What evidence is needed to inform postoperative opioid consumption guidelines? A cohort study of the Michigan Surgical Quality Collaborative

Jiyeon Song ,[1] Yi Li,[1] Jennifer F Waljee,[2,3] Vidhya Gunaseelan,[3,4] Chad M Brummett,[3,4] Michael J Englesbe,[2,3] Mark C Bicket [3,4,5]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/rapm-2023-104581).

[1]Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, Michigan, USA
[2]Department of Surgery, University of Michigan, Ann Arbor, Michigan, USA
[3]Opioid Prescribing Engagement Network, Institute for Health Policy and Innovation, Ann Arbor, MI, USA
[4]Department of Anesthesiology, University of Michigan, Ann Arbor, Michigan, USA
[5]Department of Health Management and Policy, University of Michigan School of Public Health, Ann Arbor, Michigan, USA

Correspondence to
Dr Mark C Bicket, Anesthesiology, University of Michigan Michigan Medicine, Ann Arbor, MI 48109, USA; mbicket@med.umich.edu

Received 10 April 2023
Accepted 18 May 2023

To cite: Song J, Li Y, Waljee JF, *et al*. *Reg Anesth Pain Med* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/rapm-2023-104581

ABSTRACT

Introduction To balance adequate pain management while minimizing opioid-related harms after surgery, opioid prescribing guidelines rely on patient-reported use after surgery. However, it is unclear how many patients are required to develop precise guidelines. We aimed to compare patterns of use, required sample size, and the precision for patient-reported opioid consumption after common surgical procedures.

Methods We analyzed procedure-specific 30-day opioid consumption data reported after discharge from 15 common surgical procedures between January 2018 and May 2019 across 65 hospitals in the Michigan Surgical Quality Collaborative. We calculated proportions of patients using no pills and the estimated number of pills meeting most patients' needs, defined as the 75th percentile of consumption. We compared several methods to model consumption patterns. Using the best method (Tweedie), we calculated sample sizes required to identify opioid consumption within a 5-pill interval and estimates of pills to meet most patients' needs by calculating the width of 95% CIs.

Results In a cohort of 10,688 patients, many patients did not consume any opioids after all types of procedures (range 20%–40%). Most patients' needs were met with 4 pills (thyroidectomy) to 13 pills (abdominal hysterectomy). Sample sizes required to estimate opioid consumption within a 5-pill wide 95% CI ranged from 48 for laparoscopic appendectomy to 188 for open colectomy. The 95% CI width for estimates ranged from 0.7 pills for laparoscopic cholecystectomy to 7.0 pills for ileostomy/colostomy.

Conclusions This study demonstrates that profiles of opioid consumption share more similarities than differences for certain surgical procedures. Future investigations on patient-reported consumption are required for procedures not currently included in prescribing guidelines to ensure surgeons and perioperative providers can appropriately tailor recommendations to the postoperative needs of patients.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Opioid prescribing guidelines for patients who have surgery often rely on patient-reported measures for how many pills patients consumed after discharge from surgery, but patterns of opioid consumption and the number of patients required to generate precise guidelines are not clear.

WHAT THIS STUDY ADDS

⇒ Among 10,688 patients undergoing common surgical procedures, most used no opioids, and the number of pills meeting most patients' needs ranged from 4 to 13 (95% CI 0.7 to 7.0). Sample sizes required to estimate opioid consumption within a 5-pill wide 95% CI ranged from 48 (laparoscopic appendectomy) to 188 (open colectomy).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Similar patterns of opioid prescribing suggest that some types of surgical procedures may be combined into the same category of recommendations, while sample sizes required to generate precise estimates appear small enough to encourage the development of precise guidelines for procedures not currently included in guidelines.

