Hosp Pharm 2012;47(11):855–862

www.thomasland.com
doi: 10.1310/hpj4711-855

Original Article

Cost and Quality Implications of Opioid-Based Postsurgical Pain Control in Total Abdominal Hysterectomy: A Study of Cost Outliers and Opioid-Related Adverse Events

John Reitan, PharmD[*]*; Ron Moleski, PharmD*[*]*; Arletta van Breda, RN*[†]*; Robert Adamson*[‡]*; and Indu Lew*[‡]

Abstract

Objective: A retrospective medical record review, case-control study of patients undergoing total abdominal hysterectomy was conducted to determine the relationship between opioid burden, related adverse drug effects (ADEs), and extended length of stay (LOS) and acute care costs cause(s) of LOS outliers.

Methods: Ninety-seven case patients with extended LOS (≥ 5 days) met the study eligibility criteria and were matched with case controls (patients with a LOS <5 days). The medical records of cases and controls were reviewed to collect information describing pre-established data points: opioid doses and opioid-related ADEs. Difference between cases and controls were compared using McNemar's test for matched pairs, paired *t* test, and signed rank test.

Results: Comparisons of opioid-related ADEs revealed the following statistically significant differences compared with controls: respiratory ADEs (eg, hypoxia) in 12% of cases versus 1% of controls ($P < .01$) and gastrointestinal ADEs (eg, nausea/vomiting) in 44% of cases versus 19% of controls ($P < .01$). Cases received higher doses during the 72 hours following postanesthesia care unit (PACU) discharge ($P = .04$). By hospital discharge, cases had received 2.5 times the total opioid dose of controls and, on average, remained hospitalized 132 hours (5.5 days) longer than controls. Approximately 33% of LOS difference between cases and controls occurred prior to operating room admission, whereas approximately 66% occurred between PACU admission and hospital discharge.

Conclusions: Case patients with unusually long length of hospital stay (LOS outliers) received higher opioid doses and experienced more opioid-related ADEs than controls. These factors appear to contribute to outlier status but cannot completely explain all LOS outliers.

Key Words—adverse drug effect, length of stay, opioids, pain control, postsurgical pain, total abdominal hysterectomy

Hosp Pharm—*2012;47(11):855–862*

Numerous published studies have evaluated various factors that contribute to increased hospital length of stay (LOS) and associated costs in surgical patients. Of these assessed factors, opioids have long been recognized as a factor in pre- and postsurgical complications and patient management, due in large part to their extensive use to effectively manage moderate to severe postsurgical pain. The multisystems adverse event profile of opioids generally includes central nervous system (CNS) effects (eg, sedation, euphoria, delirium), gastrointestinal (GI) effects (eg, constipation, ileus, nausea/vomiting), pruritus, urinary retention, and respiratory depression.[1] These adverse drug effects (ADEs) can produce postoperative complications in any individual patient, resulting in the need for more intensive monitoring and thus a longer, more complicated, and more costly hospital course. A strong body of evidence establishes an association between intra- and postoperative opioid use and increased LOS.

*RJM Group, LLC, Crown Point, Indiana; †van Breda Research, Bozeman, Montana; ‡Saint Barnabus Health Care System, South Plainfield, New Jersey. Corresponding author: John Reitan, PharmD, RJM Group, LLC, 768 Savannah Drive, Crown Point, IN 46307; phone: 219-662-9110; fax: 219-663-1970; e-mail: john@rjmgroupllc.com

The incidence of opioid-related ADEs varies in frequency and severity. Certain complications, such as respiratory depression, delirium, and postoperative ileus (POI), are strongly associated with increased LOS.[2,3] POI, a predictable delay in GI motility that occurs after abdominal surgery and is exacerbated by opioids, is associated with a greater incidence of postsurgical morbidity and is considered a common reason for increased LOS or readmission.[4-6]

