

# Changes in analgesic strategies for lobectomy from 2009 to 2018

Theresa Lo, MD,<sup>a,b</sup> Robin Schiller, MD, DMD,<sup>a,c</sup> Karthik Raghunathan, MBBS, MPH,<sup>a,d</sup> Vijay Krishnamoorthy, MD, MPH, PhD,<sup>a,b</sup> Oliver K. Jawitz, MD, MHS,<sup>e</sup> Srinivas Pyati, MD, FCARCSI,<sup>a,d</sup> Thomas Van De Ven, MD, PhD,<sup>a,d</sup> Raquel R. Bartz, MD,<sup>a,b</sup> Annemarie Thompson, MD,<sup>a,c</sup> and Tetsu Ohnuma, MD, MPH, PhD<sup>a,b</sup>

## ABSTRACT

**Objective:** To evaluate trends in the use of epidural analgesia and nonopioid and opioid analgesics for patients undergoing lobectomy from 2009 to 2018.

**Methods:** We queried the Premier database for adult patients undergoing open, video-assisted, and robotic-assisted lobectomy from 2009 to 2018. The outcome of interest was changes in the receipt of epidural analgesia and nonopioid and opioid analgesics as measured by charges on the day of surgery. We also evaluated postoperative daily opioid use. We used multivariable logistic and linear regression models to examine the association between the utilization of each analgesic modality and year.

**Results:** We identified 86,308 patients undergoing lobectomy from 2009 to 2018 within the Premier database: 35,818 (41.5%) patients had open lobectomy, 35,951 (41.7%) patients had video-assisted lobectomy, and 14,539 (16.8%) patients had robotic-assisted lobectomy. For all 3 surgical cohorts, epidural analgesia use decreased, and nonopioid analgesics use increased over time, except for intravenous nonsteroidal anti-inflammatory drugs. Use of patient-controlled analgesia decreased, while opioid consumption on the day of surgery increased and postoperative opioid consumption did not decrease over time.

**Conclusions:** In this large sample of patients undergoing lobectomy, utilization of epidural analgesia declined and use of nonopioid analgesics increased. Despite these changes, opioid consumption on day of surgery increased, and there was no significant reduction in postoperative opioid consumption. Further research is warranted to examine the association of these changes with patient outcomes. (JTCVS Open 2021; ■:1-13)

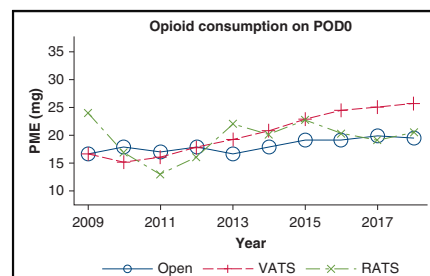
Thoracic surgery is one of the most painful surgeries a patient may experience.<sup>1</sup> Following limb amputation, thoracic surgery represents the greatest incidence of persistent post-surgical pain, which presents in 20% to 70% of patients and can last for years.<sup>2</sup> Inadequate pain control can exacerbate pulmonary complications by worsening lung restriction, decreasing ventilation, reducing clearance of secretions,

and increasing atelectasis in the perioperative period.<sup>1</sup> Poorly controlled postoperative thoracic pain may also lead to the development of chronic pain.<sup>3</sup> Since pain is a major modifiable factor affecting patients' perioperative morbidity and mortality following thoracic surgery,<sup>4</sup> this provides an opportunity for the health care team to optimize patient outcomes with a strategic pain management plan.

From the <sup>a</sup>Critical Care and Perioperative Population Health Research (CAPER) Unit, <sup>b</sup>Division of Critical Care Medicine, <sup>c</sup>Division of Cardiothoracic Anesthesiology, and <sup>d</sup>Division of Veterans Affairs Anesthesiology, Department of Anesthesiology, and <sup>e</sup>Division of Cardiovascular and Thoracic Surgery, Department of Surgery, Duke University Medical Center, Durham, NC.

Financial support from the CAPER Unit, Department of Anesthesiology, Duke University School of Medicine.

Received for publication March 19, 2021; accepted for publication March 19, 2021.



Opioid consumption on day of surgery increased from 2009 to 2018.

## CENTRAL MESSAGE

For lobectomies, epidural use declined over time, whereas nonopioid analgesic use increased and postoperative opioid use did not decrease.

## PERSPECTIVE

We queried the Premier database for adult patients undergoing open, video-assisted, and robotic-assisted lobectomy from 2009 to 2018. We found that epidural use declined over time and nonopioid analgesics use increased. Despite these changes, opioid consumption on day of surgery increased, and there was no significant reduction in postoperative opioid consumption.

See Commentary on page XXX.

Address for reprints: Tetsu Ohnuma, MD, MPH, PhD, Department of Anesthesiology, Duke University, DUMC 3094, Durham, NC 27710 (E-mail: [tetsu.ohnuma@duke.edu](mailto:tetsu.ohnuma@duke.edu)).

2666-2736

Copyright © 2021 The Author(s). Published by Elsevier Inc. on behalf of The American Association for Thoracic Surgery. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.xjon.2021.03.015>

### Abbreviations and Acronyms

COX-2	= cyclooxygenase-2
FDA	= Food and Drug Administration
ICD	= <i>International Classification of Diseases</i>
IV	= intravenous
NSAID	= nonsteroidal anti-inflammatory drug
PCA	= patient-controlled analgesia
PME	= parental morphine equivalent
PO	= per os, oral
POD	= postoperative day
RATS	= robotic-assisted thoracoscopic surgery
VATS	= video-assisted thoracoscopic surgery

There are many ways to manage postoperative pain in thoracic surgery. Thoracic epidural analgesia was considered the optimal approach for acute postoperative pain management, particularly in thoracotomy.<sup>2,4</sup> However, placement of a thoracic epidural catheter may be technically challenging or contraindicated in some patients and is not without side effects and risks.<sup>5</sup> Minimizing opioid consumption is also important to maintain adequate respiratory drive and avoid excess sedation to allow early mobilization. Given these challenges, multimodal analgesia and other regional analgesic techniques such as paravertebral blocks, intercostal nerve blocks, and intrapleural catheters have been used.<sup>6</sup> A multimodal anesthetic employs the synergistic effects of more than one analgesic compound or modality of pain control while limiting the use of opioids and reducing adverse events.<sup>2</sup> For thoracic surgery, there is currently no multicenter study that characterizes the recent usage in neuraxial techniques and multimodal analgesia in the United States. The objective of this study was to depict changes over time in the usage of epidural analgesia and nonopioid analgesics and to examine whether there was any change in opioid administration for open, video-assisted, and robotic-assisted lobectomy. We hypothesized that epidural analgesia could have a decreased trend whereas other nonopioid analgesics could have increased trends, with a decreased trend in opioid consumption.

## PATIENTS AND METHODS

### Study Design and Cohort

We conducted a retrospective observational study using the Premier Healthcare database (Premier Inc, Charlotte, NC), which contains data from approximately 20% of the annual inpatient admissions in teaching and nonteaching hospitals in rural and urban areas across the United States. This database comprises discharge-level information on patient demographics, *International Classification of Diseases (ICD), Ninth Revision, Clinical Modification* and *ICD, Tenth Revision, Clinical Modification*, diagnosis and procedure codes, costs, and hospital and provider characteristics. All billable items for therapeutic and diagnostic procedures, medication, and laboratory usage are captured as date-stamped records. This study was approved by the Duke University

Healthcare System institutional review board (Pro00101731, December 19, 2019) and was exempt from requirements for informed patient consent, as all patient data were fully deidentified.

