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A Novel Interdisciplinary Analgesic Program Reduces Pain and Improves Function in Older Adults Following Orthopedic Surgery

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Abstract

OBJECTIVES—To examine the effect of a multi-component intervention on pain and function following orthopedic surgery.

DESIGN—Controlled prospective propensity score matched clinical trial.

SETTING—New York City acute rehabilitation hospital.

PARTICIPANTS—249 patients admitted to rehabilitation following hip fracture repair (N=51) hip (N=64) or knee (N=134) arthroplasty.

INTERVENTION—Pain assessment at rest and with physical therapy (PT) by staff using numeric rating scales (1 to 5). Physician protocols for standing analgesia and pre-emptive analgesia prior to PT were implemented on the intervention unit. Control unit patients received usual care.

MAIN OUTCOME MEASURES—Pain, analgesic prescribing, gait speed, transfer time, and percent of PT sessions completed during admission. Pain and difficulty walking at 6, 12, 18, and 24 weeks following discharge.

RESULTS—In multivariable analyses compared to controls, intervention patients were significantly more likely to report no or mild pain at rest (66% versus 49%, P=.004) and with PT (52% versus 38%, P=.02) on average for the first 7 days of rehabilitation; had faster 8 foot walk

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times on days four (9.3 seconds versus 13.2 seconds, P=.02) and seven (6.9 versus 9.2 seconds, P=.02); received more analgesia (8.0 milligrams of morphine sulfate equivalents/day, P<0.001); were more likely to receive standing analgesia (98% versus 48%, P<.001); and had significantly shorter lengths of stay (10.1 versus 11.3 days, P=.005). At 6 months compared to controls, intervention patients were less likely to report moderate/severe pain with walking (15% versus 4%, P=.02), that pain did not interfere with walking (7% versus 18%, P=.004), and were less likely to be taking analgesics (35% versus 51%, P=.03).

CONCLUSION—The intervention improved post-operative pain, reduced chronic pain, and improved function.

Keywords

pain; function; orthopaedic surgery

INTRODUCTION

Uncontrolled pain is a major impediment to post-operative functional recovery and is a persistent problem in the United States.[1-3] Older adults who undergo lower extremity orthopedic surgery (e.g., hip and knee arthroplasty, hip fracture repair) experience intense post-operative pain and are at risk for sub-optimal analgesic therapy.[4-6] Higher pain levels following lower extremity orthopedic surgery have been associated with increased lengths of stay, increased complications, delays in ambulation, impaired functional recovery, and increased suffering.[4 5 7-9] Given the paucity of data with respect to the effective treatment of pain in the geriatric patient and the increasing number of elders undergoing surgery[10] we performed a controlled prospective propensity score matched case control clinical trial to examine the effect of a multi-component inter-disciplinary intervention on the treatment of pain in older adults following lower extremity orthopedic surgery. We hypothesized that this generalizable intervention would decrease pain, enhance rehabilitation, and improve post-discharge function compared to usual care.

METHODS

This controlled clinical trial enrolled all eligible and consenting patients over age 50 years admitted to the acute rehabilitation service of a large New York hospital following lower extremity orthopedic surgery (hip fracture repair (HFX), unilateral total knee replacement (TKR), unilateral total hip replacement (THR)). The intervention - a standardized pain management protocol including daily comprehensive pain assessments by nursing and physical therapy (PT) staff, a standardized analgesic protocol including guidelines for treating opioid side-effects for physicians, and daily feedback of pain scores to all clinical staff– was implemented on one acute rehabilitation unit (intervention) while two additional units served as controls. Subjects were interviewed daily about their pain, had physical performance testing conducted on days 4 and 7, and were followed by telephone every 6 weeks for 24 weeks following discharge to assess pain and walking ability. The study was approved by the Mount Sinai School of Medicine Institutional Review Board.

Study Design

This study used a prospective individual matching procedure employing propensity score methods modeled on other successful clinical trials evaluating comprehensive hospital unit based interventions.[1 11 12] We enrolled all eligible subjects admitted to our intervention and control units and at the time of analysis matched intervention to control patients by propensity scores.[13]

Setting and Patients

We prospectively screened all admissions to the acute rehabilitation service on a daily basis Monday through Friday from March 2004 through August 2006. Patients were eligible for inclusion if they were over age 50 and were admitted within seven days of: a) hip fracture repair; b) unilateral total hip arthroplasty, or c) unilateral total knee arthroplasty. We excluded non-English speaking patients, patients not cleared to fully bear weight, patients who scored less than 17 out of 22 on the telephone mini-mental state exam,14 patients with cancer-related fractures, patients with a history of substance abuse, patients with a known adverse reaction to opioids, and patients taking adjuvant agents for neuropathic pain (e.g, gabapentin, tricyclic antidepressants). Enrolled patients were not informed as to whether they were on an intervention or control unit. Study enrollment details are in Figure 1.

The acute rehabilitation service consisted of 3 self-contained units with therapeutic gyms located on the same floor as patient rooms. Orthopedic patients who met Medicare criteria for acute rehabilitation were admitted to any of the three units based solely upon bed availability. Two of the units contained dedicated beds for brain injury and spinal cord injury with the remaining beds available for orthopedic patients. We chose to place the intervention on the larger unit and the two smaller units served as controls. The units were staffed with equivalent ratios of physicians, physical and occupational therapists, physical therapy assistants, certified occupational therapy assistants, registered nurses, nurses' aides, and support associates. All team members (including physicians) were unit based and all units followed the same clinical protocols with the exception of pain management. Therapeutic rehabilitation regimens for the three conditions (HFX, TKR, THR) were identical across the 3 units as were nursing protocols (available from the authors on request).