INTRODUCTION

A critical challenge in improving the safety of surgical procedures is minimizing the risk of opioid-related harms after discharge from surgery. Morbidity and mortality linked to prescription opioids has been identified as one of the most common major concerns encountered by patients in the perioperative period. Rates of opioid dependence, abuse, or overdose after surgery, sometimes classified as 'opioid never events,' are estimated to occur with 10 times greater frequency than retention of foreign objects.[1] The goal of optimizing pain treatment, both in the perioperative setting and others, involves a delicate balancing act between minimizing these harms and maximizing pain relief.[2 3] In recognition of the challenges faced by physicians, patients, and other key groups, the National Academies of Medicine convened a committee in 2019 on the topic of generating evidence for opioid prescribing for acute pain.[4] The ensuing report identified several general surgical procedures and other types of surgery as priorities to address key gaps and the need for more robust and rigorous evidence.

Guidelines for postdischarge opioid prescribing, which list a recommended quantity of pills to prescribe to patients after surgery, build on the principle of meeting the needs of most patients who undergo surgery.[5] For example, researchers providing recommendations from a multihospital consortium advocate for a benchmark at the 75% percentile of consumption where most patients' needs would be met.[6] Similarly, Thiels *et al* reported guidelines from the Mayo Clinic that rely on categories to account for the needs of most patients while adjusting for clinical and patient characteristics.[7] While some may assume that thresholds perform as intended in meeting the needs of most patients, the sample sizes required and precision of estimates needed for guidelines is not clear. A wide range of patient factors potentially influence opioid use and increase the variation around estimates.[6 8 9] Surgeons, perioperative providers, and patients undergoing surgery deserve to know the extent to which data-driven guidelines will adequately meet their needs. However, a critical gap in knowledge is understanding how many patients who report opioid consumption are needed, without which it is not possible to adequately power quality improvement initiatives, precisely calculate of consumption, and generate robust clinical guidelines.

To address this gap, we sought to compare different surgical procedures based on estimates of patient-reported consumption of opioid pills as collected from 65 hospitals participating in the Michigan Surgical Quality Collaborative (MSQC) to evaluate the sample sizes required to calculate precise estimates for opioid consumption. The secondary objective was to compare the precision of measures used in existing recommendations intended to guide postdischarge opioid prescribing. In both cases, analysis specific to the type of surgery provides the most clinically informative results while sharing additional insight on the extent that various types of surgical procedures differ in the patterns of consumption and levels of precision for opioid use after surgery. The results may inform the reproducibility of the results and facilitate the making of future data-driven guidelines.

METHODS

Data source and cohort selection

This study used data from the clinical registry maintained by the MSQC. MSQC is a statewide quality improvement program that includes 65 major hospitals in Michigan with standard procedures for the collection of perioperative data including outcomes for patients undergoing surgery at these hospitals. The registry provides a pragmatic perspective on real-world evidence about care in surgical settings through convenience sampling of patients. The study cohort included adult patients aged 18 years and older who underwent 1 of 15 surgical procedures between January 1, 2018 and May 31, 2019 across the state of Michigan. Surgical procedures included laparoscopic appendectomy, laparoscopic cholecystectomy, inguinal/femoral hernia repair, ventral/incisional hernia repair, laparoscopic colectomy, laparoscopic antireflux surgery, open cholecystectomy, open appendectomy, open colectomy, open small bowel procedures, colostomy procedures, laparoscopic hysterectomy, vaginal hysterectomy, total abdominal hysterectomy, and thyroidectomy.[9–11] Patients reported data by completing postoperative surveys that were administered via a combination of telephone, email, or mail between postoperative days 30–90.[12]

Outcome

The primary outcome was the number of pills of opioids consumed after discharge from surgery as reported by patients. Patient-reported opioid consumed was calculated for each included procedure. The amount of opioids was standardized by calculating the standardized doses of oral morphine equivalents based on the type of opioid and number of pills consumed by the patient.[13] For convenience of analysis and reporting in this investigation, this amount of opioids was converted into the number of pills of oxycodone 5 mg, which is equivalent to 7.5 mg of oral morphine. The main focus for this investigation was the pattern of opioid consumption, which included the proportion of patients who reported consuming no opioids, as well as the amount of opioids that would satisfy the needs for 75% of patients (ie, the 75th percentile). We also had an additional focus on additional clinically relevant percentiles (ie, the 50th percentile, the 90th percentile).

