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Post-Discharge Pain Management After Thoracic Surgery – A Patient-Centered Approach

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Abstract

Background: Postoperative analgesia is paramount to recovery following thoracic surgery, and opioids play an invaluable role in this process. Yet, current one-size-fits-all prescribing practices produce large quantities of unused opioids, increasing the risk of nonmedical use and overdose. Here, we hypothesized that patient and perioperative characteristics, including 24-hour before discharge opioid intake, could inform more appropriate post-discharge prescriptions after thoracic surgery.

Methods: We conducted a prospective observational cohort study in 200 adult thoracic surgery patients. The cohort was divided into three groups based on 24-hour before discharge opioid intake in morphine milligram equivalents (MME): 1) no (0 MME), 2) low (>0–22.5 MME), or 3) high (>22.5 MME) before discharge opioid intake. Logistic regression was used to analyze the association of patient and perioperative characteristics with self-reported after discharge opioid use.

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Results: Univariate analysis showed preoperative opioid use, 24-hour before discharge acetaminophen and gabapentinoid intake, and 24-hour before discharge opioid intake were associated with higher after discharge opioid use. Multivariable modeling demonstrated that 24-hour prior to discharge opioid intake was most significantly associated with after discharge opioid use. For example, compared to patients who took high amounts of opioids prior to discharge, patients who took no opioids prior to discharge were 99% less likely to take a high amount of opioids after discharge compared to taking none (OR 0.011; 95% CI 0.003–0.047; $P < 0.0001$).

Conclusions: Assessment of 24-hour before discharge opioid intake may inform patient requirements after discharge. Opioid prescriptions after thoracic surgery can thereby be targeted based on anticipated needs.

Safe and effective pain management strategies are paramount to recovery following thoracic surgery. Poorly controlled pain can greatly impair respiratory mechanics, leading to complications such as atelectasis and pneumonia.¹ In addition, ineffective pain management in the immediate postoperative period may contribute to the development of chronic pain syndromes, especially, post-thoracotomy pain.^{2, 3} To this end, the appropriate use of opioid and non-opioid pain medications after thoracic surgery represents a cornerstone of postoperative therapy.⁴

However, there is also significant morbidity and mortality associated with opioid use,^{5, 6} and, unfortunately, even well intentioned postoperative opioid prescriptions may contribute to adverse outcomes. For example, for opioid naïve patients, the number of days of opioid medication supplied from the initial prescription correlates with a higher risk for development of chronic opioid use.⁷ Both open and minimally invasive thoracic procedures have been associated with a higher risk of prolonged postoperative opioid use compared to other surgical patient populations.^{8, 9} In addition, there is a risk of nonmedical use of opioids.¹⁰ The risk of diversion and nonmedical use of opioid medications have been shown to parallel the amount of opioids distributed legally by way of prescriptions.⁶

It has been demonstrated across a variety of surgical procedures that many patients do not take a significant proportion of the opioids prescribed to them.^{11, 12} Specifically, 67% to 92% of postoperative patients report unused opioid medications, and 73% to 77% of patients store these medications in unlocked locations.¹³ These unused opioids can become a source for nonmedical opioid use. According to the National Survey on Drug Use and Health 49.5% of people aged 12 – 17 years and 51.4% of those 18 years or older obtained the opioids for non-medical use from a relative or family member.¹⁴

A more targeted, patient-specific approach to opioid prescriptions after any type of surgery could yield significant benefits toward limiting the amount of these medications in the community without compromising the management of pain. Because of the unique variability in regards to open versus minimally invasive procedures, medical comorbidities, susceptibility to chronic pain syndromes, and malignant versus non-malignant pathologies we chose to specifically study thoracic surgery patients. The objective of this study was to examine if patient and perioperative characteristics, including 24-hour before discharge opioid intake, could inform appropriate and safe post-discharge prescriptions for patients

following thoracic surgery. We hypothesized that the amount of opioids (in morphine milligram equivalents - MME) taken in the weeks after discharge.