Usual Care

Patients admitted to the control units received the standard nursing pain assessment as mandated by the Joint Commission on Accreditation of Healthcare Organizations.15 Patients were assessed for pain at rest, worst pain, and pain relief on every nursing shift using 5 point numeric rating scales. Analgesia was prescribed based upon the treating physicians' preference.

Intervention

The intervention was based upon published guidelines, 16¯18 studies,5 19 20 and our prior research.1 The intervention consisted of a pain protocol for standing, pre-emptive, rescue, and titrated analgesia with training and feedback to clinical staff as supporting systems.

Analgesic Protocol—Patients admitted to the intervention unit were placed on a standard analgesic protocol detailed in Appendix 1. The protocol was available only to intervention unit physicians and was contained within their set of admitting orders. The protocol called for standing analgesia based upon patients' self-reported pain levels, as needed analgesia for breakthrough pain (i.e., intermittent pain flares that occur despite regularly scheduled analgesia), and pre-emptive analgesia administered one hour before PT. Analgesia was titrated as in Appendix 1. Protocols for tapering of opioids to prevent withdrawal symptoms (Appendix 1) and for treating opioid-induced side effects were also provided (Appendix 2). All medications were prescribed by the treating physiatrist.

Staff Training and Pain Assessment

Additional support was provided to clinical staff through education, enhanced pain assessment, and audit and feedback interventions developed in a prior study.1 At baseline, all intervention unit staff received education on pain management and additional training

was provided at regular intervals for newly hired staff. 1 Four additional questions (pain with transfer, pain with ambulation, and the degree to which pain interfered with transferring and walking) were added to the hospital's existing nursing pain assessment to capture the more dynamic nature of pain present in this patient population. Physical therapists queried patients about their pain at the start and conclusion of therapy, the worst pain experienced during therapy, and the degree to which pain interfered with therapy. Pain ratings were charted with vital signs as in the usual care group. Additionally a daily report detailing patients who reported severe pain at rest or pain that interfered moderately/completely with transfer or PT over the prior 24 hours was provided to the intervention interdisciplinary team on morning rounds.

Data Collection and Measures

All patients, intervention and control, were asked to rate their pain at rest, with transfer, and with physical therapy on 5 point numeric rating scales (1-none to 5-very severe) at admission and daily throughout their admission by clinical research interviewers. Additionally, clinical interviewers performed daily assessments of opioid side effects.1

Patient characteristics were obtained from interviews and medical record review. Comorbid conditions were measured using the RAND comorbidity score.21 Functional status prior to surgery, at admission to rehabilitation, and at discharge was measured using the motor subscales of the Functional Independence Measure (FIM). Cognitive status was assessed by the telephone version of the Mini-mental State Examination, depression by the 15 item Geriatric Depression Scale, and overall health related quality of life by self-report using excellent, very good, good, fair, or poor. 14 22 23

Physical performance was assessed prior to the patient's first PT session on rehabilitation days four and seven by a research physical therapist who was not a member of the rehabilitation staff and who was blinded to the patients' intervention status using two measures - the timed 8 foot walk and single and repetitive standing from chair. 24-26 These measures have both been shown to be reliable and valid measures of lower extremity performance following HFX and TKR/THR.24-26 Performance on these tasks was scored as described in prior published studies.25 26 Finally, we collected data on the number of missed or shortened physical therapy sessions.8

Patients were interviewed by telephone by a clinical interviewer blinded to the patients' intervention status following discharge every 6 weeks for 24 weeks. Patients were queried as to their pain at rest and with walking (1-none to 5-very severe), and the degree to which pain interfered with walking (1-none to 4-completely).

Analyses

Matching—Within each type of surgery, (HFX, TKR, THR) we computed a propensity score for each intervention and control subject.13 27 Propensity scores were determined by regressing whether patients received the intervention on variables of patient age, gender, ethnicity, medical insurance, modified RAND comorbidity score, GDS score, self-perceived health related quality of life score, admission rest pain, admission FIM score, overall FIM score prior to surgery, and 8 foot walk and sit to stand times at study entry. As more intervention than control patients were enrolled given the larger size of the intervention unit, we employed one to many matching without replacement.28 Each patient on the control unit was matched to one or more patients on the intervention unit whose logit of their propensity score was within ±0.2 standard deviations of the logit of the control patient's score. All analyses of the intervention's effect included only matched subjects.

Main Analyses—Pain scores used in the analyses were obtained from the clinical research interviewers and data were weighted to account for the one-to-many propensity matching. We employed multivariable logistic regression and multivariable ordered logistic regression for categorical outcomes, generalized linear models for continuous outcomes (GLM), and generalized estimating equations (GEE) for longitudinal outcomes to examine the association between the independent variables and our outcomes of interest. Covariates were selected based on prior studies.8 21 29 30

Confirmatory Analyses—To supplement to the propensity score analyses, we also performed multivariable modeling as described above using all subjects, not just those matched by propensity score.