### Study Population

Adult patients included in the study underwent elective open, video-assisted thoracoscopic surgery (VATS), or robotic-assisted thoracoscopic surgery (RATS) from 2009 to 2018. We used ICD, *Ninth Revision, Clinical Modification*, and ICD, *Tenth Revision, Clinical Modification*, procedure codes to identify the procedures and distinguish between open, VATS, and RATS lobectomies (Table E1). Patients who had ICD codes for conversions from thoracoscopic to open thoracotomy were classified as open thoracotomy (Table E1). We applied the following exclusion criteria: (1) absent charge codes for opioid prescription on the day of surgery ( $n = 6886$  or 7.7%), indicating likely missing data or extreme cases; or (2) opioid doses greater than the 99th percentile ( $n = 871$  or 0.98%), indicating extreme outliers.

### Study Variables

The outcome of interest was changes in the receipt of epidural analgesia, nonopioid, and opioid analgesics as measured by charges on the day of surgery. The following analgesics were identified using billing information: patient-controlled analgesia (PCA), acetaminophen (intravenous [IV] or oral [per os, PO]), opioid/acetaminophen combination products (eg, codeine/acetaminophen, hydrocodone/acetaminophen, or oxycodone/acetaminophen), nonsteroidal anti-inflammatory drugs (NSAIDs, intravenous or oral), cyclooxygenase-2 (COX-2) inhibitors, ketamine, liposomal bupivacaine, dexmedetomidine, gabapentinoids, dexamethasone, and total opioid consumption on the day of surgery. We also examined opioid consumption on postoperative day (POD) 1, 2, and 3. Opioid doses were converted to parenteral morphine equivalents (PMEs) using dose conversion formulae.<sup>7</sup>

### Covariates

Patient demographic characteristics include age, sex, race (White, African American, other), payer category (managed care organization, Medicaid, Medicare, other), and the Elixhauser Comorbidity Index,<sup>8</sup> which were entered into models as binary variables. Hospital characteristics included hospital bed size (<100, 100-199, 200-299, 300-399, 400-499, and  $\geq 500$ ), hospital teaching status, and hospital location (rural or urban).

### Statistical Analysis

We used descriptive statistics to present the baseline demographic information, with counts (and proportion) for categorical variables and means (and standard deviation) for continuous variables. We applied multivariable logistic regression models to examine the use of each analgesic modality as the dependent variable by year, adjusting for all covariates described above. Opioid consumption on the day of surgery and POD 1, 2, and 3 by each year was modeled using multivariable linear regression models adjusting for all covariates described above. Fiscal year was included in the different models as categorical and continuous variables separately to calculate predicted estimates each year and evaluate linear trends. We performed all data analyses using SAS, version 9.4 (SAS Institute, Cary, NC). All analyses used 2-sided statistical tests.

## RESULTS

We identified 86,308 patients undergoing lobectomy from 2009 to 2018 in 607 hospitals within the Premier database. Of these, a total of 35,818 (41.5%) patients underwent open lobectomy, 35,951 (41.7%) patients received VATS lobectomy, and 14,539 (16.8%) patients had RATS

TABLE 1. Patient baseline characteristics and comorbidities and hospital-related characteristics

	Open lobectomy (n = 35,818)	VATS lobectomy (n = 35,951)	RATS lobectomy (n = 14,539)
Age, y, mean $\pm$ SD	65.6 $\pm$ 11.8	64.9 $\pm$ 12.8	65.2 $\pm$ 12
Male, n (%)	17,896 (50)	16,311 (45.4)	6695 (46)
Race, n (%)			
African American	2655 (7.4)	2843 (7.9)	1133 (7.8)
White	29,101 (81.2)	29,760 (82.8)	11,506 (79.1)
Other	4062 (11.3)	3348 (9.3)	1900 (13.1)
Payor, n (%)			
Managed care organization	7861 (21.9)	8638 (24)	3871 (26.6)
Medicaid	2421 (6.8)	2517 (7)	985 (6.8)
Medicare	22,129 (61.8)	21,239 (59.1)	8421 (57.9)
Other	3407 (9.5)	3557 (9.9)	1262 (8.7)
Comorbidity			
Congestive heart failure	1596 (4.5)	1399 (3.9)	624 (4.3)
Valvular disease	1298 (3.6)	1212 (3.4)	617 (4.2)
Pulmonary circulation disease	420 (1.2)	218 (0.6)	189 (1.3)
Peripheral vascular disease	3203 (8.9)	2442 (6.8)	972 (6.7)
Paralysis	55 (0.2)	48 (0.1)	21 (0.1)
Other neurologic disorders	1402 (3.9)	1284 (3.6)	460 (3.2)
Chronic pulmonary disease	18,143 (50.7)	15,445 (43)	5742 (39.5)
Diabetes without chronic complications	6115 (17.1)	5544 (15.4)	2409 (16.6)
Diabetes with chronic complications	1293 (3.6)	1461 (4.1)	611 (4.2)
Hypothyroidism	4287 (12)	4424 (12.3)	1784 (12.3)
Renal failure	2328 (6.5)	2073 (5.8)	888 (6.1)
Liver disease	607 (1.7)	682 (1.9)	250 (1.7)
Peptic ulcer disease excluding bleeding	73 (0.2)	88 (0.2)	21 (0.1)
Acquired immune deficiency syndrome	34 (0.1)	48 (0.1)	25 (0.2)
Lymphoma	296 (0.8)	325 (0.9)	124 (0.9)
Metastatic cancer	5395 (15.1)	3371 (9.4)	1233 (8.5)
Solid tumor without metastasis	4771 (13.3)	4101 (11.4)	1329 (9.1)
Rheumatoid arthritis/collagen vascular disease	1270 (3.5)	1378 (3.8)	489 (3.4)
Coagulopathy	574 (1.6)	520 (1.4)	234 (1.6)
Obesity	4144 (11.6)	4194 (11.7)	1771 (12.2)
Weight loss	1337 (3.7)	810 (2.3)	292 (2)
Fluid and electrolyte disorders	1953 (5.5)	1322 (3.7)	474 (3.3)
Chronic blood loss anemia	122 (0.3)	80 (0.2)	31 (0.2)
Deficiency anemias	3016 (8.4)	2072 (5.8)	943 (6.5)
Alcohol abuse	1043 (2.9)	795 (2.2)	264 (1.8)
Drug abuse	426 (1.2)	352 (1)	157 (1.1)
Psychoses	700 (2)	697 (1.9)	235 (1.6)
Depression	4063 (11.3)	4040 (11.2)	1513 (10.4)
Hypertension	22,491 (62.8)	20,980 (58.4)	8775 (60.4)
Teaching hospital	18,001 (50.3)	21,406 (59.5)	9742 (67)
Rural hospital	3242 (9.1)	2874 (8)	662 (4.6)
Hospital number of beds, n (%)			
0-99	348 (1)	311 (0.9)	1 (0)
100-199	2000 (5.6)	1703 (4.7)	474 (3.3)
200-299	4673 (13)	4016 (11.2)	1379 (9.5)
300-399	6759 (18.9)	5557 (15.5)	2354 (16.2)
400-499	7235 (20.2)	5692 (15.8)	1488 (10.2)
500+	14,803 (41.3)	18,672 (51.9)	8843 (60.8)
Length of stay, d, median, (IQR)	6 (5, 9)	4 (2, 3)	3 (2, 5)