Patterns of consumption and estimating their distribution

One shortcoming of the field is that no models have traditionally been used in the past to estimate opioid consumption after surgery. Conventional methods to calculate estimates and precision in medical fields rely on central measures of tendency (ie, 50th percentile), but recommendations for opioid consumption after surgery typically anchor to the 75th percentile to accommodate the needs of most patients, which requires a different statistical approach. To address this gap, estimates of the distribution of opioid consumption were calculated for each surgical procedure after examining descriptive statistics. We visualized opioid consumption data specific to each procedure, which revealed positively skewed patterns and a significant proportion of patients reporting no opioid use.

To account for the characteristics of the data, we considered both parametric and non-parametric methods to approximate the pattern of consumption.[14] The parametric approach used two predefined approaches: (1) the Tweedie model, which has been previously described as a special case of an exponential distribution model with flexibility to adapt to various commonly used continuous distributions (eg, normal, Poisson, Gamma)[15 16] and (2) the zero-inflated Poisson model, which allows for frequent observations for values of zero, which happens when many patients report consuming zero opioids.[17 18] For a non-parametric (or distribution-free) approach, we employed the kernel density estimation.[19]

We then compared distribution density plots, quantile-quantile plots and Kolmogorov-Smirov test statistics to identify the best model.[20] We found that the Tweedie model performed better than the zero-inflated Poisson model across all types of surgical procedures, and the values from the Tweedie model were also close to the values from the non-parametric estimation (see online supplemental materials eTable 1 and eTable 2 for comparison data). For further comparison of the Tweedie and non-parametric estimation, we computed variations of sample size estimates using resampling (bootstrap) approach (see online supplemental materials eMethods for additional explanation).

Sample size determination

We calculated the sample size required to yield a desired precision of opioid consumption that would meet the need of most patients across a range of precisions, in which the width of the 95% CIs was specified. We considered several fixed interval lengths to calculate sample sizes, including a 5-pill interval as the most clinically relevant 95% CI width. Calculations used the Tweedie model and were procedure specific. Sample sizes were then compared by procedure type for various percentiles.

Estimates of precision

The width of the 95% CI for percentile was used to represent the main measure of precision. We calculated 95% CIs for

Table 1 Characteristics of opioid consumption by type of surgical procedure

Procedure type	Descriptive statistics			Zero values	Range and percentiles				
	N	Mean	SD	N (%)	Min	p25	p50	p75	Max
Laparoscopic appendectomy	957	4.7	5.2	261 (27)	0	0	3	7	59
Open small bowel resection or enterolysis	90	5.9	6.8	34 (38)	0	0	3	10	28
Open appendectomy	65	4.9	5.7	21 (32)	0	0	3	8	24
Creation, resiting, or closure of ileostomy or colostomy	85	7.1	8.4	29 (34)	0	0	5	12	36
Open cholecystectomy	64	6.9	7.2	17 (27)	0	0	5.5	10	30
Laparoscopic cholecystectomy	2792	4.5	5.5	773 (28)	0	0	3	7	75
Abdominal hysterectomy	371	8.6	8.8	73 (20)	0	2	6	13	53
Minor hernia	3308	5.1	6.3	911 (28)	0	0	3	8	73
Major hernia	465	5.9	7.1	129 (28)	0	0	4	9	40
Open colectomy	351	7.7	10.2	105 (30)	0	0	5	11	80
Laparoscopic hysterectomy	1008	6.0	7.3	248 (25)	0	1	4	10	100
Vaginal hysterectomy	476	6.1	6.7	120 (25)	0	0	4	10	37
Laparoscopic antireflux	87	4.0	5.6	31 (36)	0	0	1	6	30
Thyroidectomy	155	3.3	5.9	62 (40)	0	0	1	4	40
Laparoscopic colectomy	414	5.8	8.9	162 (39)	0	0	2	8	60

Opioid consumption measured as oxycodone 5 mg pills, equivalent to 7.5 oral morphine equivalents.

patient-reported opioid consumption that would satisfy the needs of most patients (ie, the 75th percentile), as well as other relevant percentiles, using the Tweedie model. We considered a significance level of 0.05. All analyses were performed using R statistical software (R core team, 2020).