All analyses were performed using STATA 9.2.31

RESULTS

Eighty eight of 98 patients on the control unit (90%) were matched to 129 of 150 patients (85%) on the intervention units (Table 1). There were no significant differences observed between the two matched groups. Specifically, baseline pain scores and performance measures were not significantly different between the two groups. All results presented below reflect the propensity score matched normalized weighted data.

Figure 2 displays rest pain and pain with PT scores through hospital day 7. Intervention patients reported significantly less pain at rest and with PT than usual care patients. In multivariable analyses compared to controls, intervention patients on average were significantly more likely to report no or mild pain at rest (66% (95% CI 64.8% to 66.9%) versus 51% (50.0% to 52.9%); parameter estimate = .63; P=.004) and with PT (52% (50.8% to 52.8%) versus 38% (36.8% to 39.1%); parameter estimate = .47; P=.02) for the first 7 days of rehabilitation. Compared to control patients, intervention patients were significantly less likely to report moderate to very severe pain at discharge (21% versus 37%; odds ratio = .42; 95% CI .24 to .74; P=.003) and during their last PT session prior to discharge (37% versus 56%; odds ratio = .47; 95% CI .29 to .77; P=.002).

Table 2 presents the multi-variable adjusted in-hospital performance outcomes for the two groups. Compared to controls, patients in the intervention arm had significantly faster 8 foot walk times at rehabilitation day 4 (9.3 seconds (95% CI 8.13 to 10.50) versus 13.2 seconds (11.98 to 14.44)) and day 7 (6.9 seconds (6.17 to 7.64) versus 9.2 seconds (8.31 to 10.18)). Intervention patients were significantly less likely to have a PT session missed or shortened (81% versus 73% of controls, odds ratio = 0.08; 95% CI .004 to.17; P=.04). Intervention patients had significantly shorter mean length of stay as compared to control patients (10.1 days (9.6 to 10.5) versus 11.3 days (11.0 to 11.7)).

Intervention patients received 8.0 milligrams (95% CI for difference 1.8 to 14.2) more oral morphine sulfate equivalents per day (23.6 milligrams/day versus 15.6 milligrams/day, parameter estimate = 6.48; P<0.001 respectively) and were significantly more likely to receive regularly scheduled opioid analgesia (98% versus 48%, odds ratio = 295.18; 95% CI 34.12 to 2553.44; P<.001 respectively) than control patients. For the 52% of control patients who did not receive any standing analgesia, 21% were ordered an “as needed opioid”, 77% were ordered an “as needed” combination product (acetaminophen with codeine, acetaminophen with oxycodone); and 3% were ordered “as needed” acetaminophen. Intervention patients were significantly more likely to have concurrent laxatives prescribed while receiving opioids (92% versus 83%, odds ratio=2.54, 95% CI 1.04 to 6.20 P=.03) than control patients. There were no significant differences between the two groups with respect

to opioid side effects of constipation (e.g., 3 or more days without a bowel movement) (32% of intervention patients versus 25% of controls, P=.06), delirium (4% of intervention versus 7% of controls, P=.30), nausea (16% of intervention patients versus 17% of controls, P=.31), somnolence (33% of intervention patients versus 36% of controls, P=.55), or thought clarity (6% of intervention patients versus 6% of controls, P=.96).

At 6 months, intervention patients were less likely to report moderate to very severe pain with walking (4% versus 15% of controls, odds ratio =.16; 95% CI .05 to.56; P=.02), that pain interfered with walking (7% versus 18% of controls, odds ratio =.16; 95% CI .05 to.56; P=.004), and were less likely to be taking analgesics (35% versus 51% of controls; odds ratio = 0.50; 95% CI .26, .94; P=.03) as compared to control patients. Figure 3 presents pain and interference with walking for intervention and control patients for the six months following discharge.

Results from multivariable analyses that included all subjects were qualitatively similar to those of the propensity score matched analyses across all outcome measures (i.e., the parameter estimates were contained within the 95% confidence intervals of the estimates of the primary propensity score analyses).

DISCUSSION

This study of a generalizable interdisciplinary pain management program is one of the first rigorous clinical trials to demonstrate significant reductions in post-operative pain, reduction in chronic pain, and improved lower extremity mobility both acutely and 6 months following discharge. This study makes several valuable contributions to the evidence base for pain treatment. First, it is one of the only controlled clinical trials published to date that describes generalizable interventions that routinely identify and scale pain, result in appropriate analgesic medication prescribing, and are associated with reduced pain severity. Second, it is the largest study to date to show that improved pain control results in enhanced rehabilitation for older adults following surgery and shorter lengths of stay. Finally, this study is the first to our knowledge that demonstrates that reducing acute post-operative pain results in a lower prevalence of chronic pain and improved walking at 6 months following discharge.

Strengths and Limitations

There are several limitations to this study that should be noted. This was not a randomized trial and it is possible that an unmeasured confounder may have accounted for the results observed. As others have noted, it is impractical to randomize patients on admission to unit based interventions in settings where fiscal pressures require that patients be assigned to the first available open bed.12 Although patient assignment was based upon the random availability of an open bed and was out of our control, it is possible that measured and unmeasured confounders were not randomly distributed across intervention and control units. To account for this possibility, our study employed a prospective individual matching procedure to achieve a balanced allocation of subjects11 and used newly developed propensity score methods to ensure even more stringent balancing between intervention and control groups.32 As shown in Table 1, subjects in the two arms were well matched and there were no significant difference in observable characteristics between the two groups.