Patients and Methods

The Institutional Review Board approved this study. All patients enrolled provided informed consent. Study design and reporting were conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology Statement.¹⁵

Population

We report on a prospective single center cohort study of patients undergoing thoracic surgery between 2017 and 2018. All patients undergoing inpatient thoracic surgical procedures were eligible, with the exception of isolated bronchoscopy. Patients were not eligible if they were under the age of 18 years, returning to institutional environments after discharge, non-English speaking, pregnant, deemed to lack decision-making capacity, or status post tracheostomy. To avoid selection bias in prioritizing the order that patients were contacted on the floor, we randomized the contact order of eligible patients at the beginning of a recruitment day.

Procedures and Measurements

Postoperative pain control regimens were not standardized for the study and were instead managed at the discretion of the individual surgeons. Patients typically received intravenous opioids via patient-controlled analgesia pumps and were subsequently transitioned to oral opioids (usually Oxycodone 5mg tablets) that were titrated based on patient requirements. Barring an allergy or physiologic contraindication, acetaminophen and NSAIDs were routinely offered as needed. In addition, the Department of Anesthesiology's inpatient pain service provided epidural catheters or other regional nerve blocks when deemed appropriate by the surgeon.

After consent and enrollment, patients completed the study survey in one-week intervals beginning after hospital discharge, for a total of four weeks (Figure 1). Participants received a U.S. \$10 gift card or money order for each completed survey (U.S. \$40 total). The survey was administered per the individual patient's preference using mailed paper, online, or by telephone.

Patient characteristics, and details on the surgical procedure and perioperative care were obtained from the electronic medical record. Characteristics included age, body mass index, gender, race, ethnicity, insurance status, American Society of Anesthesiology (ASA) physical status, and pre-operative medications. Procedural and perioperative information included emergency status, type of surgical procedure, duration of the procedure, use of nerve block, paravertebral block, or epidural catheter, before discharge opioid and non-opioid pain medications, and type and amount of opioids prescribed at discharge. According to published recommendations,¹⁶ we categorized the amount of opioids taken over the last 24 hours prior to discharge as: 1) no before discharge opioid intake (0 MME), 2) low before discharge opioid intake (>0 – 22.5 MME, equivalent to up to three oxycodone 5mg tablets),

and 3) high before discharge opioid intake (>22.5 MME, or more than 3 oxycodone 5mg tablets).

Outcomes were collected for four weeks after discharge using a survey instrument that was created by combining existing questions (PROMIS tools for pain intensity and interference)¹⁷ with additional questions designed to assess pain medication intake, storage, and disposal. Readability of the questions was evaluated by the Flesch-Kincaid grade level.¹⁸ The primary outcome, cumulative after discharge opioid intake over four weeks was measured in MME. Secondary outcomes included the quality of pain management after discharge, intake of nonopioids, as well as opioid storage and disposal patterns.

Data Analysis

A simplified power analysis for logistic regression was made assuming only a sample size of $n=100$, a probability for H_0 of 0.3, an odds ratio of 3, and given the two group assumption in this calculation, a conservative two-tailed alpha of 0.025 using G*Power 3.1.¹⁹ Using these parameters, power was calculated at 98%.

We used chi-square tests and analysis of variance (ANOVA) as appropriate to compare patient, procedural, and perioperative characteristics across the primary outcome, after discharge opioid intake, categorized as: 1) no after discharge opioid intake (0 MME), 2) low after discharge opioid intake (>0–112.5 MME, or up to 15 oxycodone 5mg tablets), and 3) high after discharge opioid intake (>112.5 MME or more than 15 oxycodone 5mg tablets), according to guidelines developed for general surgery patients.¹⁶

We developed multivariable logistic regression models to examine the association between 24-hour before discharge opioid intake and after discharge opioid intake (up to 4 weeks), controlling for age group (60 years and older), ASA physical status (III-IV vs. I-II), pain intensity of surgical procedure (Thoracotomy or major open procedure vs. others), 24-hour prior to discharge gabapentin or pregabalin use (yes/no), and pre-operative opioid usage (yes/no). We chose multinomial logistic regression as opposed to ordinal logistic regression. Although our outcome variable is ordered, the effects of the explanatory variables, in particular the amount of opioids taken 24 hours before discharge, was not proportional across the thresholds of opioids taken after discharge (none, up to 112.5 MME, and >112.5 MME).