Independent, patient-specific risk factors that contribute to extended LOS include sleep apnea, malignancy, age greater than 65 years, urgent hospital admission, presence of diabetes mellitus, and diagnostic codes suggesting respiratory, gastrointestinal, and genitourinary ADEs and inadequate pain control.[3] One study of cost outliers (subgroup of patients who utilize a disproportionate amount of resources) among persons undergoing gastric bypass demonstrated that comorbidities (especially diabetes, sleep apnea, and degenerative joint disease) were associated with increased hospital costs and LOS.[7] Use of intra- and postoperative opioids may exacerbate these predisposing risk factors, predictably leading to an increased LOS. As such, identification of comorbidities that place patients at a greater risk of experiencing an opioid-related adverse event can guide clinicians to utilize an opioid-sparing regimen in these patients, helping to better ensure positive outcomes while controlling hospital costs.

The current study describes a retrospective medical record review, case-control study that was conducted to determine the occurrence of and cause(s) of cost outliers in a group of patients undergoing total abdominal hysterectomy (TAH) in a large health system of acute care hospitals. Because opioid use is common in patients undergoing TAH, the primary objective of this study was to assess the relationship between opioid burden, related ADEs, and extended LOS as well as acute care costs.

METHODS

An electronic database from a large, 6-site acute care health system was queried to identify all patients undergoing a TAH procedure (*ICD-9* 68.49) during a 4-year period (January 1, 2007 to December 31, 2010). Patients who met the pre-established criteria as an outlier for TAH (defined by longest LOS [≥5 days]) were identified. LOS was determined by standard criteria accepted by the health care industry and payers and did not include any time in the emergency department (ED) for the covered hospital stay. Patients who met the eligibility criteria were assigned case numbers. The patient with the longest LOS was identified as case 1, the second longest as case 2, and so on. Similarly, a second cohort of 97 control patients (LOS <5 days) was randomly selected from the remaining (nonoutlier) population of TAH patients and was "matched" with the case group based on predetermined criteria (see below) to allow a comparion between groups that were as similar as reasonably possible. A record review of the 97 cases and 97 matched controls was conducted and compared to identify specific contributing factors to outlier status.

Patient Selection

Female patients aged 18 to 80 years were included if they underwent a TAH (*ICD-9* 68.49) performed between January 1, 2007 through December 31, 2010. Patients were excluded if they had procedures other than TAH; underwent laparoscopic, radical, or other hysterectomy; had any evidence of genitourinary cancer (eg, ovarian, cervical, uterine); or underwent procedures prior to January 1, 2007 or after December 31, 2010.

Matching Cases With Controls

Cases were matched with similar control patients within the remaining TAH (*ICD-9* 68.49) patients using the following criteria:

1. Age: "younger" (>18 to 49 years) or "older" (>49 to 80 years)
2. Diabetes mellitus: presence or absence
3. Urgency of admission: elective versus urgent or emergency

After the 97 matched pairs of cases and controls were identified, medical records for the included cases and controls were reviewed by clinical chart reviewers/data collectors who were specifically trained on the protocol. Data were collected and recorded using the approved case report form designed for this study.

Data Elements

Medical records of the matched pairs were examined and reviewed for the following data points:

1. Patient demographics (eg, age, body mass index [BMI] status)
2. Insurance type
3. Admission type (ie, emergency, urgent, elective)
4. Duration of surgical procedure
5. LOS (time of admission to discharge, excluding any time in the ED)
6. Total patient charges
7. Opioid use
8. Drug

9. Dose
10. Route of administration
11. Preoperative (during admission), intraoperative, or postoperative (during admission) use
12. Number of doses during admission
13. Total dosage for entire admission
14. Pain scores (when available) with date obtained
15. Opioid ADEs
    a. Respiratory effects
    b. Gastrointestinal effects
    c. Central nervous system effects
    d. Indicators of inadequate pain control
    e. Other possible adverse effects

Data were identified and entered into the study case report form when any of the above terms relative to opioid ADEs appeared in the patient chart, either as a quantitative data point or qualitative term entered into the notes section of the chart by the health care team managing the patient pre-, intra-, and postoperatively from admission to discharge.