RESULTS

A total of 10,688 patients from 15 types of surgery contributed data included in this analysis. Sample sizes specific to each procedure ranged from 64 for open cholecystectomy to 3308 for inguinal/femoral hernia (table 1). The median number of pills of opioids reported as consumed by patients in the first 30 days after discharge from surgery was lowest for two types of surgery, laparoscopic antireflux surgery and thyroidectomy, at 1 pill and was highest for abdominal hysterectomy at 6 pills. Opioid consumption to satisfy the needs for most patients (ie, the 75th percentile) ranged from 4 pills for thyroidectomy to 13 pills for total abdominal hysterectomy.

Patterns of patient-reported opioid consumption after surgery

The pattern of patient-reported opioid consumption included a high proportion of patients who consumed no pills, which ranged from 20% for abdominal hysterectomy to 40% for thyroidectomy. This feature, combined with overall low quantities of pills consumed after surgery, resulted in positively skewed distributions for all fifteen surgical procedures. For example, laparoscopic cholecystectomy had a larger sample size and more compact distribution when compared with open cholecystectomy, resulting in greater estimates of precision for the former surgical procedure (figure 1).

Sample sizes required for patient-reported opioid consumption after surgery

Sample sizes for opioid consumption to meet the needs of most patients within a 5-pill 95% CI identified laparoscopic appendectomy and laparoscopic cholecystectomy as the surgical procedures with the need for the smallest number of patients, with samples of 48 and 62, respectively (table 2). In contrast, a sample of 188 was required to achieve a similar 5-pill 95% CI for open colectomy. Compared with laparoscopic cholecystectomy, approximately threefold more patients would be required for the sample size for open cholecystectomy to be sufficient to estimate opioid consumption within a 5-pill 95% CI for most patients, and the difference increased when considering meeting the needs at the 90th percentile (figure 2). Overall, these relationships appeared similar for sample sizes required to estimate opioid consumption within precise intervals at the 50th and 90th percentiles for other surgeries (online supplemental materials eTables 3–5). Examination of sample sizes for 50th, 75th, and 90th percentiles revealed that the Tweedie model generally performed to a better degree than the non-parametric model (see online supplemental materials eTables 6–8).

Estimates of precision for patient-reported opioid consumption after surgery

The width of 95% CIs for opioid consumption to meet the needs of most patients (ie, at 75th percentile) ranged from 0.7 pills for laparoscopic cholecystectomy to 7.0 pills for creation, resiting, or closure of ileostomy or colostomy (figure 3). Estimates for the width of 95% CIs were less than or equal to 5 pills for 73% (11/15) of procedures, including laparoscopic hysterectomy, laparoscopic appendectomy, minor hernia, and laparoscopic cholecystectomy. These relationships were generally consistent when estimating the number of pills required to meet the consumption needs of patients at the 50th and 90th percentiles (online supplemental materials eTable 9).

DISCUSSION

This analysis of patient-reported opioid consumption from a large sample of patients undergoing 15 common surgical procedures suggests that only small to moderate sample sizes are required to generate evidence to inform opioid prescribing guidelines. For example, sample sizes needed to inform opioid prescribing guidelines to satisfy most patients after surgery were under 200 at 5-pill intervals for all procedures. Further, many patients reported not consuming opioids after different types of procedures. Several estimates have robust precision for opioid