Results

The participants were most often white, female, 60 years of age, and most often presented for non-emergent, minimally invasive thoracic operations as opposed to thoracotomy or other major open procedures. Zero post-discharge opioid use defined the “no after discharge opioid intake” group. The cumulative amounts of opioids taken during the four-week period post-discharge (in MME/7.5, equivalent to one oxycodone 5mg tablet) taken in the “low” vs. “high” after discharge opioid intake groups (25th / 50th / 75th percentile) were 2 / 5 / 10 vs. 27 / 42 / 88 respectively. Univariate comparisons between the three after discharge opioid intake groups (none, low, and high) revealed the following pre-discharge variables as significant: preoperative opioid use, 24hour prior to discharge acetaminophen and

gabapentinoid use, pain intensity of the procedure (correlating with open versus minimally invasive approaches), and 24-hour before discharge opioid intake (Table 1). The 25th / 50th / 75th percentiles for the cumulative 4-week opioid intake in MME/7.5 (equivalent to one oxycodone 5mg tablet) was 1 / 27 / 74 after thoracotomy surgery (n=43) and 0 / 5 / 30 after videoscopic assisted surgery (n=143). The rate of commercial insurance in responders (n=200) vs. non-responders (n=28) to the survey was 48% and 43% respectively (p=0.69). Combined intake of NSAIDs and acetaminophen and PROMIS pain intensity and pain interference scores were collected weekly for each after discharge opioid intake group (Table 2). Overall, both pain intensity and pain interference scores down-trended across all three after-discharge-opioid-intake groups over time.

The reasons for cessation of opioid use, as well as storage and disposal patterns were assessed at weekly intervals (Table 3). The most common reason for cessation of opioid use was: “my pain was controlled without taking opioid pain pills.” In addition, a locked storage location was used by only 9–11% of patients, and only 3% or fewer patients reported disposing of leftover opioid medication.

Total opioid intake over the 4 weeks post-discharge was graphed according to the amount taken during the 24 hours prior to discharge (Figure 2). The majority of patients who took no opioids after discharge also took no opioids over the 24 hours prior to discharge. Conversely, most of the patients who took high amounts of opioids after discharge also took high amounts in the 24 hours prior to discharge. The multivariable logistic regression model confirms a similar pattern (Table 4):

Compared to patients who took a high amount of opioids prior to discharge, patients who took no opioids prior to discharge were:

- 99% less likely to take a high amount of opioids post discharge compared to taking none, and
- 93% less likely to take a low amount of opioids post discharge compared to taking none.

Compared to patients who took a high amount of opioids prior to discharge, patients who took a low amount of opioids prior to discharge were:

- 86% less likely to take a high amount of opioids post discharge compared to taking none, and
- 56% less likely to take a low amount of opioids post discharge compared to taking none.

Comment

Following thoracic surgery, the intake of opioids in the 24 hours prior to discharge is useful to estimate the amount of opioids taken after discharge. This is an important finding because it assists clinicians to gauge which patients will likely not require a post-discharge opioid prescription, or possibly only require a small quantity of opioids. Our hypothesis that amounts of opioids taken in the 24 hours prior to discharge would be associated with the

amounts of opioid taken in the four weeks after discharge was confirmed. Our findings could be included into opioid prescribing decision aids used at discharge.

In a recent study in cardiothoracic surgery patients, the size of perioperative opioid prescriptions was one of the strongest predictors for new persistent opioid use.²⁰ An individualized approach to post-discharge opioid prescribing is an essential step toward mitigating the risks associated with over-prescribing of these medications. However, we realize that the chosen model is not perfect, and its application risks undertreatment of some patients' pain. In Figure 2, specifically, patients who took no opioids in the 24 hours prior to discharge, ended up taking high amounts of opioids after leaving the hospital. As a safety measure to limit the number of patients who will potentially fall into this category, we propose that patient/provider shared decision-making techniques be employed to help guide post-discharge prescriptions.²¹

Non-opioid adjuncts as part of multimodal perioperative pain regimens play an important role in minimizing opioid consumption in surgical patients, and their use is recommended.²² Our findings that patients who received acetaminophen or gabapentinoids 24 hours prior to discharge were less likely to fall into the zero after discharge opioid intake group may appear counterintuitive at first. However, we are not concluding that acetaminophen and gabapentinoids increase postoperative opioid usage. Instead, the use of these adjuncts likely highlights a subgroup of patients with more difficult to control pain, which therefore would be associated with higher opioid requirements after discharge. A separate, but likely related predictor of this subgroup exhibiting more challenging pain control includes those undergoing thoracotomy or other major open procedures, as demonstrated by our univariate analysis. While multivariate analysis showed a similar trend, it was not statistically significant.