VATS, Video-assisted thoracoscopic surgery; RATS, robotic-assisted thoracoscopic surgery; SD, standard deviation; IQR, interquartile range.

lobectomy. Patient baseline characteristics, comorbidities, and hospital-related characteristics are shown in Table 1. Patient demographics were similar in age, race, and sex. Chronic pulmonary disease was present in 50.6% of the open cohort, 43% of the VATS cohort, and 40% of the RATS cohort. Percentage for metastatic cancer was 15% for open, 9.4% for VATS, and 8.5% for RATS. Fifty percent of open lobectomy, 60% of VATS lobectomy, and 67% of RATS lobectomy were done in teaching hospitals. Average length of stay was 6 days for open lobectomy, 4 days for VATS, and 3 days for RATS.

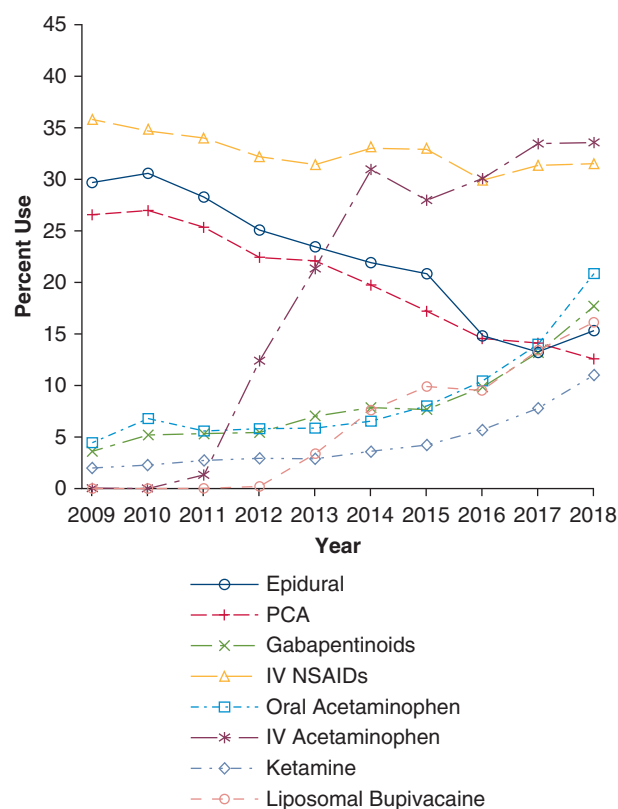
### Open Lobectomy

The predicted probabilities and values of employed analgesic techniques, medications, and opioid consumption by year were estimated using multivariable logistic and linear regression models, as shown in Figures 1 and 2 for open lobectomy. Figure 1 shows a decrease in epidural analgesia use from 30% in 2009 to 15% in 2018 ( $P < .0001$ ), a decrease in PCA use from 27% in 2009 to 13% in 2018 ( $P < .0001$ ), and a decrease in IV NSAIDs use from 36% in 2009 to 21% in 2018 ( $P < .0001$ ) for open lobectomy. The use of IV acetaminophen increased following Food and Drug Administration (FDA) approval in November 2010; by 2018 it was used in 34% of open lobectomy. Use of PO acetaminophen increased after the surge of IV acetaminophen; it went from 4% in 2009 to 21% in 2018. The use of ketamine, liposomal bupivacaine, and gabapentinoids also increased over time for open lobectomy. Figure E1 shows the use of dexmedetomidine, dexamethasone, COX-2 inhibitors, PO NSAIDs, and opioid/acetaminophen combination products increased over time.

Figure 2 shows an increase in total opioid use (expressed in PME) on the day of surgery, which went from 16.5 mg in 2009 to 19.5 mg in 2018 for open lobectomy ( $P < .0001$ ). POD 1 daily opioid use increased from 22 mg in 2009 to 31 mg in 2018 ( $P < .0001$ ). POD 2 daily opioid use decreased from 27 mg in 2009 to 24 mg in 2012 but increased to 32 mg by 2018 ( $P < .0001$ ). POD 3 daily opioid use remained unchanged, ranging from 30 to 33 mg throughout the years ( $P = .73$ ).

### VATS Lobectomy

The predicted probabilities and values of employed analgesic techniques, medications, and opioid consumption by year were estimated using multivariable logistic and linear regression models, as shown in Figures 3 and 4 for VATS lobectomy. Figure 3 depicts a decrease in epidural analgesia use from 15% in 2009 to 5% in 2018 ( $P < .0001$ ). A decrease in PCA and IV NSAIDs and increase in use of IV and PO acetaminophen, ketamine, liposomal bupivacaine, and gabapentinoids were observed. Figure E2 shows use of dexmedetomidine, dexamethasone,



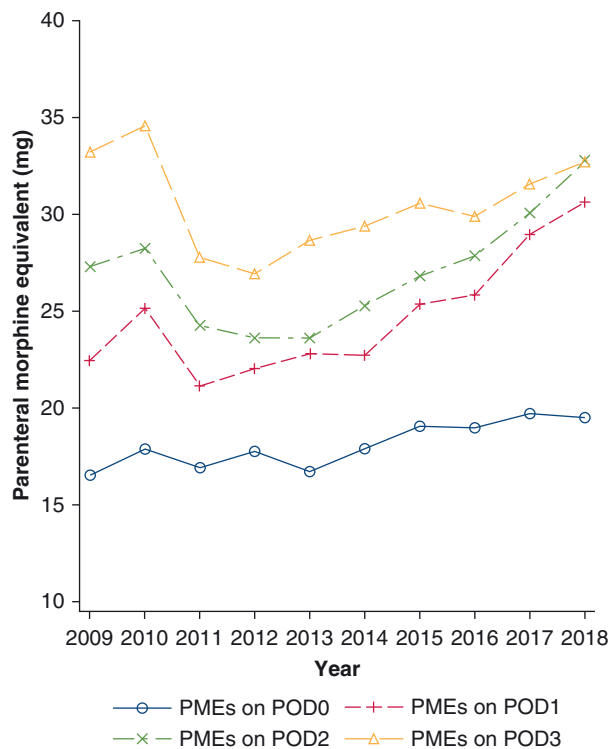
**FIGURE 1.** Trend in nonopioid analgesics for open lobectomy on day of surgery. Plot of predicted probabilities of use in nonopioid analgesics for open lobectomy on day of surgery from 2009 to 2018. Use of epidural, PCA, and IV NSAIDs decreased over time ( $P < .0001$ ). Use of IV and oral acetaminophen, ketamine, gabapentinoids, and liposomal bupivacaine increased over time ( $P < .0001$ ). PCA, Patient-controlled analgesia; IV, intravenous; NSAID, nonsteroidal anti-inflammatory drug.

COX-2 inhibitors, PO NSAIDs, and opioid/acetaminophen combination products increased over time.