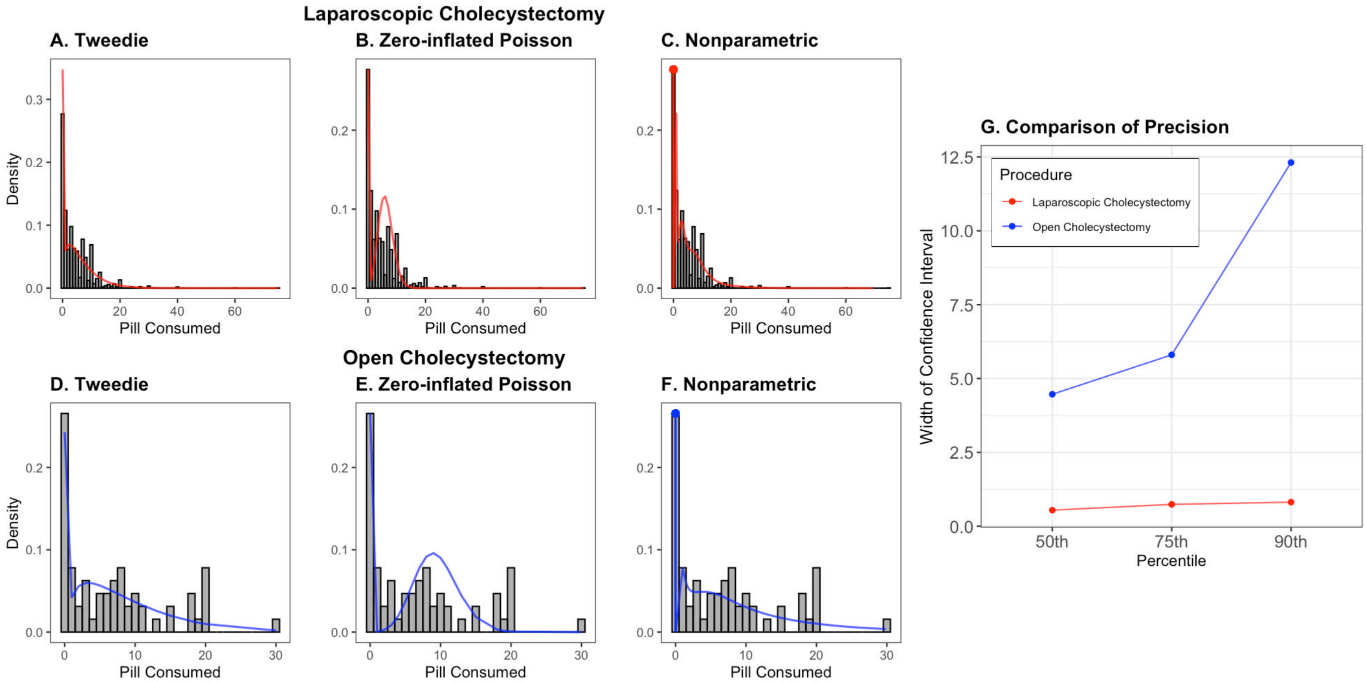


Figure 1 Comparing the patterns of consumption and CIs for laparoscopic cholecystectomy (N=2792) and open cholecystectomy (N=64) the patterns of consumption (ie, density) of laparoscopic cholecystectomy samples estimated through the Tweedie model, the ZIP model, and the non-parametric method are plotted, respectively (A, B, C). The pattern of consumption for open cholecystectomy was also estimated and plotted through the above three methods (D, E, F). Finally, estimates length for 95% CIs at the 50th, 75th, and 90th percentiles differ for laparoscopic cholecystectomy and open cholecystectomy (G). ZIP, zero-inflated Poisson.

consumption to satisfy the needs of most patients after surgery (ie, the 75th percentile). The pattern of how many opioids patients consumed after each type of surgery aligned the best with the same distribution model. This suggests that while many aspects of recovery after surgery may differ based on the type of procedure, characteristics associated with opioid consumption likely share more similarities than differences among the group of surgical procedures included in this analysis. Moving forward, combining certain types of surgical procedures into the same category of recommendations, such as laparoscopic appendectomy and laparoscopic cholecystectomy, may be appropriate given such overlap in distributions without compromising the validity of the prescribing thresholds.