Our study demonstrated a low disposal rate of unused (leftover) opioid medications. A recent systematic review investigating unused opioids after surgery found that only 4–30% of patients planned to or actually disposed of their unused medications, and only 4–9% of them employed a method of disposal recommended by the Food and Drug Administration.¹³ The 1–3% disposal rate identified at our institution suggests a need for increasing patient education and resources for proper disposal of unused opioid medications.

Our study has important strengths and limitations. Much of the strengths can be credited to the prospective design, with efforts to limit selection bias and subject dropout. In addition, the results provide clinically relevant findings that are relatively straightforward in their tangible application to patient care.

There are also important limitations of this study. First, the provision of gift cards to subjects to improve survey response may produce participation bias by preferentially recruiting patients from lower socioeconomic backgrounds. Indeed, incentive payments tend to have a greater impact on participation rates for this particular demographic. But, because these individuals are also less likely at baseline to participate in surveys, incentive payments may in fact balance response rates with higher socioeconomic groups.²³ In addition, our study showed similar rates of commercial insurance (a surrogate for socioeconomic status) in

responders and non-responders. Other forms of bias stem from employing multiple patient-reported variables, in particular, recall bias and social desirability bias. Yet, the application of patient-reported outcomes in clinical research continues to expand, as these measures often provide more complete descriptions of clinical interventions compared to traditional variables. Furthermore, patient-reported outcomes have demonstrated similar degrees of reliability as more objective clinical measures, including bedside glucose monitoring and diastolic blood pressure.²⁴ Another limitation is that our study was observational and lacked randomization or controls. While the suggested approach to post-discharge prescribing seems to be supported by our findings, it needs to be further studied in a randomized controlled fashion. Further research should also examine the ideal timeframe over which prior to discharge opioid use should be assessed. We chose the 24-hour prior to discharge period based on previously published work.¹⁶ Also, opioid-sparing effects from epidural or intercostal nerve blockade would likely be less relevant on the day prior to discharge. As a final limitation, we did not specifically incorporate preoperative performance status descriptors in our analysis. However, we did include an assessment of the ASA physical status, which has been shown to be a reasonable proxy for more established measures of functional status, such as the Eastern Cooperative Oncology Group performance status.²⁵

In summary, our results suggest that potential improvements in opioid prescribing patterns after thoracic surgery may be made through assessment of 24-hour prior to discharge opioid requirements. Limiting opioid availability may reduce a patient's risks of nonmedical use and overdose, and more broadly, represents an important contribution to reversing the current opioid epidemic by reducing the availability of excess opioids. Future work might reveal further opportunities to more precisely individualize post-discharge opioid prescriptions after thoracic surgery. The concept of limiting opioid usage while ensuring high-quality postoperative analgesia should also extend to other surgical patient populations.

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Figure 1.
Study flow diagram. Final cohort n=200 patients.

Figure 2.

Post-discharge opioid intake. Results of 4-week self-reported after discharge opioid intake are grouped as follows: 1) none (0 MME), 2) low ADOI (> 0 to 112.5 MME), or up to 15 oxycodone 5mg tablets), and 3) high ADOI (>112.5 MME, or more than 15 oxycodone 5mg tablets). Abbreviations: MME, morphine milligram equivalents; ADOI, after discharge opioid intake.

Table 1:

Patient, procedural, and perioperative characteristics.