Figure 4 exhibits an increase in total opioid use (expressed in PME) on the day of surgery, which went from 17 mg in 2009 to 26 mg in 2018 for VATS lobectomy ( $P < .0001$ ). POD 1 daily opioid use increased from 29 mg in 2009 to 36 mg in 2018 ( $P < .0001$ ). POD 2 daily opioid use decreased from 31 mg in 2009 to 23 mg in 2012 but increased to 35 mg by 2018 ( $P < .0001$ ). POD 3 daily opioid use decreased from 35 mg in 2009 to 24 mg in 2012 but increased to 33 mg in 2018 ( $P = .005$ ).

### RATS Lobectomy

The predicted probabilities and values of employed analgesic techniques, medications, and opioid consumption by year were estimated using multivariable logistic and linear regression models, as shown in Figures 5 and 6 for RATS lobectomy. Figure 5 shows an initial increase in epidural use to 16% in 2012 followed by a decrease to 1.3% in 2018 ( $P < .0001$ ). A decrease in PCA and IV NSAIDs



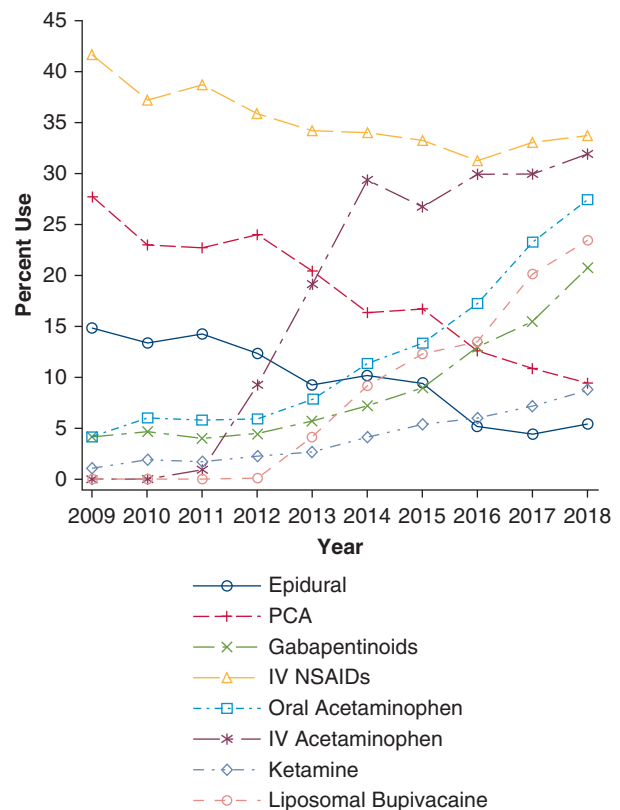
**FIGURE 2.** Trend in opioid consumption for open lobectomy on POD 0, 1, 2, and 3. Plot of predicted probabilities of values in opioid consumption, expressed in PMEs, on day of surgery and POD 1, 2, and 3 for open lobectomy. Total opioid use on day of surgery went from 17 mg in 2009 to 20 mg in 2018 ( $P < .0001$ ). POD 1 opioid use increased from 22 mg in 2009 to 31 mg in 2018 ( $P < .0001$ ). POD 2 opioid use decreased from 27 mg in 2009 to 24 mg in 2012 and then increased to 33 mg in 2018 ( $P < .0001$ ). POD 3 opioid use decreased from 33 mg in 2009 to 27 mg in 2012 and increased back to 33 mg in 2018 ( $P = .73$ ). *POD*, Postoperative day; *PME*, parenteral morphine equivalents.

and an increase in the use of IV and oral acetaminophen, ketamine, liposomal bupivacaine, and gabapentinoids were observed. Figure E3 depicts the increased use of dexmedetomidine, dexamethasone, COX-2 inhibitors, oral NSAIDs, and opioid/acetaminophen combination products from 2009 to 2018.

Figure 6 shows that total opioid use (expressed in PMEs) on day of surgery increased from 24 mg in 2009 to 13 mg in 2011 and then increased to 20 mg in 2018 ( $P < .0001$ ). Opioid consumption on POD 1 decreased from 33 mg in 2009 to 20 mg in 2011, then increased to 31 mg in 2018 ( $P < .0001$ ). POD 2 daily opioid use decreased from 29 mg in 2009 to 21 mg in 2012 but increased to 26 mg in 2018 ( $P = .05$ ). POD 3 daily opioid use decreased from 26 mg in 2009 to 16 mg in 2011 and increased to 25 mg in 2018 ( $P = .21$ ).

## DISCUSSION

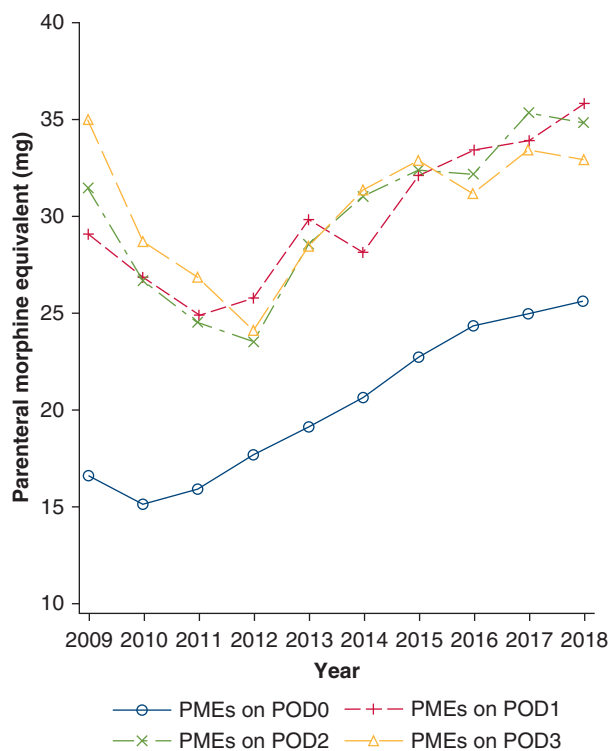
In this study, we examined the use of epidural, nonopioid, and opioid analgesia from 2009 to 2018 in patients



**FIGURE 3.** Trend in nonopioid analgesics for video-assisted lobectomy on day of surgery. Plot of predicted probabilities of use in nonopioid analgesics for video-assisted lobectomy on day of surgery from 2009 to 2018. Use of epidural, PCA, and IV NSAIDs decreased over time ( $P < .0001$ ). Use of IV and oral acetaminophen, ketamine, gabapentinoids, and liposomal bupivacaine increased over time ( $P < .0001$ ). *PCA*, Patient-controlled analgesia; *IV*, intravenous; *NSAID*, nonsteroidal anti-inflammatory drug.

undergoing open, VATS, and RATS lobectomy in a broad cross-section of US hospitals between 2009 and 2018. Overall, the use of epidural analgesia decreased over time whereas the use of nonopioid local and systemic analgesics increased. For opioid-based analgesia, the percentage of PCA use declined. However, opioid use on the day of surgery increased and opioid consumption on POD 1, 2, and 3 did not decrease over time.