Quality and safety initiatives to better align opioid use with patient needs after surgery have shown significant promise in reducing prescriptions given by surgeons while preserving the ability of patients to obtain sufficient relief after several types of procedures.[21] Prior to these efforts, patients reported

Table 2 Sample sizes for opioid consumption at the 75th percentile by type of surgical procedure

	Width of 95% CI						
Procedure type	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill
Laparoscopic appendectomy	6	12	48	75	132	297	1186
Laparoscopic cholecystectomy	7	16	62	96	170	382	1527
Laparoscopic antireflux	8	18	71	110	195	438	1751
Open appendectomy	8	18	71	111	197	442	1765
Minor hernia	10	21	83	129	229	515	2058
Open cholecystectomy	10	22	87	136	241	542	2166
Thyroidectomy	11	24	93	146	258	581	2322
Major hernia	11	25	98	153	272	612	2445
Vaginal hysterectomy	12	26	101	158	280	629	2516
Open small bowel resection or enterolysis	13	28	111	173	307	689	2755
Laparoscopic hysterectomy	14	32	125	195	346	778	3110
Abdominal hysterectomy	16	36	144	225	399	898	3590
Laparoscopic colectomy	19	42	166	260	461	1037	4145
Creation, resiting, or closure of ileostomy or colostomy	19	42	168	263	467	1050	4197
Open colectomy	21	47	188	293	521	1172	4685

Estimates use the Tweedie model.

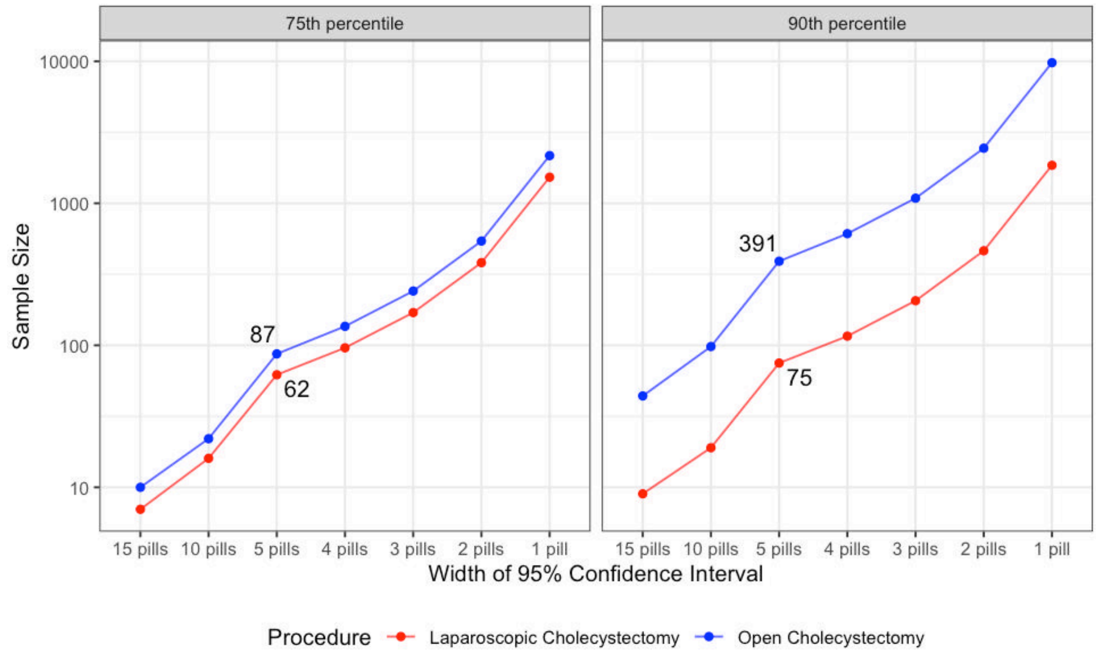


Figure 2 Comparing required sample size and CIs for laparoscopic cholecystectomy and open cholecystectomy the graph depicts the sample size required to obtain a CI at or below the estimated width for laparoscopic cholecystectomy (red line) and open cholecystectomy (blue line) at both the 75th percentile and 90th percentile. Estimates of sample size were computed using the Tweedie distribution. The y-axis is set to the log10 scale.