Data Collection and Analysis

Demographic data elements were collected and recorded in the patient's medical record. Recorded ADEs were grouped into the following categories: respiratory effects (apnea, which included insomnia, sleep disturbance, and hypersomnia), bradypnea, pulmonary insufficiency following surgery and trauma, respiratory complications and hypoxia, gastrointestinal effects (constipation/postoperative ileus, dry mouth, nausea/vomiting, stomatitis), central nervous system effects (nervousness, delirium, confusion, altered mental status, dizziness/vertigo/accidental fall), genitourinary effects (urinary retention/oliguria, nephropathy), other possible adverse effects (hypotension, postoperative bradycardia, rash/itching, opioid dependency), and indicators of inadequate pain control (hypertension, tachycardia, agitation).

Opioid use was assessed by recording all doses indicated in the surgical record and the medication administration record (MAR). (By law, all doses of controlled substances must be recorded in the surgical record and MAR, regardless of drug or method of administration.) Quantification of total opioid "load" was determined as follows. Total opioid dosage was first calculated summating all doses recorded in the administration records and, depending on the agent and using standard equi-dosage calculators, converted to the equivalent dosage of intravenous (IV) morphine sulfate. The "total opioid burden" was then calculated for the case and control groups for comparison. Opioid use prior to hospital admission, even when recorded, was not included in data collection. Opioid ADEs were recorded exactly as written in each patient's medical record.

Financial Analysis

During the record review portion of the evaluation, electronic patient billing records for each patient were analyzed to determine primary cost contributors for patients in each group. Assessed charges represent what was actually billed to the patient or insurance company.

Patient-billed amounts were compared between the 2 groups to determine significance of any of the cost contributors. This analysis included a review of charges by type and quantity, as well as an evaluation of payer mix and differences based on payer mix. Total admission costs were determined by the total billing for that admission in the billing database.

Statistical Methods

Baseline characteristics measured on an interval scale (eg, BMI) were compared using the paired *t* test, whereas those measured on categorical scales (eg, race) were compared using McNemar's test for matched pairs. For risk factors defined on categorical scales (eg, presence of nausea), the difference between cases and controls for incidence of possible opioid-related ADEs was compared using McNemar's test for matched pairs. For risk factors defined on interval scales (eg, duration of surgery), different scores were calculated by subtracting the value for each control from the matched case. Differences in hospital charges and payments were tested for statistical significance using the paired *t* test as the resulting difference score was normally distributed. Because equi-analgesic opioid units (opioid burden) were not normally distributed (as determined by Kolmogorov D), comparisons were made using the signed rank test.

RESULTS

A total of 3,654 patients met the study entry criteria. Of these, 2,241 patients were treated at the 2 largest sites within the 6-site acute care health care system. Due to the availability of electronic medical records and to minimize variability across sites, only these patients (case outliers and controls) were included in the study.

Baseline demographics (**Table 1**) were similar in the case outliers and control groups, with the exception of private insurance, which was more prevalent

Table 1. Baseline characteristics of outliers and controls

	Outliers n = 97	Controls n = 97	
	Mean (*SD*)	Mean (*SD*)	*P*
Age, years	49.6 (10.2)	48.7 (7.8)	.64[a]
Height, m	1.6 (0.1)	1.6 (0.1)	.59[a]
Weight, kg	82.9 (23.6)	78.6 (16.8)	.15[a]
Body mass index (kg/m^2)	31.2 (8.6)	29.7 (6.1)	.15[a]
	n (%)	n (%)	*P*
White race	58 (60%)	60 (62%)	.76[b]
Diabetes	13 (13%)	10 (10%)	.26[b]
Private insurance	73 (75%)	94 (97%)	<.01[b]

[a]Paired *t* test.
[b]McNemar's test for matched pairs.

in the control (97%) versus the case outlier (75%) group ($P < .01$).

