperative morphine use and hyperalgesia are reduced by preoperative but not intraoperative epidural analgesia: Implications for preemptive analgesia and the prevention of central sensitization. Anesthesiology 2003;98(6):1449–60.

81 Gatti A, et al. Controlled-release oxycodone and pregabalin in the treatment of neuropathic pain: Results of a multicenter Italian study. Eur Neurol 2009;61(3):129–37.

82 Andersen LJ, et al. Postoperative analgesia in total hip arthroplasty: A randomized double-blinded, placebo-controlled study on peroperative and postoperative ropivacaine, ketorolac, and adrenaline wound infiltration. Acta Orthop 2007;78(2):187–92.

83 Beaussier M, et al. Continuous preperitoneal infusion of ropivacaine provides effective analgesia and accelerates recovery after colorectal surgery: A randomized, double-blind, placebo-controlled study. Anesthesiology 2007;107(3):461–8.

84 Buvanendran A, et al. Effects of perioperative administration of a selective cyclooxygenase 2 inhibitor on pain management and recovery of function after knee replacement: A randomized controlled trial. JAMA 2003;290(18):2411–8.

85 Carney J, et al. The transversus abdominis plane block provides effective postoperative analgesia in patients undergoing total abdominal hysterectomy. Anesth Analg 2008;107(6):2056–60.

86 Iohom G, et al. Effect of perioperative administration of dexketoprofen on opioid requirements and inflammatory response following elective hip arthroplasty. Br J Anaesth 2002;88(4):520–6.

87 Mathiesen O, et al. Pregabalin and dexamethasone in combination with paracetamol for postoperative pain control after abdominal hysterectomy. A randomized clinical trial. Acta Anaesthesiol Scand 2009;53(2):227–35.

88 McDonnell JG, et al. The analgesic efficacy of transversus abdominis plane block after cesarean delivery: A randomized controlled trial. Anesth Analg 2008;106(1):186–91. table of contents.

89 Paech MJ, et al. Postcesarean analgesia with spinal morphine, clonidine, or their combination. Anesth Analg 2004;98(5):1460–6. table of contents.

90 Safdar B, et al. Intravenous morphine plus ketorolac is superior to either drug alone for treatment of acute renal colic. Ann Emerg Med 2006;48(2):173–81. 181 e1.

91 Siddiqui ZI, et al. Continuous lumbar plexus block provides improved analgesia with fewer side effects compared with systemic opioids after hip arthroplasty: A randomized controlled trial. Reg Anesth Pain Med 2007;32(5):393–8.

92 Sinatra RS, et al. Preoperative rofecoxib oral suspension as an analgesic adjunct after lower abdominal surgery: The effects on effort-dependent pain and pulmonary function. Anesth Analg 2004;98(1):135–40. table of contents.

93 Sinatra RS, et al. Evaluation of the effect of perioperative rofecoxib treatment on pain control and clinical outcomes in patients recovering from gynecologic abdominal surgery: A randomized, double-blind, placebo-controlled clinical study. Reg Anesth Pain Med 2006;31(2):134–42.

94 Wang JJ, et al. Intraarticular triamcinolone acetonide for pain control after arthroscopic knee surgery. Anesth Analg 1998;87(5):1113–6.

95 Rawal N. Organization, function, and implementation of acute pain service. Anesth Clin North Am 2005; 23(1):211–25.

96 USDHHS. Making Health Care Safer: A Critical Analysis of Patient Safety Practices Evidence Report. Technology Assessment. •• No. 43. Chapter 37, Subchapter 2 . Available at: http://www.ahrq.gov/clinic/ptsafety/index.html#toc (accessed •••). [7]

97 Rawal N. Acute pain services revisited—Good from far, far from good? Reg Anesth Pain Med 2002;27(2):117–21.

98 Bardiau FM, et al. An intervention study to enhance postoperative pain management. Anesth Analg 2003;96(1):179–85. table of contents.

99 Bardiau FM, et al. Effectiveness of an acute pain service inception in a general hospital. J Clin Anesth 1999;11(7):583–9.

100 Gould TH, et al. Policy for controlling pain after surgery: Effect of sequential changes in management. BMJ 1992;305(6863):1187–93.

101 Tighe SQ, et al. The acute pain service: Effective or expensive care? Anaesthesia 1998;53(4):397–403.

102 Stadler M, et al. A cost-utility and cost-effectiveness analysis of an acute pain service. J Clin Anesth 2004;16(3):159–67.