It is also possible that cross-contamination could have occurred with providers caring for patients on more than on floor and applying the intervention or some variant to the control group as a result of weekend or holiday coverage. We believe that such contamination is unlikely. It was extremely rare for nursing or physician staff to “float” from intervention to control units – even during times of cross-coverage - during the study period. Even if such

cross-contamination had occurred the resulting bias would favor the null hypothesis and as such, our results would reflect a more conservative estimate of the true intervention effect.

Finally, our study was limited to the sub-set of older adults admitted to acute rehabilitation. It is possible that the long-term pain and functional outcomes that we observed might not generalize to other settings or patient populations. Nevertheless, our intervention was designed so that it could be easily incorporated into standard rehabilitation protocols for lower-extremity orthopedic surgery in other settings (peri-operatively in the hospital, sub-acute rehabilitation). Although empirical testing of our intervention in these other settings is warranted, we are cautiously optimistic that similarly positive results will be obtained.

Relationship to Other Studies

Pain Severity and Analgesic Prescribing—After more than 2 decades of panels, symposia, and editorials calling for remedial action,15 33-36 inadequate treatment of pain remains a serious problem in the United States and world-wide.1 37 38 A recent systematic review of institutional interventions to improve the management of pain in hospitalized adults did not identify a single generalizable intervention that successfully and consistently improved patients' pain severity.2 We believe our intervention was effective because it targeted the entire interdisciplinary team rather than nursing staff alone,2 employed interventions that have been previously shown to be effective in improving pain assessment, 1 and unlike other studies, targeted physicians by giving them guidance regarding both opioid prescribing and side effect management. Although this study was conducted in the rehabilitation setting, the intervention could be easily implemented in the immediate postoperative period and in sub-acute rehabilitation. Future studies are needed to confirm our finding in these additional settings.

Rehabilitation—Prior observational studies have found that post-operative pain in older adults undergoing lower extremity orthopedic surgery is associated with an increased the risk of delirium,7 39 40 longer hospital and rehabilitation length of stay, 8 41 higher probability of a PT session being missed or shortened,8 delays in ambulation post-operatively,8 impaired functional recovery,8 41 and greater pain at 6 months 42 Data from controlled studies examining the effect of improving postoperative pain on functional outcomes in older adults are sparse. The few small studies that have been performed suggest that improved pain management is associated with reduced length of stay, earlier mobilization, and improved range of motion in patients undergoing knee arthroplasty.5 43 44 Our study both confirms and extends these preliminary reports by enrolling patients who underwent hip and knee arthroplasty and hip fracture repair, being of adequate size to adjust for confounding variables, and using validated performance measures of lower extremity function. Patients in the intervention arm not only had better pain control, but were noted to have increased gait speed, faster transfer times, were significantly more likely to complete their regularly scheduled PT sessions, and had shorter lengths of stay.

Chronic Pain and Six Month Function—Despite the prevalence (over one million surgeries annually in the United States) and reported success rates of knee and hip arthroplasty and hip fracture repair, a substantial number of patients undergoing these procedures report chronic pain at six months.45 46 The prevalence of chronic pain has been reported to be as high as 28.1% following hip arthroplasty, 18.4% following knee arthroplasty, and 26% following hip fracture repair.8 46 These rates are comparable to those observed in the control arm of this study.

Why chronic pain syndromes develop following surgery is not well understood. It is hypothesized that chronic pain results from the interaction of prolonged peripheral and

central nervous system sensitization that subsequently leads to the development of permanent aberrant excitatory synaptic connections.46 Observational data suggest that enhanced post-operative pain management is associated with improved functional outcomes at six months in older adults.8 Our study confirms and amplifies these findings by demonstrating that patients exposed to the intervention reported less pain, improved function, and less analgesic requirements 6 months after receiving our analgesic protocol. We postulate that our intervention, by providing effective analgesia in the immediate post-operative period, prevented the development of central sensitization and contributed to the reduction of chronic pain and improved 6 month function observed in our intervention group (Figure 3). Studies are needed to confirm these results and explore the underlying pathophysiology for them in both animal models and additional clinical trials.

CONCLUSIONS

The inability of health care providers and the health care system to address the problem of untreated pain has been well documented. This failure is partly a reflection of the emphasis in medicine on diagnosis and treatment of causative factors rather than on symptomatic treatment. The common belief that acute pain is merely a symptom, will resolve as healing occurs, and is not harmful in itself relegates the relief of acute pain to a minor level of priority in the minds of many doctors and nurses.47 The absence of data linking untreated pain to adverse clinical and functional outcomes has further reinforced these beliefs. This study of an interdisciplinary unit based intervention to improve the treatment of pain revealed important and novel findings. It is the largest and most rigorously designed study to date to identify an effective systematic intervention to reduce post-operative pain in older adults. Second, it supplements existing observational data by providing direct evidence that reducing post-operative pain improves functional outcomes in older adults and reduces rehabilitation length of stay. Finally, and perhaps most intriguingly, it suggests that aggressive pain management in the post-operative setting may reduce the development of chronic post-operative pain. Additional research focused on replicating these results in other patient populations and settings and on the underlying biological mechanisms that underlie these clinical findings is required.