With respect to time parameters outlined in **Table 2**, the outlier group (vs control group) had longer LOS; it was 3 times longer than the control group (191.6 vs 60.1 hours; $P < .01$). The outlier group also had greater time in hospital prior to operating room (OR) admission (44.7 vs 3.4 hours; $P < .01$) and prolonged time from postanesthesia care unit (PACU) to hospital discharge (142.0 vs 51.4 hours). No difference in OR or PACU time was noted between the outlier and control groups.

With regard to opioid-related outcomes (**Table 3** and **4**), the outlier group had a markedly higher incidence of gastrointestinal ADEs (44% vs 19%; $P < .01$) and respiratory ADEs (12% vs 1%; $P < .01$) compared with the control group. Inadequate pain control was reported in 12% of cases versus 6% of controls ($P = .16$). Overall, the outlier group received twice the amount of opioids, expressed in terms of IV morphine, compared with the control group. The difference in total opioid use occurred prior to the OR and following discharge from the PACU. When comparing opioid burden prior to going to the OR, only 16 of 97 controls received any opioid as compared to 40 of 97 outliers ($P < .01$). When all patients admitted from the ED were eliminated, the trends for greater time prior to entry into OR and time after OR, as well as total opioid use and opioid ADEs, were the same, indicating that emergency admission did not have an impact on the results. As noted in **Table 5**, the outlier group (vs control group) had higher total charges ($14,289 vs $5,745), direct charges ($9,385 vs $3,854), and total payments ($14,379 vs $5,684).

DISCUSSION AND CONCLUSION

Analysis of LOS and cost outliers relating to opioid use and the efforts to eliminate or manage factors that prolong hospitalization represent an important approach to improving the overall quality and efficiency of care among surgical patents. To better understand factors contributing to increased resource

Table 2. Entire length of hospital stay segments for outliers and controls

	Outliers		Controls		
	n	Mean (*SD*)	n	Mean (*SD*)	*P*
Time from admission to OR, hours	96	44.7 (67.6)	96	3.4 (3.1)	<.01[a]
OR time, hours	95	2.4 (1.0)	96	2.3 (0.8)	.28[a]
PACU time, hours	93	2.9 (2.1)	96	3.1 (1.8)	.11[a]
PACU to hospital discharge, hours	93	142.0 (77.0)	96	51.4 (12.4)	<.01[a]
Entire length of stay, hours	97	191.6 (88.4)	97	60.1 (12.4)	<.01[a]

Note: OR = operating room; PACU = postanesthesia care unit.
[a]Paired *t* test.

Table 3. Proportion of outliers and controls identified to experience an adverse effect by adverse effect category and number of adverse effects identified

Adverse effect	Outliers (n=97)	Controls (n=97)	
	n[a] (%)	n[a] (%)	*P*[b]
Respiratory effects	12 (12)	1 (1)	<.01
Pulmonary insufficiency	3	0	
Respiratory complications	5	0	
Hypoxia	6	1	
Gastrointestinal effects	43 (44)	18 (19)	<0.01
Constipation/postoperative ileus	26	2	
Nausea/vomiting	35	19	
Central nervous system effects	5 (5)	3 (3)	0.48
Nervousness	3	1	
Altered mental status	3	1	
Dizziness/vertigo/accidental fall	2	3	
Genitourinary effects	3 (3)	4 (4)	0.71
Urinary retention/oliguria	3	3	
Nephropathy	0	1	
Other possible adverse effects	11 (11)	11 (11)	1.00
Hypotension	4	1	
Postoperative bradycardia	1	0	
Rash/itching	7	11	
Indicators of inadequate pain control	12 (12)	6 (6)	0.16
Hypertension	4	3	
Tachycardia	8	5	
Agitation	4	2	

[a]Indicates number of effects, not number of patients.
[b]McNemar's test for matched pairs.

utilization in postsurgical patients, we examined the degree to which opioid burden and related ADEs were responsible for unusually long LOS and charges among patients undergoing TAH in an acute care health system.