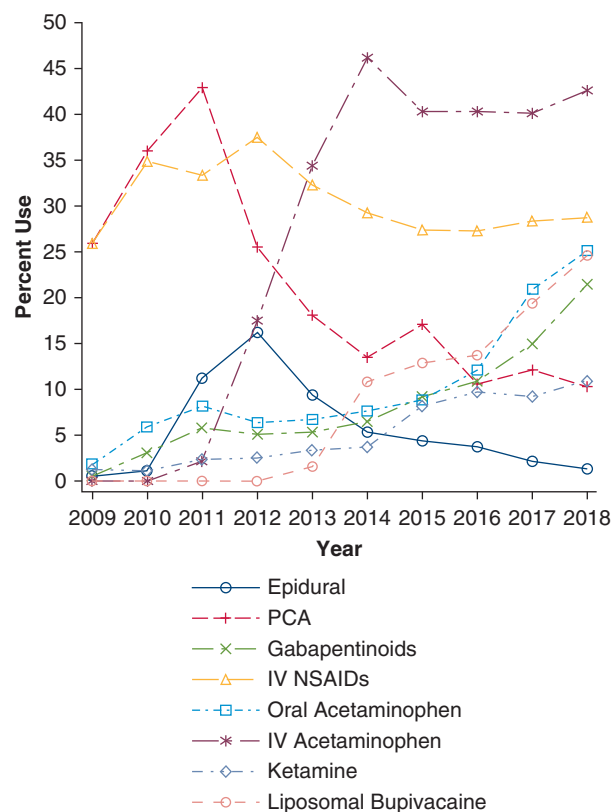
First, we found that epidural use is declining. This is consistent with smaller studies in this surgical population,<sup>9,10</sup> and in other populations (eg, radical cystectomy).<sup>11</sup> The reason for this observed decline in epidural use is multifactorial: (1) potential for complications, including dural perforation, epidural hematoma, hypotension, and urinary retention, which sometimes necessitates catheterization of the urinary bladder, leading to greater risk for urinary tract infections<sup>12,13</sup>; (2) delay in operating room time if placement is difficult; and (3) financial pressures from dedicated pain service and provision from pharmacy.<sup>14</sup> It can also be of limited effectiveness if the catheter becomes dislodged or



**FIGURE 4.** Trend in opioid consumption for video-assisted lobectomy on POD 0, 1, 2, and 3. Plot of predicted probabilities of values in opioid consumption, expressed in PMEs, on day of surgery and POD 1, 2, and 3 for video-assisted lobectomy. Total opioid use on day of surgery went from 17 mg in 2009 to 26 mg in 2018 ( $P < .0001$ ). POD 1 opioid use decreased from 29 mg in 2009 to 25 mg in 2012 and increased to 36 mg in 2018 ( $P < .0001$ ). POD 2 opioid use decreased from 31 mg in 2009 to 23 mg in 2012 and increased to 35 mg in 2018 ( $P < .0001$ ). POD 3 opioid use decreased from 35 mg in 2009 to 24 mg in 2012 and increased to 33 mg in 2018 ( $P = .005$ ). *POD*, Postoperative day; *PME*, parenteral morphine equivalents.

is inaccurately placed. In fact, the more recent Enhanced Recovery after Surgery guidelines broadened their recommendations to include other regional techniques, such as paravertebral, intercostal, serratus anterior plane, and erector spinae blocks, as alternatives to thoracic epidural analgesia.<sup>15</sup> The administration of liposomal bupivacaine, given its slow release of bupivacaine, may also preclude the practice of thoracic epidural infused with local anesthetics due to concern for local anesthetic toxicity.

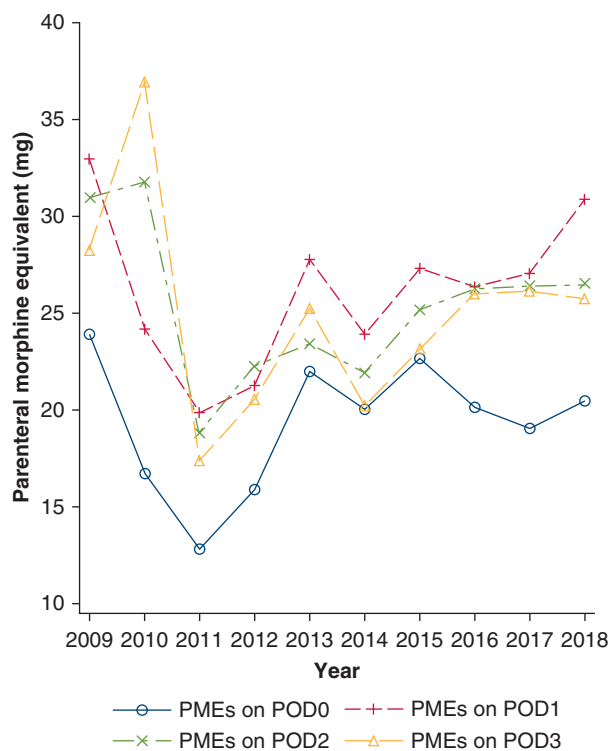
Second, we observed an increase in the use of nonopioid local and systemic analgesics. The concept of multimodal analgesia was first introduced in 1993,<sup>16</sup> and it has been accelerated by the recent opioid epidemic. Studies on total hip or knee arthroplasty have shown that a greater number of analgesic modalities is more effective in sparing opioid consumption.<sup>17,18</sup> We observed an increase in the use of IV acetaminophen and liposomal bupivacaine, similar to recent findings on total joint replacement.<sup>7,19</sup> This may be due to aggressive marketing after approval of these drugs



**FIGURE 5.** Trend in nonopioid analgesics for robotic-assisted lobectomy on day of surgery. Plot of predicted probabilities of use in nonopioid analgesics for robotic-assisted lobectomy on day of surgery from 2009 to 2018. Use of epidural, PCA, and IV NSAIDs decreased over time ( $P < .0001$ ). Use of IV and oral acetaminophen, ketamine, gabapentinoids, and liposomal bupivacaine increased over time ( $P < .0001$ ). *PCA*, Patient-controlled analgesia; *IV*, intravenous; *NSAID*, nonsteroidal anti-inflammatory drug.

by the FDA, combined with the perceived potential for these drugs to reduce opioid consumption.<sup>20,21</sup> Liposomal bupivacaine also obviates the need for infusion pump or catheter management, thereby reducing the need for dedicated acute pain services.<sup>14</sup> Although there are retrospective studies comparing thoracic epidural analgesia with liposomal bupivacaine given as intercostal nerve block for lobectomies, large multicenter randomized controlled trials are lacking.<sup>22</sup> In addition, the use of NSAIDs, a treatment with proven efficacy, has also decreased.<sup>23</sup> In sum, whereas nonopioid treatments may be increasing in an overall sense, there is a significant heterogeneity in how specific treatments are changing over time. There is a lack of high-quality comparative effectiveness studies examining whether the combination of newer analgesic treatments is sufficient to replace epidural analgesia.

Lastly, for opioid use, we observed a steep decrease in the percentage of PCA use on the day of surgery, which might be indicative of providers' intention to order less PCAs.