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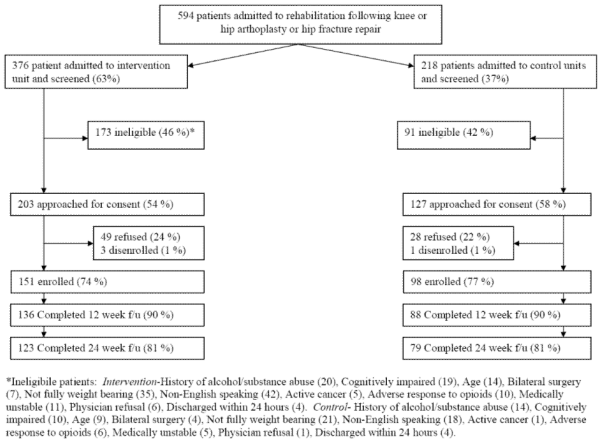


Figure 1.
Details of Subject Enrollment

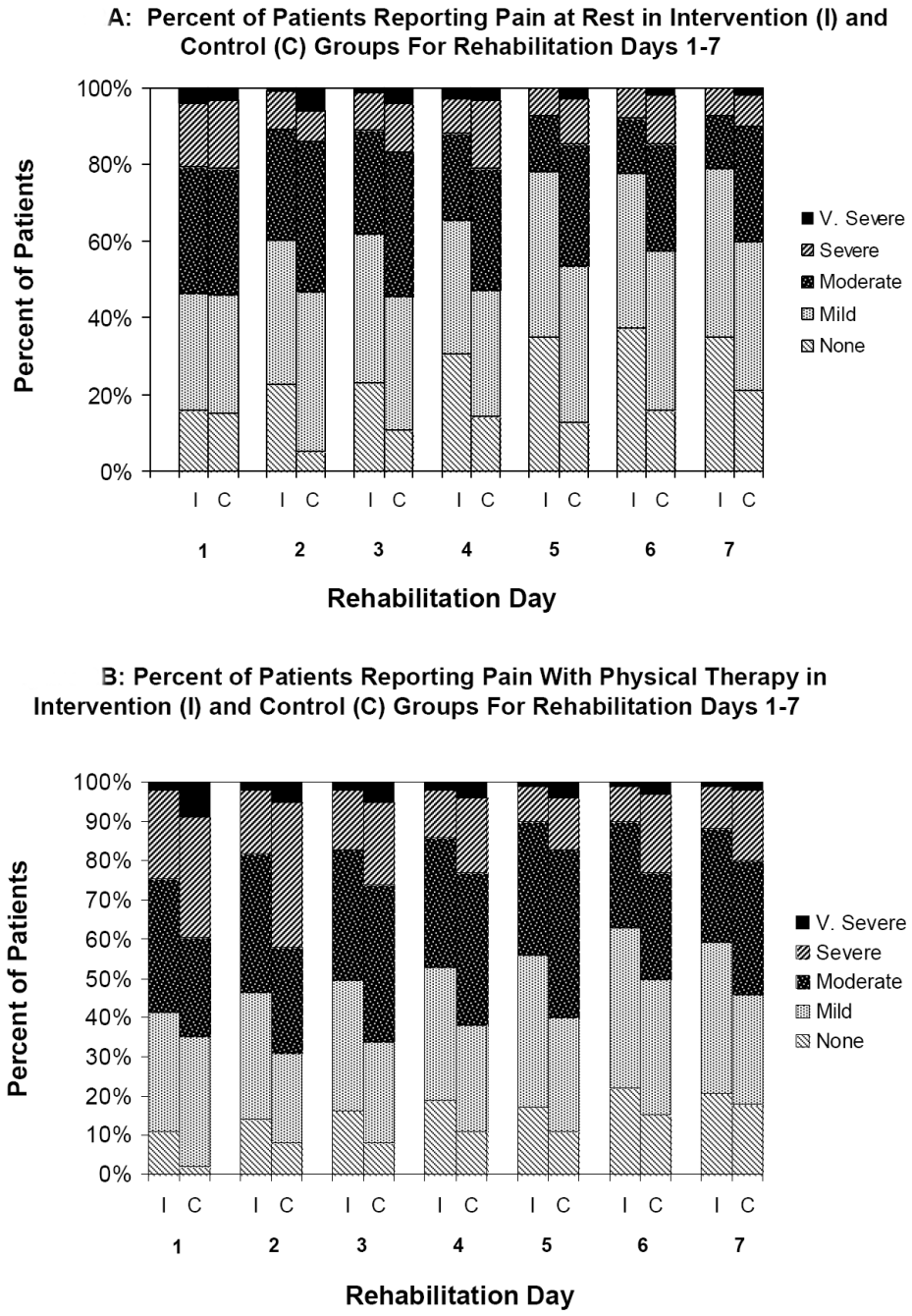
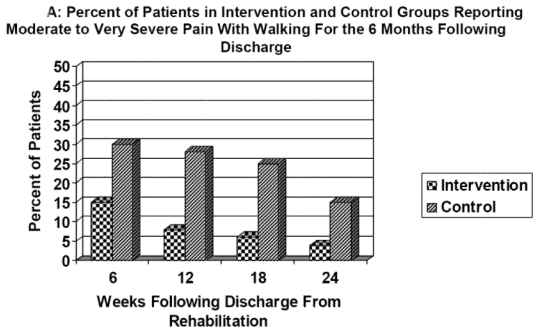


Figure 2.