significant amounts of leftover opioid pills after surgery, with estimates ranging from two-thirds to three-fourths of all opioid pills.[22 23] Prescribing guidelines created by surgeons and other perioperative team members serve as one of the most prominent tools to tackle this problem within the surgical community. Prescribing guidelines have evolved over time, from relying on the consensus of caregivers to tracking actual consumption of patients.[10 24–26] Improving the base of evidence for these recommendations has led to a reduction in the recommended number of pills to prescribe after some of the most commonly performed surgical procedures. For example, the number of pills recommended to prescribe after laparoscopic colectomy in 2016 was 25 pills in October 2017, 20 pills in March 2018, 0–15 pills in January 2019, and more recently 0–10 pills in

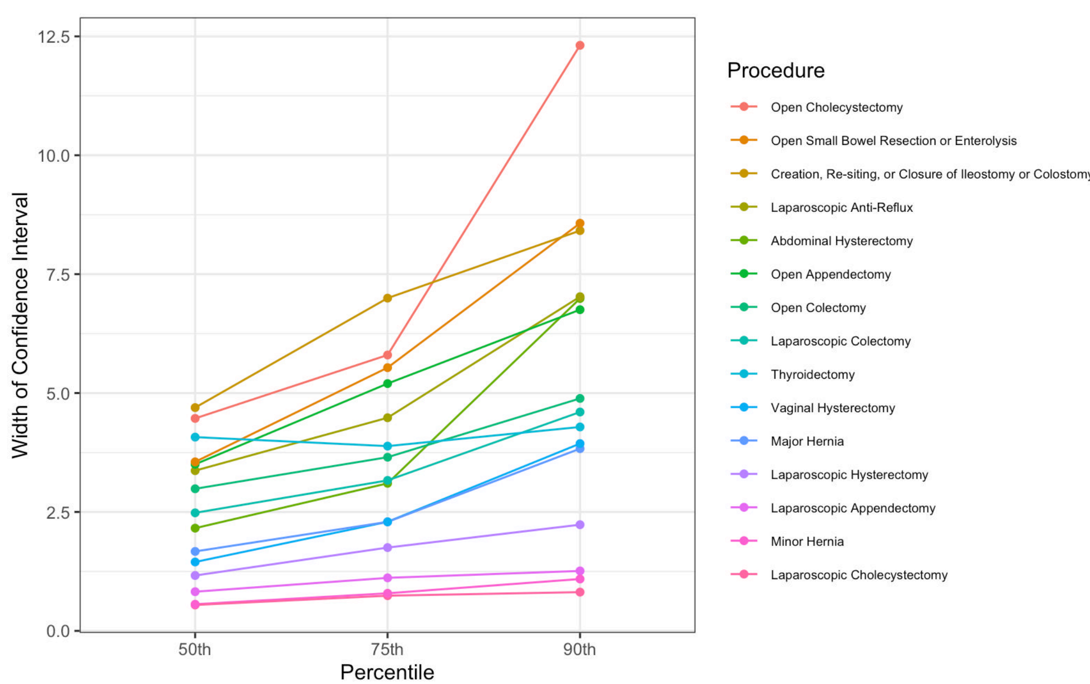


Figure 3 Width of CIs in pills of opioids consumed at the 50th, 75th, and 90th percentiles by type of surgical procedure lines display widths of 95% CIs for opioid consumption at the 50th, 75th and 90th percentiles specific to each type of surgical procedure based on study data. For example, the 95% CI width for opioid consumption to meet the needs of most patients (ie, at the 75th percentile) for laparoscopic cholecystectomy was 0.7 pills, while the same estimate for creation, resiting, or closure of ileostomy or colostomy was 7.0 pills. Estimates of CI widths were computed using the Tweedie distribution.