In this group of TAH patients, those who were LOS outliers were found to have more complicated admissions based on an extended time in the hospital prior to surgery. In addition, time from admission to surgery was longer in the outlier patients compared with controls. This may indicate that the outliers, at baseline, presented with more complications and were potentially sicker than control patients prior to TAH surgery. Overall, the outlier patient group was found to have increased usage of opioid drugs prior to surgery and after PACU and yet was also more likely to have indicators of inadequate pain control, which may also have contributed to the extended LOS. This finding is most likely related to the fact that, as previously noted, outlier patients had more complicated admissions compared with the matched controls. In addition, the opioid burden (expressed as total mgs morphine sulfate administered during hospitalization) in outlier patients was higher in the 72 hour period post discharge from the PACU. It is therefore not surprising that outlier patients also experienced a higher incidence of opioid-related respiratory and gastrointestinal ADEs. It is clear that as a result of these and other opioid-related complications, use of these analgesics may contribute to longer LOS and higher charges in patients undergoing TAH. As a result, patients in the outlier group (vs control group) had almost a 3-fold increase in hospital charges.

In the current study, the accuracy of the medication administration records, as enforced by control substances regulations, ensured accurate quantification of

Table 4. Administration of opioids[a] to outliers and controls by hospital stay

Hospital stay	Outliers n = 97	Controls n = 97	
	Median (Q1-Q3)	Median (Q1-Q3)	*P*
Full length of stay	9.0 (6.8-12.3)	6.3 (4.4-9.0)	<.01[b]
Prior to operating room	0.0 (0.0-0.8)	0.0 (0.0-0.0)	<.01[b]
In operating room	2.0 (1.0-3.5)	2.0 (1.0-2.5)	.07[b]
In PACU	1.3 (0.7-2.0)	1.2 (0.7-2.0)	.87[b]
72 hours post PACU	4.0 (2.3-7.0)	2.7 (1.3-5.3)	.04[b]
More than 72 hours post PACU	0.0 (0.0-0.7)	0.0 (0.0-0.0)	<.01[b]

Note: PACU = postanesthesia care unit.
[a]Opioids quantified in terms of mgs of intravenous morphine sulfate (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1163279).
[b]Signed rank test.

the opioid load and thus contributed to the reliability of outcomes data. The data presented here are consistent with other reports in the published literature. One study examined the impact of opioid-related ADEs on total hospital costs and LOS and demonstrated that surgical patients experiencing opioid-related ADEs had significantly increased median total hospital costs (7.4% increase; $P < .001$) and increased median LOS (10.3% increase; $P < .001$) compared with matched non-ADE controls.[1] The increased costs attributable to ADEs, by surgery type, were orthopedics ($861.50), general surgery ($676.51), and obstetrics/gynecology ($540.90). Similarly, increased LOS attributable to ADEs, by surgery type, included general surgery (0.64 days), orthopedics (0.52 days), and obstetrics/gynecology (0.53 days). Higher doses of opioids were associated with increased risk of experiencing ADEs.[2] A similar study of more than 60,000 patients receiving opioids during surgical hospitalization also found that patients who experienced opioid-related ADEs (the most common being nausea/vomiting, rash, hives, itching) had statistically significant increases in LOS (0.53 days; $P < .01$) and total hospital costs (16%; $P < .001$).[3] An analysis of a large national database revealed that patients with coded POI experienced an increase in LOS (an additional 6 days) and higher health care costs (an additional $9,417) per hospital stay compared with patients without coded POI.[6] Postoperative delirium, considered one of the most common postsurgical complications in older patients, is also associated with increased morbidity and LOS, as well as increased mortality and likelihood of nursing home placement.[8] Similarly, an analysis of cost outliers was conducted in an institution that used a clinical pathway for gastric bypass surgery.[9] The data revealed that despite use of the clinical pathway, 16% of patients in the study were cost outliers and that the factors associated with increased hospital costs included severe medical comorbidities, notably diabetes and sleep apnea and the occurrence of major postoperative complications.