Pain at rest (Figure 2A) and pain with PT (Figure 2B) for intervention and control patients for intervention and control patients from rehabilitation day 1 to rehabilitation day 7. Overall adjusted mean pain at rest scores from admission through day 7 were 2.2 (95% CI 2.14 to 2.30) for intervention patients and 2.6 (2.46 to 2.63) for control patients (parameter estimate = -.33; 95% CI -.52 to -14; P<.001). Overall adjusted mean pain scores during PT for rehabilitation days 1-7 were 2.6 (2.48 to 2.65) for intervention patients and 2.8 (2.72 to 2.91) for control patients (parameter estimate = -.20; -.34 to -01; P=.04). All values reflect propensity score matched normalized weighted data.



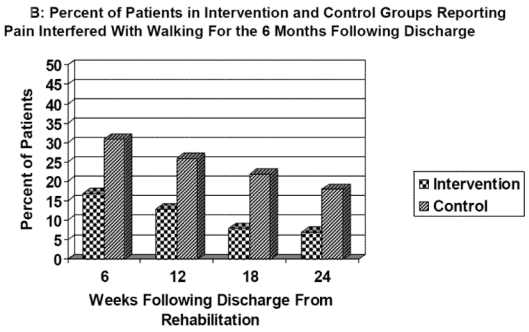
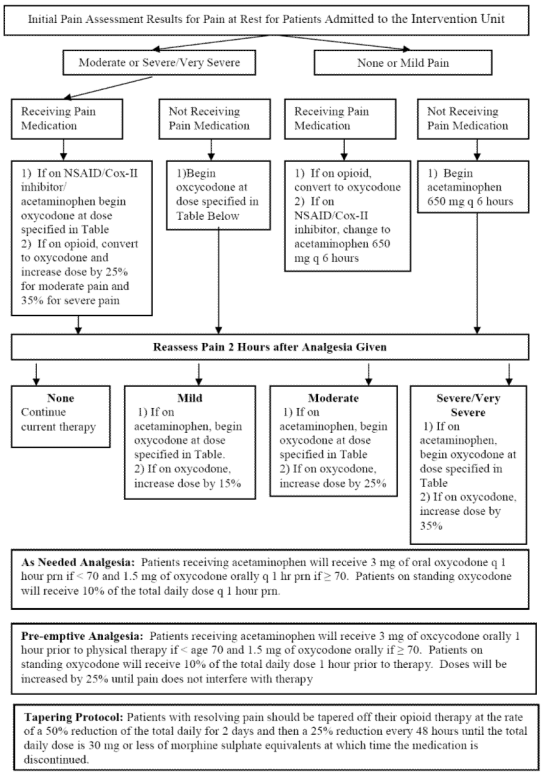


Figure 3.

Percent of patients reporting moderate to very severe pain with ambulation (Figure 3A) and percent of patients reporting pain interfered with ambulation (Figure 3B) for intervention and control patients for the 24 weeks following hospital discharge. Overall adjusted mean pain with ambulation scores over the 24 weeks were 1.50 (95% CI 1.47 to 1.53) for intervention patients and 1.77 (1.73 to 1.81) for control patients (parameter estimate = -.27; 95 CI -.46, -.05; P=.01). Overall adjusted mean interference scores over the 24 weeks were 1.18 (1.16 to 1.20) for intervention patients and 1.48 (1.45 to 1.51) for control patients (parameter estimate =-.25; 95 CI -.41, -.10; P=.001). All values reflect propensity score matched normalized weighted data.



Starting Doses of Oxycodone For Opioid Naive Patients

		Pain Intensity		
Patient Age		Mild and Receiving Acetaminophen/NSAID/ Cox-II inhibitor	Moderate	Severe
< 70 years	Standing oral dose	5 mg q 4 hours	7.5 mg q 4 hours	10 mg q 4 hours
	As needed oral dose	3 mg q 1hour prn	5 mg q 1hour prn	7.5 mg q 1 hour prn
	Pre-emptive oral dose before PT	3 mg 1 hour before PT	5 mg 1 hour before PT	7.5 mg 1 hour before PT
∃ 70 years	Standing oral dose	3 mg q 4 hours	5 mg q 4 hours	7.5 mg q 4 hours
	As needed oral dose	1.5 mg q 1 hour prn	2 mg q 1 hour prn	5 mg q 1 hour prn
	Pre-emptive oral dose before PT	1.5 mg 1 hour before PT	3 mg 1 hour before PT	5 mg 1 hour before PT