**FIGURE 6.** Trend in opioid consumption for robotic-assisted lobectomy on POD 0, 1, 2, and 3. Plot of predicted probabilities of values in opioid consumption, expressed in PMEs, on day of surgery and POD 1, 2, and 3 for robotic-assisted lobectomy. Total opioid use on day of surgery went from 24 mg in 2009 to 13 mg in 2011, and then increased to 20 mg in 2018 ( $P < .0001$ ). POD 1 opioid use decreased from 33 mg in 2009 to 20 mg in 2011, and then increased to 31 mg in 2018 ( $P < .0001$ ). POD 2 opioid use decreased from 29 mg in 2009 to 21 mg in 2012, and then increased to 26 mg in 2018 ( $P = .05$ ). POD 3 opioid use decreased from 26 mg in 2009 to 16 mg in 2011, and then increased to 25 mg in 2018 ( $P = .21$ ). *POD*, Postoperative day; *PME*, parenteral morphine equivalents.

However, the amount of opioid use on the day of surgery increased over time. The absence of epidural analgesia might have increased the intraoperative opioid consumption.

The amount of opioid consumption on POD 1, 2, and 3 did not decrease over time. It initially declined from 2009 to 2012, which might be due to policies being implemented to address the opioid epidemic. For example, in 2009, the FDA initiated a process under the FDA Amendments Act to require manufacturers of high-potency opioids to implement risk-evaluation and mitigation strategies.<sup>24</sup> However, even with the increasing use in nonopioid local and systemic analgesics, postoperative opioid use re-ascended after 2012; by 2018, its amount was similar to that in 2010. This was observed across the open, VATS, and RATS cohorts. Bykov and colleagues<sup>25</sup> also reported similar findings in patients undergoing various types of inpatient surgeries from 2007 to 2017. Thus, recent changes in analgesic strategies

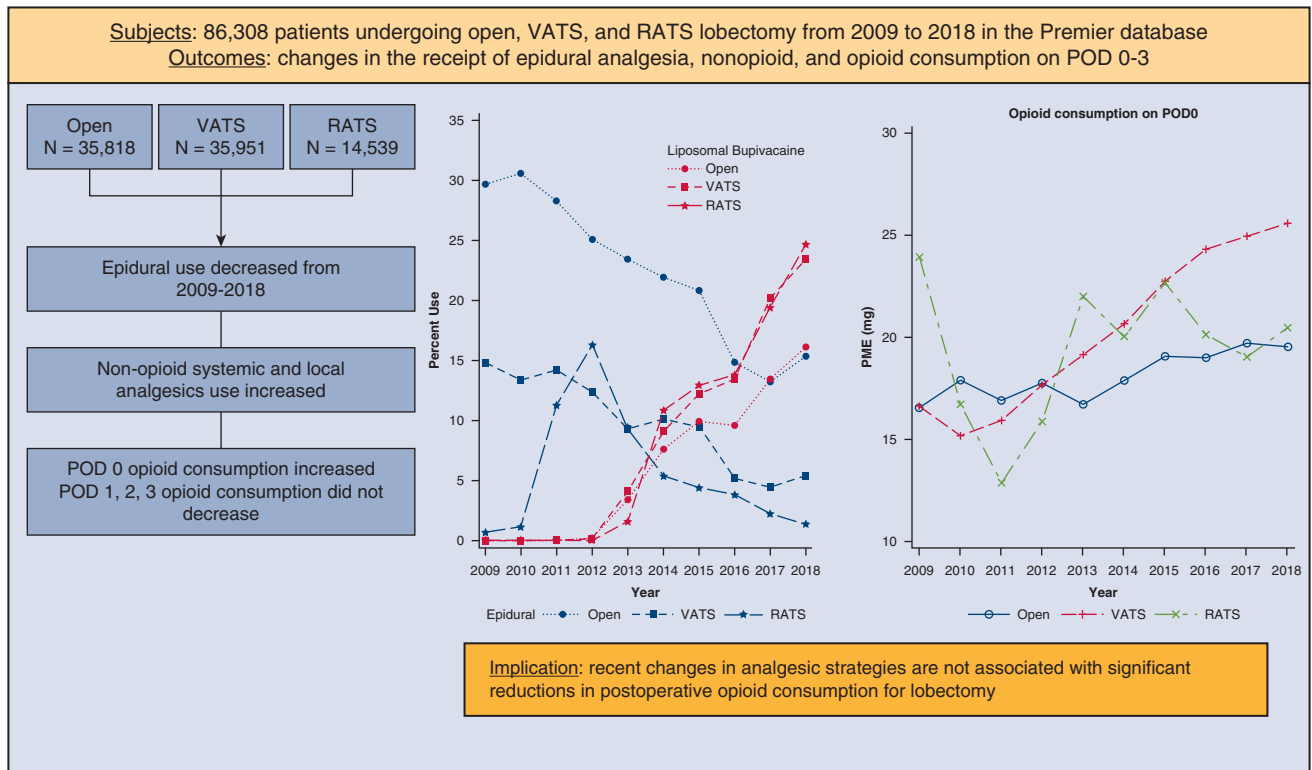
are not associated with significant reductions in postoperative inpatient opioid consumption for lobectomy. This is an important issue to address because opioid consumption prior to discharge is often the best predictor for home opioid use.<sup>26</sup>

Postoperative opioid use was lower in the RATS group than the open and VATS groups, as seen in Figures 2, 4, and 6. This was similar to the findings from a recent study by Rajaram et al,<sup>27</sup> who performed propensity-matched analysis on open, VATS, and RATS lobectomy patients from 2013 to 2015, using the Premier database. It is important to note that our study was not designed to compare these 3 surgical cohorts, but instead, we aimed to analyze changes in analgesic use over time within each surgical cohort.

There are several limitations in our study. First, since we identified the receipt of epidural analgesia and other analgesics by charge codes in the database, there might be incomplete data capture due to deficiency in billing, coding bias, or error in data entry. However, it is unlikely that this explains the observed changes in pain management over time because these systemic biases should be consistent throughout the years. Second, the centers that are included in the Premier database may not be consistent throughout the years, thereby making the underlying population unstable. In addition, the numbers of RATS cases from 2009 to 2011 were small, so the data for RATS during these 3 years might be skewed. Third, we were only able to identify 34 patients who received paravertebral blocks or other regional techniques in the database. We were unable to capture the intercostal, interpleural, paravertebral blocks placed by surgeons, either as a single injection or catheter-based infusion (eg, On-Q pump). This is likely due to a lack of billing for these procedures. Lastly, we treated year as an independent variable, but this may create some biases due to interactions with other variables.

In conclusion, our study demonstrated a decline in epidural analgesia use for patients undergoing open, VATS, and RATS lobectomy from 2009 to 2018. Concomitantly, the use of nonopioid analgesics increased, and postoperative opioid use did not decrease over time. Opioid consumption on the day of surgery increased despite great use of multimodal analgesia. This suggests that the analgesics chosen to replace epidurals for lobectomy patients might not be as effective at reducing opioid use (Figure 7). If our goal as providers is to minimize perioperative opioid use, we have failed to achieve this goal with the current analgesic strategies. To reach this goal, we may have to: (1) pursue a more vigorous multimodal analgesia regimen, (2) advocate for a defined Enhanced Recovery After Surgery protocol, and (3) consider reestablishing epidural analgesia or expanding other regional analgesic techniques. To evaluate the clinical impact of our observed changes in analgesic approach, future studies are required to examine

## Changes in analgesic strategies for lobectomy from 2009 to 2018



**FIGURE 7.** Changes in analgesic strategies for lobectomy from 2009 to 2018. A retrospective observational study was conducted using the Premier database for adult patients undergoing open, video-assisted, and robotic-assisted lobectomy from 2009 to 2018. Epidural use declined over time, and nonopioid analgesics use increased. Despite these changes, opioid consumption on day of surgery increased, and there was no significant reduction in postoperative opioid consumption. VATS, Video-assisted thoracoscopic surgery; RATS, robotic-assisted thoracoscopic surgery; POD, postoperative day.

outcomes such as pain score, postoperative complications, and cost.

### Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

We thank Drs Michelle McGauvran and Selby Johnson for their insightful inputs for research question formulation and preparation for the manuscript.

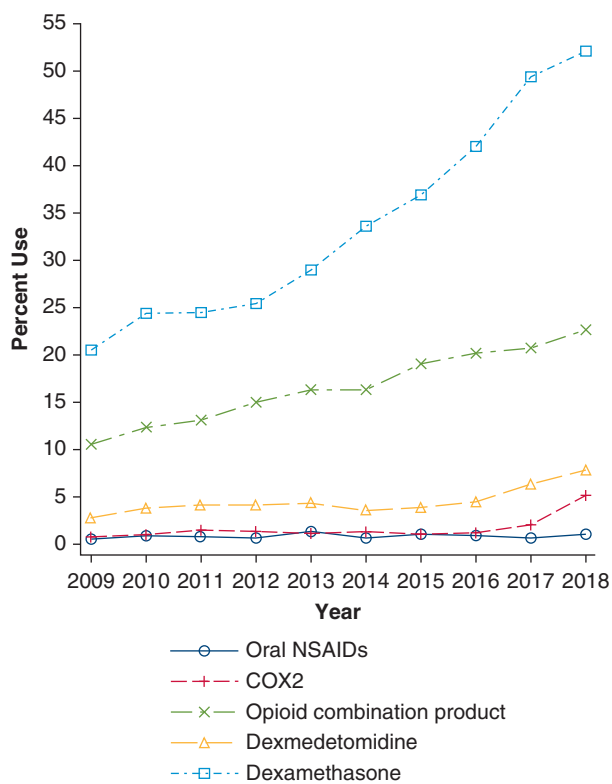
### References

- Thompson C, French DG, Costache I. Pain management within an enhanced recovery program after thoracic surgery. *J Thorac Dis.* 2018;10(suppl 32):S3773-80.
- Wenk M, Schug SA. Perioperative pain management after thoracotomy. *Curr Opin Anaesthesiol.* 2011;24:8-12.
- Richebe P, Capdevila X, Rivat C. Persistent postsurgical pain: pathophysiology and preventative pharmacologic considerations. *Anesthesiology.* 2018;129:590-607.
- Kaiser AM, Zollinger A, De Lorenzi D, Largiadèr F, Weder W. Prospective, randomized comparison of extrapleural versus epidural analgesia for postthoracotomy pain. *Ann Thorac Surg.* 1998;66:367-72.
- Goto T. What is the best pain control after thoracic surgery? *J Thorac Dis.* 2018; 10:1335-8.
- Rayaz H, Bravos ED, Gottschalk A. The role of liposomal bupivacaine in thoracic surgery. *J Thorac Dis.* 2019;11(suppl 9):S1163-8.
- Ohnuma T, Raghunathan K, Ellis AR, Whittle J, Pyati S, Bryan WE, et al. Effects of acetaminophen, NSAIDs, gabapentinoids, and their combinations on postoperative pulmonary complications after total hip or knee arthroplasty. *Pain Med.* 2020;21:2385-93.
- van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. *Med Care.* 2009;47:626-33.
- Wijeyesundera DN, Beattie WS, Austin PC, Hux JE, Laupacis A. Epidural anaesthesia and survival after intermediate-to-high risk non-cardiac surgery: a population-based cohort study. *Lancet.* 2008;372:562-9.
- Blackshaw WJ, Bhawnani A, Pennefather SH, Al-Rawi O, Agarwal S, Shaw M. Propensity score-matched outcomes after thoracic epidural or paravertebral analgesia for thoracotomy. *Anaesthesia.* 2018;73:444-9.
- Miller BL, Abel EJ, Allen G, Schumacher JR, Jarrard D, Downs T, et al. Trends in epidural anesthesia use at the time of radical cystectomy and its association with perioperative and survival outcomes: a population-based analysis. *Am J Clin Exp Urol.* 2020;8:28-37.
- Júnior Ade P, Erdmann TR, Santos TV, Brunharo GM, Filho CT, Losso MJ, et al. Comparison between continuous thoracic epidural and paravertebral blocks for postoperative analgesia in patients undergoing thoracotomy: systematic review. *Braz J Anesthesiol.* 2013;63:433-42.
- Zaouter C, Kaneva P, Carli F. Less urinary tract infection by earlier removal of bladder catheter in surgical patients receiving thoracic epidural analgesia. *Reg Anesth Pain Med.* 2009;34:542-8.