In a previously published study of 4,108 admissions to a stratified random sample of 11 medical and surgical units in 2 tertiary care hospitals over a 6-month period, investigators found that 29% of preventable ADEs were associated with analgesics (the most common of which was morphine), which were associated with an increase in LOS and costs.[10] For preventable ADEs, the increases were 4.6 days in LOS, with annual costs (in pre-1997 dollars) attributable to all ADEs and preventable ADEs totaling

Table 5. Hospital charges, costs, and reimbursements for outliers and controls

	Outliers (n = 97)	Controls (n = 97)	
	Mean (*SD*)	Mean (*SD*)	*P*
Total charges	14,289 (6,729)	5,745 (1,502)	<.01[a]
Direct costs	9,385 (4,730)	3,854 (1,048)	<.01[a]
Total payments	14,379 (7,991)	5,684 (2,842)	<.01[a]

[a]Paired *t* test.

$5.6 million and $2.8 million, respectively.[10] Although this study was published more than 15 years ago, studies conducted since then, including the findings in the current study, indicate that opioid-related ADEs continue to have substantial impact on patient outcomes and health care costs.

As previously noted, studies have been conducted that demonstrate that opioids are associated with extended LOS.[2,3] Researchers in one study, using methodologies similar to these reported here (ie, retrospective matched case cohort study using data from computerized medical records with primary outcomes of costs and hospital LOS associated with opioid-related ADEs), reported that patients with ADEs related to opioids had increased median total hospital costs (7.4% increase; 95% CI, 3.83 to 10.96; $P < .001$) and increased median LOS (10.3% increase; 95% CI, 6.5 to 14.2; $P < .001$) compared with matched non-ADE controls.[2] For patients undergoing obstetrical/gynecological surgeries, the increased cost attributable to opioid-related ADEs was $540.90 (95% CI, 281.40 to 800.40) and increased LOS attributable was 0.53 days (95% CI, 0.33 to 0.72). In addition, a critically important finding of this study was that opioid-related ADEs following surgery occurred more frequently in patients who received higher dose of opioids. Yet another study examining costs associated with opioid-related errors involving patient-controlled analgesia found the most costly cause of error to be related to opioid ADEs ($13,803), where harmful events were approximately 250 times more costly than nonharmful events ($6,943 vs $28).[11] Although this particular study focused on medication errors, the findings here reaffirm the association between opioid-related ADEs and increased costs. From these data and the data from the current study, it is found that opioid use contributes to higher rates of complications and increased LOS in surgical patients undergoing hospitalization. Hospital pharmacy programs that involve clinical pharmacist interventions focused on implementation of opioid protocols as well as incorporation of alternative pain management strategies, such as use of regional anesthesia,[12] and other therapies such as nonsteroidal anti-inflammatories could be beneficial in optimizing opioid use in the hospital setting. Our findings are consistent with the above mentioned studies but appear different due to our study design. We identified all patients with long LOS ($\geq$5 days) and compared them with patients with normal LOS in an attempt to identify factors that may have impacted the LOS. Among other factors, we found that gastrointestinal and respiratory adverse events were significantly more common in patients with long LOS.

Although the current study provides important clinical insights regarding the impact of opioid use on LOS and costs in patients undergoing TAH, several limitations should be considered. First, with the exception of BMI (which may be used to indicate potential obesity) and diabetes, data on other comorbidities (eg, sleep apnea, age-related illnesses such as osteoporosis and osteoarthritis) that may impact opioid-related outcomes were not captured. Surgical technique and the skill of the surgeon, which may have impacted predisposition to opioid-related ADEs, LOS, and costs, were also not captured or quantified. In addition, because this was a retrospective chart review study, the specific factors that affected the early admissions rate in the study group versus the control group could not be determined.