Appendix 1.
Analgesic Prescribing Protocol for Intervention Unit

Constipation	With few exceptions all patients on opioid therapy need an individualized bowel regimen. Start with the STEP 1 regimen. When an effective regimen is found it must be continued for the duration of the opioid therapy. STEP 1: Docusate 100 mg bid plus Senna 1 tab qd or bid. STEP 2: Docusate 100 mg bid plus Senna 2 tab bid. STEP 3: Docusate 100 mg bid plus Senna 3 tab bid. STEP 4: Docusate 100 mg bid, Senna 4 tab bid plus Lactulose (or Sorbitol) 15 cc bid. STEP 4: Add: sodium phosphate or oil retention enema; if no results add a high colonic tap water enema. STEP 5: Docusate 100 mg bid, Senna 4 tab bid plus Lactulose (or Sorbitol) 30 cc bid. STEP 6: Docusate 100 mg bid, Senna 4 tab bid plus Lactulose (or Sorbitol) 30 cc qid. Maintain a high index of suspicion for the possibility of bowel obstruction or fecal impaction. Rule out impaction with digital rectal examination or abdominal x-ray when clinical suspicion exists. Rectal disimpaction must occur before treating constipation with an oral laxative regimen. If a patient has not been on a bowel regimen, the step 1 regimen should be started. If there is no response in 24 hours move to the next step. At any given time if there has been no bowel movement in 3 or more days a sodium phosphate or mineral oil enema should be administered. If this is not effective a high colonic tap water enema should be administered.
Nausea	metoclopramide 5-10 mg PO/IV q 6-8 h (consider around the clock administration if nausea is recurrent). *Caution if CNS disorder, Parkinson=s Disease, impaired liver function, blood dyscrasia, or hypersensitivity to drug class.* Alternatively: prochlorperazine 5-10 mg PO/IV q 6-8 h (consider around the clock administration if nausea is recurrent). *Caution if CNS depression, adrenergic blocker use, cardiovascular disease, glaucoma, bone marrow depression, seizure disorder, or sensitivity to drug class.*
Sedation	methylphenidate 2.5-5 mg po q 8AM and noon. May titrate upward 2.5 mg every 24-48 hr as needed. Do not exceed 15 mg po q 8AM and noon. *Caution if patient has heart disease, hypertension, Tourette=s syndrome, seizure disorder, hyperthyroidism, severe anxiety, psychosis, history of MAO inhibitor use in last 2 weeks, history of substance abuse, or sensitivity to drug class.*
Delirium	1. Through thorough history and examination, attempt to identify and treat any and all reversible aetiologies for delirium. 2. Review the medication list and eliminate or reduce agents known to predispose patients to delirium (e.g. anticholinergic agents, benzodiazepines, steroids). 3. Begin: a. olanzapine 2.5 mg po qd-BID. Titrate up if necessary 2.5-5 mg per day to maximum 20 mg/day *Caution if paralytic ileus, GI/GU obstruction, narrow-angle glaucoma, history of neuroleptic malignant syndrome, cardiovascular disease, seizure history, impaired liver function, hypotension, hypovolemia, dehydration, aspiration pneumonia risk, CNS depression, or sensitivity to drug class.* Alternatively b. risperidone or haloperidol 0.5 mg po BID. Titrate up if necessary 1 mg/day to maximum of 3 mg BID. *Caution if prolonged QT or on other agents that prolong QT, impaired renal function, impaired liver function, history of neuroleptic malignant syndrome, seizure disorder, cardiac disease, cerebrovascular disease, hypotension, hypovolemia, dehydration, CNS depression or aspiration risk, sensitivity to drug class.*

Appendix 2.
Protocols for Management of Opioid Related Side Effects

Table 1

Characteristics for Propensity Score Matched and Unmatched Control and Intervention Patients

	Propensity Score Matched Patients			Unmatched Patients	
	Control (N=88) Weighted Value	**Intervention (N=129) Weighted Value**	**P**	**Control (N=10)**	**Intervention (N=21)**
Women	74.4 %	76.7 %	.72	10 (100 %)	9 (43 %)
Mean age in years (sd)	70.9 (8.3)	70.9 (9.9)	.95	76 (10.6)	71 (11.5)
Race			.71		
White	58.6 %	63.2 %		9 (90 %)	7 (33 %)
African American	21.8 %	23.0 %		0	9 (43 %)
Hispanic	14.9 %	9.2 %		0	1 (5 %)
Other	4.6 %	4.6 %		1 (10 %)	4 (19%)
Insurance			.56		
Medicare	81.4 %	76.7 %		10 (100%)	13 (62%)
Medicaid	5.8 %	4.7 %		0	1 (5 %)
Other	12.8 %	18.6 %		0	7 (33 %)
Surgery			.99		
Hip fracture repair	20.9 %	20.9 %		8 (80 %)	4 (19 %)
Total hip replacement	24.4 %	24.4 %		1 (10 %)	5 (24 %)
Total knee replacement	54.7 %	54.7 %		1 (10 %)	12 (57)
Pre-hospital residence			.55		
Home/apartment	88.8 %	86.5 %		10 (100)	20 (94 %)
Nursing home	1.2 %	3.5 %		0	1 (5 %)
Self-perceived health related quality of life			.83		
Excellent	14.9 %	14.1 %		3 (30)	3 (14)
Very Good	24.1 %	31.8 %		3 (30)	5 (24)
Good	39.1 %	35.3 %		2 (20)	5 (24)
Fair	14.9 %	14.1 %		1 (10)	8 (38)
Poor	6.9 %	4.7 %		1(10)	0