	All n=200	No ADOI n=64	Low ADOI 112.5mg n=52	High ADOI >112.5mg n=84	P value
Age 60 and older	115, 58%	40, 63%	30, 58%	45, 54%	0.55
Body mass index	25.9 (5.8)[24.9]	25.9 (5.6)[25.0]	25.8 (5.9)[24.7]	26.0 (5.9)[24.7]	0.97
Female: n, %	116, 58%	41, 64%	32, 62%	43, 51%	0.24
Race					
White	178, 89%	56, 88%	45, 87%	77, 92%	0.58
Ethnicity					
Hispanic	12, 6%	4, 6%	3, 6%	5, 6%	>0.99
Insurance: Commercial	96, 48%	27, 42%	23, 44%	46, 55%	0.26
Pre-operative opioids	22, 11%	1, 2%	6, 12%	15, 18%	0.007
Pre-operative benzodiazepines	28, 14%	7, 11%	7, 14%	14, 17%	0.60
Pre-operative SSRI or SNRI	33, 17%	9, 14%	10, 19%	14, 17%	0.76
ASA physical status (III-IV vs I-II)	135, 68%	49, 77%	31, 60%	55, 66%	0.13
Emergency	5, 3%	1, 2%	1, 2%	3, 4%	0.86
Surgical procedure duration (min)	137 (79)[128]	129 (80)[124]	134 (84)[120]	145 (75)[140]	0.45
Thoracotomy or other major open procedure	55, 28%	15, 23%	8, 15%	32, 38%	0.01
Type of procedure*					
Segmentectomy / wedge	71, 36%	20, 31%	23, 44%	28, 33%	0.30
Lobectomy	61, 31%	18, 28%	18, 35%	25, 30%	0.74
Pneumonectomy	4, 2%	1, 2%	1, 2%	2, 2%	>0.99
Pleurectomy / decortication	13, 7%	3, 5%	5, 10%	5, 6%	0.58
Thymectomy	13, 7%	5, 8%	0, 0%	8, 10%	0.05
Lymphadenectomy	12, 6%	5, 8%	2, 4%	5, 6%	0.65
Esophagectomy	4, 2%	1, 2%	1, 2%	2, 2%	>0.99
Nuss procedure	8, 4%	0, 0%	1, 2%	7, 8%	0.02
Lung transplant	8, 4%	3, 5%	1, 2%	4, 5%	0.73
Heller myotomy / hernia repair / Nissen fundoplication	10, 5%	4, 6%	4, 8%	2, 2%	0.35
Other	35, 18%	13, 20%	7, 14%	15, 18%	0.62
Epidural, paravertebral, or nerve block	153, 77%	43, 67%	42, 81%	68, 81%	0.11
24-hour before discharge opioids					
None	52, 26%	38, 59%	10, 19%	4, 5%	<.0001

	All n=200	No ADOI n=64	Low ADOI 112.5mg n=52	High ADOI >112.5mg n=84	P value
22.5 MME	63, 32%	19, 30%	22, 42%	22, 26%	
> 22.5 MME	85, 43%	7, 11%	20, 38%	58, 69%	
24-hour prior to discharge acetaminophen	183, 92%	54, 84%	49, 94%	80, 95%	0.04
24-hour prior to discharge NSAIDs	62, 31%	19, 30%	14, 27%	29, 35%	0.62
24-hour prior to discharge gabapentin or pregabalin	154, 77%	42, 66%	44, 85%	68, 81%	0.03
Type of discharge opioid prescribed					
None	18, 9%	18, 28%	0, 0%	0, 0%	<.0001
Oxycodone	147, 74%	34, 53%	39, 75%	74, 88%	<.0001
Other	41, 21%	12, 19%	15, 29%	14, 17%	0.21
Scaled Discharge Opioid Prescription MME/7.5	93 (178)[60]	80 (174.9)[33]	65 (72.1)[48]	122 (219.0)[63]	0.15

^aMultiple procedures possible.

Continuous variables are reported using mean $\pm$ SD, and median in brackets; χ^2 tests and analysis of variance were conducted to determine significance. Categorical values are n (%).

ADOI, after-discharge opioid intake; ASA, American Society of Anesthesiologists; MME, morphine milligram equivalents; NSAIDs, nonsteroidal anti-inflammatory drugs; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

Table 2.

Post-discharge non-opioid analgesic intake and pain scores.