It interesting to note that subset data analysis eliminating all patients admitted from the ER revealed that the trends for greater time prior to entry into OR and time after OR, as well as total opioid use and opioid ADEs, were the same. This could be related to factors that were outside of the study scope, such as in-depth analysis of baseline illness in the ED patients, impact of comorbidities or nosocomial events, overall complication rate post-TAH, or impact of scheduled versus nonscheduled surgery on patient outcomes. Other limitations of the current study include the findings that data recorded into the patient chart varied in both quality and quantity. As such, data such as time to first bowel movement after leaving PACU or patient pain scores were frequently not available for assessment. In addition, time from admission to the OR was greater among the outliers. This may have been because these patients were sicker, had more underlying complications, or were at risk for complications. Again, however, the data to allow determination of the reasons were not available in most of the patient charts, and so no conclusion can be made from the current study. Last, due to personnel resource limitations for data collection, we were unable to cross-check data collection to validate the accuracy of the data. Further investigation, in the form of prospective studies, examining intra- and postoperative opioid use in a larger patient population with various comorbidities is needed to further establish the impact of opioids on patient outcomes and costs in the surgical setting.

In conclusion, this retrospective chart review of TAH patients treated in a large acute care health system demonstrated that outlier patients had more complicated admissions and increased usage of opioid

drugs prior to surgery and after PACU. The data from this study found a substantial relationship between LOS, time to OR, and time from PACU to discharge and opioid burden in these patients, indicating that opioid burden is a driver of overall LOS as well as postsurgical course. In addition, outlier patients experienced a higher incidence of opioid-related respiratory and gastrointestinal ADEs and had almost a 3-fold increase in charges.

ACKNOWLEDGMENTS

The authors thank Marissa Seligman, PharmD, and R. Jake Jacobs for their editorial assistance.

REFERENCES

1. Davies EC, Green CF, Taylor S, et al. Adverse drug reactions in hospital in-patients: a prospective analysis of 3695 patient-episodes. *PLoS ONE*. 2009;4(2):e4439.

2. Oderda G, Said Q, Evans R, et al. Opioid-related adverse drug events in surgical hospitalizations: impact on costs and length of stay. *Ann Pharmacother*. 2007;41:400-407.

3. Oderda G, Evans S, Lloyd J, et al. Cost of opioid-related adverse drug events in surgical patients. *J Pain Sympt Manage*. 2003;25(3):276-283.

4. Chang SS, Baumgartner RG, Wells N, et al. Causes of increased hospital stay after radical cystectomy in a clinical pathway setting. *J Urol*. 2002;167(1):208-211.

5. Kariv Y, Wang W, Senagore AJ, et al. Multivariable analysis of factors associated with hospital readmission after intestinal surgery. *Am J Surg*. 2006;191(3):364-371.

6. Delaney CP, Senagore AJ, Viscusi ER, et al. Postoperative upper and lower gastrointestinal recovery and gastrointestinal morbidity in patients undergoing bowel resection: pooled analysis of placebo data from 3 randomized controlled trials. *Am J Surg*. 2006;191(3):315-319.

7. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. *Am J Surg*. 2002;183(6):630-641.

8. Jankowski CJ. Delirium and postoperative cognitive dysfunction in geriatric anesthesia. In: Sieber FE, ed. *Geriatric Anesthesia*. New York: McGraw-Hill; 2007:267-279.

9. Cooney ER, Haluck R, Ku J, et al. Analysis of cost outliers after gastric bypass surgery: What can we learn? *Obesity Surg*. 2003;13:29-36.

10. Bates DW, Spell N, Cullen DJ, et al. The cost of adverse drug events in hospitalized patients. *JAMA*. 1997;277:307-311.

11. Meissner B, Nelson W, Hicks R, et al. The rate and costs attributable to intravenous patient-controlled analgesia errors. *Hosp Pharm*. 2009;44:312-324.

12. Viscusi ER, Jan R, Schechter L, Lenart S, Willoughby PH. Organization of an acute pain management service incorporating regional anesthesia techniques. http://www.nysora.com/pain_management/3055-organization_acute_pain_management.html. Posted December 3, 2009. Accessed September 11, 2012. ■