	Propensity Score Matched Patients			Unmatched Patients	
	Control (N=88) Weighted Value	Intervention (N=129) Weighted Value	P	Control (N=10)	Intervention (N=21)
Geriatric depression score (sd)	2.9 (2.8)	2.6 (2.5)	.38	3.8 (4.0)	3.2 (3.4)
Rand comorbidity index (sd)	1.7 (1.1)	1.6 (1.1)	.45	1.7 (1.2)	2.1 (1.7)
Fim total score prior to surgery (sd)	85.0 (7.3)	85.4 (5.8)	.66	86.1 (9.7)	82.1 (11.8)
Fim locomotion score prior to surgery (sd)	11.3 (2.6)	11.7 (2.0)	.18	12.9 (1.9)	10.8 (2.9)
Fim locomotion score on admission to rehabilitation (sd)	4.0 (2.5)	4.4 (2.9)	.44	2.3 (1.1)	3.4 (2.5)
Pain at rest on admission			.57		
None	12.8 %	17.4 %		1 (10 %)	2 (9.5 %)
Mild	31.4 %	32.6 %		4 (40 %)	7 (33 %)
Moderate	27.9 %	25.6 %		1 (10 %)	6 (28.6 %)
Severe-very severe	27.9 %	24.4%		4 (40 %)	6 (28.6 %)
Pain with transfer from bed to chair on admission			.38		
None	1.2 %	5.9 %		0	0
Mild	25.9 %	17.6 %		3 (30 %)	5 (23.8 %)
Moderate	29.4 %	30.6 %		3 (30 %)	5 (23.8 %)
Severe-very severe	43.8 %	45.8 %		4 (40 %)	11 (52.3 %)
Pain with walking on admission			.87		
None	8.3 %	7.3 %		0	1 (4.8 %)
Mild	27.4 %	23.2 %		1 (10 %)	6 (28.6 %)
Moderate	27.4 %	32.9 %		5 (50 %)	4 (19 %)
Severe-very severe	36.9 %	36.7 %		4 (40 %)	10 (47.6 %)
Sit to stand time			.95		
Unable to perform task	12.9 %	11.6 %		4 (40 %)	5 (22.7 %)
> 56 seconds	15.3 %	15.1 %		3 (30 %)	10 (45.5 %)
36-55.9 seconds	23.5 %	20.9 %		0	5 (22.7 %)
26-35.9 seconds	23.5 %	29.1 %		2 (20 %)	1 (4.5 %)

	Propensity Score Matched Patients			Unmatched Patients	
	Control (N=88) Weighted Value	Intervention (N=129) Weighted Value	P	Control (N=10)	Intervention (N=21)
< 26 seconds	24.7 %	23.3 %		1 (10 %)	1 (4.5 %)
Average time for 8 foot walk			.97		
Unable to perform task	12.6 %	10.6 %		4 (40 %)	3 (13.6 %)
> 19 seconds	16.1 %	16.5 %		3 (30 %)	9 (40.9 %)
12.0 to 18.9 seconds	21.8 %	21.2 %		0	5 (22.7 %)
7.5 to 11.9 seconds	31.0 %	29.4 %		2 (20 %)	3 (13.6 %)
<7.5 seconds	18.4 %	22.4 %		1 (10 %)	2 (9.1 %)

Table 2

Multivariable Adjusted Performance Outcomes For Propensity Score Matched Subjects*

	Control (N=88)	Intervention (N=129)	Parameter estimate (95% CI) or Odds Ratio (95% CI)	P
8 Foot Walk Performance				
8 ft walk performance on day 4			3.03 (1.78, 5.19)	<.001
Unable to complete task	13.8%	5.8%		
Over 13 seconds to complete task	25.3%	12.8%		
7.5 to 13 seconds to complete task	26.4%	22.1%		
5.6 to 7.4 seconds to complete task	21.8%	20.9%		
5.5 seconds or less to complete task	12.6%	38.4%		
Mean 8 ft walk time (sec) on day 4 for those able to complete the task (sd)	13.2 (7.0)	9.3 (4.9)	-.28 (-.51, -.04)	.02
8 ft walk performance on day 7†			2.77 (1.45, 5.28)	.002
Unable to complete task	11.1	10.4		
Over 13 seconds to complete task	31.7	11.9		
7.5 to 13 seconds to complete task	28.6	17.9		
5.6 to 7.4 seconds to complete task	15.9	28.4		
5.5 seconds or less to complete task	12.7	31.3		
Mean 8 ft walk time (sec) on day 7 for those able to complete the task (sd)†	9.2 (3.7)	6.9 (2.9)	-.21 (-.39, -.03)	.02
Sit to Stand Performance				
Sit to stand performance on day 4			1.87 (1.08, 3.2)	.03
Unable to complete task	16.1%	9.3%		
Over 40 seconds to complete task	23%	15.1%		
28 to 40 seconds to complete task	17.2%	19.8%		
19-27 seconds to complete task	28.7%	26.7%		
18 seconds or less to complete task	14.9%	29.1%		
Sit to stand time (sec) on day 4 for those able to complete the task (sd)	34.7 (13.0)	32.7 (13.4)	-.08 (-.25, .08)	.34
Sit to stand performance on day 7†			1.08 (.56, 2.1)	.81
Unable to complete task	13.5%	15%		
Over 32 seconds to complete task	23.1%	21.7%		
23 to 31 seconds to complete task	26.9%	21.7%		
16 to 22 seconds to complete task	34.6%	30%		
15 seconds or less to complete task	1.9%	11.7%		
Sit to stand time (sec) on day 7 for those able to complete the task (sd)†	26.0 (10.0)	27.8 (14.5)	-.02 (-.22, .18)	.85

	Control (N=88)	Intervention (N=129)	Parameter estimate (95% CI) or Odds Ratio (95% CI)	P
Mean length of stay in days (sd)	11.3 (1.8)	10.1 (2.2)	-1.52 (-2.57, -.46)	.005

*Variables included in the multivariable models: FIM locomotion score at admission to rehabilitation, modified RAND comorbidity score, age, sex, type of surgery (hip fracture repair, hip replacement, knee replacement), race/ethnicity, and GDS score

†Sample size on day 7 was 168 (64 control and 104 intervention patients) due to discharges