	Week 1 (n=199)				Week 2 (n=198)				Week 3 (n=195)				Week 4 (n=194)			
	No ADOI	Low ADOI 112.5 mg	High ADOI >112.5 mg		No ADOI	Low ADOI 112.5 mg	High ADOI >112.5 mg		No ADOI	Low ADOI 112.5 mg	High ADOI >112.5 mg		No ADOI	Low ADOI 112.5 mg	High ADOI >112.5 mg	
NSAIDs and Acetaminophen taken (n, %)	9 (14%)	10 (20%)	20 (24%)		7 (11%)	10 (20%)	18 (22%)		4 (6%)	7 (14%)	11 (13%)		6 (9%)	3 (6%)	11 (13%)	
PROMIS (t-score) Pain Intensity score	45	50	52		43	48	50		41	45	48		39	42	46	
PROMIS (t-score) Pain Interference score	54	60	63		53	59	61		51	56	59		50	54	58	

Abbreviations: ADOI, after discharge opioid intake; NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 3.
Post-discharge opioid cessation, storage and disposal patterns.

MME/7.5 depicts the equivalent of one oxycodone 5mg tablet.

	Week 1	Week 2	Week 3	Week 4
Opioids left over (MME/7.5)				
25 th percentile	0	0	0	0
50 th percentile	22	19	17	15
75 th percentile	51	51	51	50
Reason for not taking any opioid pain pills (n, %)				
a. My pain was controlled without taking opioid pain pills	56(66%)	87(71%)	107(71%)	119(73%)
b. Side effects were too strong	17(20%)	15(12%)	20(13%)	14(9%)
c. I was concerned about becoming addicted	6(7%)	10(8%)	13(9%)	18(11%)
d. I had no opioid pain pills left	0(0%)	3(2%)	4(3%)	8(5%)
e. Other	6(7%)	7(6%)	7(5%)	5(3%)
Storage location of left-over opioid pain pills (n, %)				
a. Cupboard or wardrobe	43(29%)	46(32%)	51(37%)	53(40%)
b. Medicine cabinet/other box	76(51%)	67(47%)	61(44%)	51(39%)
c. Fridge	1(1%)	1(1%)	1(1%)	2(2%)
d. Other	21(14%)	19(13%)	20(14%)	19(14%)
e. Left-over pills were disposed of	2(1%)	5(3%)	3(2%)	4(3%)
f. Don't have any leftover pain pills	7(5%)	5(3%)	2(1%)	3(2%)
Locked Storage Location (n, %)	13(9%)	15(11%)	13(10%)	13(10%)

Abbreviations: MME, morphine milligram equivalents.

Table 4.
Multinomial logistic regression model.

24-hour prior to discharge opioid intake was grouped as None, Low (≤ 22.5 MME, or up to 3 oxycodone 5mg tablets), or high (> 22.5 MME or more than 3 oxycodone 5mg tablets). Associations are made with 4-week self-reported after discharge opioid intake according to the following grouping: 1) none, 2) low (>0 to ≤ 112.5 MME, or up to 15 oxycodone 5mg tablets), and 3) high (>112.5 MME, or more than 15 oxycodone 5mg tablets).

Predictors	Comparison		
	High After Discharge Opioid Intake vs. None	Low After Discharge Opioid Intake vs. None	
	OR (95% CI)	OR (95% CI)	P value
Age (<60 years old vs. ≥60 years old)	0.432 (0.167–1.113)	0.542 (0.209–1.41)	0.22
ASA physical status (I-II vs. III-IV)	2.678 (0.999–7.178)	2.718 (1.046–7.062)	0.09
Pre-operative opioid use (no vs. yes)	0.175 (0.019–1.641)	0.216 (0.022–2.082)	0.31
24-hour prior to discharge gabapentinoid (no vs. yes)	0.601 (0.222–1.623)	0.397 (0.139–1.133)	0.22
Surgical approach (minimally invasive vs. open)	0.598 (0.22–1.622)	1.671 (0.546–5.112)	0.08
24-hour prior to discharge opioid intake (none vs. high)	0.011 (0.003–0.047)	0.075 (0.022–0.261)	<0.0001
24-hour prior to discharge opioid intake (low vs. high)	0.138 (0.047–0.412)	0.438 (0.138–1.391)	

Abbreviations: MME, morphine milligram equivalents; OR, odds ratio; CI, confidence interval.