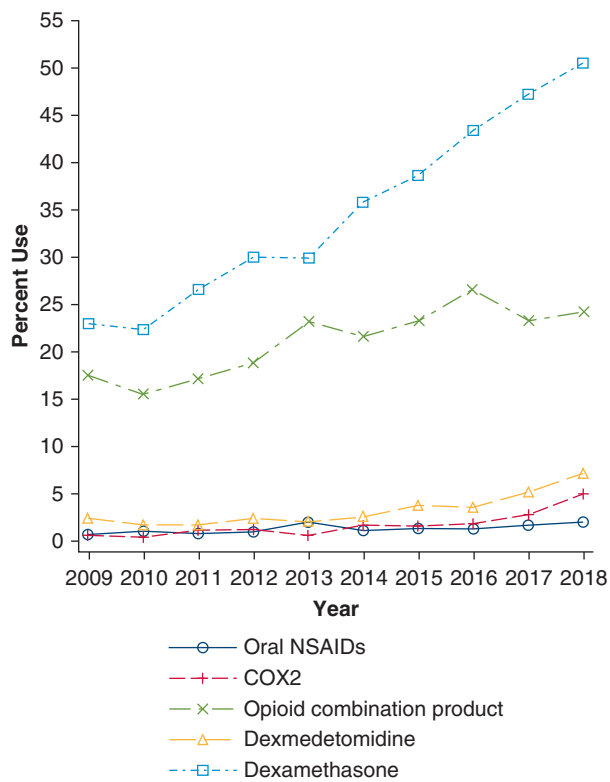


14. Rice DC, Cata JP, Mena GE, Rodríguez-Restrepo A, Correa AM, Mehran RJ. Posterior intercostal nerve block with liposomal bupivacaine: an alternative to thoracic epidural analgesia. *Ann Thorac Surg.* 2015;99:1953-60.
15. Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, Brunelli A, Cerfolio RJ, Gonzalez M, et al. Guidelines for enhanced recovery after lung surgery: recommendations of the Enhanced Recovery After Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). *Eur J Cardiothorac Surg.* 2019; 55:91-115.
16. Kehlet H, Dahl JB. The value of “multimodal” or “balanced analgesia” in postoperative pain treatment. *Anesth Analg.* 1993;77:1048-56.
17. Memtsoudis SG, Poeran J, Zubizarreta N, Cozowicz C, Mörwald EE, Mariano ER, et al. Association of multimodal pain management strategies with perioperative outcomes and resource utilization: a population-based study. *Anesthesiology.* 2018;128:891-902.
18. Cozowicz C, Poeran J, Zubizarreta N, Liu J, Weinstein SM, Pichler L, et al. Non-opioid analgesic modes of pain management are associated with reduced postoperative complications and resource utilisation: a retrospective study of obstructive sleep apnoea patients undergoing elective joint arthroplasty. *Br J Anaesth.* 2019;122:131-40.
19. Pichler L, Poeran J, Zubizarreta N, Cozowicz C, Sun EC, Mazumdar M, et al. Liposomal bupivacaine does not reduce inpatient opioid prescription or related complications after knee arthroplasty: a database analysis. *Anesthesiology.* 2018;129:689-99.
20. Kelley TM Jr, Bailey DW, Sparks P, Rice R, Caddell E, Currier H, et al. Intercostal nerve blockade with Exparel(R) results in lower opioid usage during the first 24 hours after video-assisted thoracoscopic surgery. *Am Surg.* 2018;84:1433-8.
21. Khalil KG, Boutrous ML, Irani AD, Miller CC III, Pawelek TR, Estrera AL, et al. Operative intercostal nerve blocks with long-acting bupivacaine liposome for pain control after thoracotomy. *Ann Thorac Surg.* 2015;100: 2013-8.
22. Campos JH, Seering M, Peacher D. Is the role of liposomal bupivacaine the future of analgesia for thoracic surgery? An update and review. *J Cardiothorac Vasc Anesth.* 2020;34:3093-103.
23. Barak M, Ziser A, Katz Y. Thoracic epidural local anesthetics are ineffective in alleviating post-thoracotomy ipsilateral shoulder pain. *J Cardiothorac Vasc Anesth.* 2004;18:458-60.
24. Woodcock J. A difficult balance—pain management, drug safety, and the FDA. *N Engl J Med.* 2009;361:2105-7.
25. Bykov K, Patomo E, Franklin JM, Vine SM, Bateman BT. Postoperative inpatient utilization of opioid and opioid-sparing analgesics in the United States hospitals, 2007-2017. *Pharmacoepidemiol Drug Saf.* 2021;30:390-4.
26. Hill MV, Stucke RS, Billmeier SE, Kelly JL, Barth RJ Jr. Guideline for discharge opioid prescriptions after inpatient general surgical procedures. *J Am Coll Surg.* 2018;226:996-1003.
27. Rajaram R, Rice DC, Li Y, Bruera E, Liu E, Song C, et al. Postoperative opioid use after lobectomy for primary lung cancer: a propensity-matched analysis of Premier hospital data. *J Thorac Cardiovasc Surg.* May 16, 2020 [Epub ahead of print].

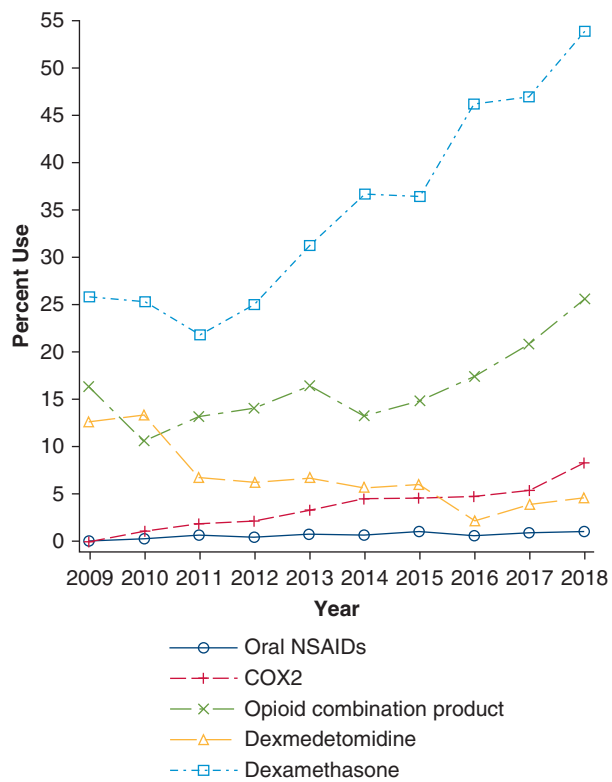
**Key Words:** multimodal analgesia, epidural analgesia, nonopioid analgesia, thoracic surgery, lobectomy, thoracotomy, video-assisted thoracoscopic surgery, robotic-assisted thoracoscopic surgery



**FIGURE E1.** Trend in nonopioid analgesics for open lobectomy on day of surgery. Plot of predicted probabilities of use in other nonopioid analgesics for open lobectomy on day of surgery from 2009 to 2018. Use of COX-2 inhibitors, opioid combination product, dexmedetomidine, and dexamethasone increased over time ( $P < .0001$ ). Use of oral NSAIDs remained low and did not change significantly over time ( $P = .45$ ). COX-2, Cyclooxygenase-2; NSAID, nonsteroidal anti-inflammatory drug.



**FIGURE E2.** Trend in nonopioid analgesics for video-assisted lobectomy on day of surgery. Plot of predicted probabilities of use in other nonopioid analgesics for video-assisted lobectomy on day of surgery from 2009 to 2018. Use of oral NSAIDs, COX-2 inhibitors, opioid combination product, dexmedetomidine, and dexamethasone increased over time ( $P < .0001$ ). NSAID, Nonsteroidal anti-inflammatory drug; COX-2, cyclooxygenase-2.



**FIGURE E3.** Trend in nonopioid analgesics for robotic-assisted lobectomy on day of surgery. Plot of predicted probabilities of use in other non-opioid analgesics for robotic-assisted lobectomy on day of surgery from 2009 to 2018. Use of oral NSAIDs increased over time ( $P = .01$ ). Use of COX-2 inhibitors, opioid combination product, and dexamethasone increased over time ( $P < .0001$ ). Use of dexmedetomidine decreased over time ( $P < .0001$ ). NSAID, Nonsteroidal anti-inflammatory drug; COX-2, cyclooxygenase-2.

**TABLE E1. ICD-9 and ICD-10 codes for procedures and conversions**

Procedures	ICD-9 codes	ICD-10 codes
Open lobectomy	32.4 32.49	0BTC0ZZ, 0BTD0ZZ, 0BTF0ZZ, 0BTG0ZZ, 0BTH0ZZ, 0BTJ0ZZ
VATS	32.41	0BJ04ZZ, 0BJ14ZZ, 0BJK4ZZ, 0BJL4ZZ, 0BJQ4ZZ, 0BJT4ZZ
Robotic-assisted procedure codes*	17.41, 17.43, 17.44, 17.45, 17.49	8E0W0CZ, 8E0W3CZ, 8E0W4CZ, 8E0W4CZ, 8E0W7CZ, 8E0W8CZ, 8E0WXCZ
Conversions from VATS/RATS to open	V64.41 V64.42	Z53.32

ICD-9, *International Classification of Diseases, Ninth Revision*; ICD-10, *International Classification of Diseases, Tenth Revision*; VATS, video-assisted thoracoscopic surgery; RATS, robotic-assisted thoracoscopic surgery. \*RATS was identified if a patient had both ICD procedure codes for robotic assisted procedure and ICD procedure codes for VATS/open lobectomy.