January 2020.[11 21] This evolution in recommendations builds on continued efforts to engage with surgical stakeholders, track consumption, and monitor patient-reported outcomes after surgery, a feedback loop essential to monitor for the potential for such reductions to result in increases in uncontrolled pain. Advances in the approach to measuring consumption and providing accurate recommendations in guidelines represent the next step in enhancing the quality and safety of patient recovery after surgery.

Prescription opioids have historically been emphasized as the gold standard for pain relief, despite evidence that other types of medications may confer superior pain relief for acute pain.[27] For example, taking a combination of non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen results in better acute pain relief than certain doses of opioids like oxycodone. The ability to maximize the use of NSAIDs and acetaminophen may also impact how much opioids are consumed by patients after surgery, though such non-opioid alternatives remain underused despite recommendations for their use as first-line analgesics in the postoperative period. Opioid prescribing guidelines represent a key tool among many others in efforts to optimize pain control while maximizing patient safety after discharge from surgery. Utilization of minimally invasive surgical techniques, peripheral nerve blocks and catheters, and non-pharmacological treatments such as cold and cryo-based therapies all have the potential to spare opioids and improve pain-related outcomes for patients after surgery.

Estimating how many pills of opioids are consumed by patients after surgery, and the pattern of consumption, is critical to determine an optimal number of sample sizes for each procedure. The three methods to estimate the distribution of opioid consumption after surgery have different strengths. Parametric techniques rely on certain assumptions about the pattern of consumption that may not always be met. This method is useful when the model approximates the data well, which was the case in this analysis. However, if the pattern of consumption does not align well, this method can lead to improper estimates of precision and sample size. The gold standard is a non-parametric approach, but it has the downside of increasing the required sample size when compared with parametric methods that fit the data well. Findings in this study support the use of a specific parametric approach (ie, Tweedie), which may be applied in future investigations to determine the precision of estimates and adequate sample sizes to analyze patient-reported opioid consumption after surgery.

This analysis should also be considered in light of certain limitations. First, data on consumption reflects the characteristics of surgical procedures performed across several different hospitals that all reside within the state of Michigan. While common to one state, these surgical settings vary by rurality, practice environment, and payor type, and some of these characteristics may differ from other states, though the multicenter recruitment and large sample size allow for more reliable estimates across more than a dozen types of procedures. Second, data on opioid consumption, which is derived from patient reports, may be subject to recall bias, though clinical initiatives using these data sources have yielded improvements in clinical outcomes without adversely affecting pain outcomes. Third, this work did not focus on creating postoperative prescribing guidelines, and our methodology is not a traditional power analysis to determine the sample size based on a desired CI, given many initiatives to improve opioid prescribing include quality improvement initiatives that may include small sample sizes.

CONCLUSIONS

Estimates of sample size and precision for postdischarge opioid prescribing using the models described above provide important information to complement thresholds in prescribing guidelines. These estimates may directly inform patients about the range of needs that they experience when recovering at home after surgery, surgeons about the confidence of their recommendations, and other key stakeholders working to improve the safety and quality of surgical care. This knowledge also sharpens our understanding of the trade-off between sample sizes and precision essential to conducting more rigorous studies to improve quality and safety outcomes for patients undergoing general surgery and other types of surgical procedures.

Twitter Chad M Brummett @drchadb and Mark C Bicket @MarkBicket

Contributors JS helped design the study, acquire, analyze, and interpret the data, draft the initial manuscript, and critically revise the manuscript, and serves as the guarantor. YL helped design the study, draft the initial manuscript, and critically revise the manuscript. JFW helped interpret the data and critically revise the manuscript. VG helped acquire, analyze, and interpret the data, and critically revise the manuscript. CMB helped interpret the data and critically revise the manuscript. MJE helped interpret the data and critically revise the manuscript. MCB helped design the study, interpret the data, draft the initial manuscript, and critically revise the manuscript.

Funding This work was funded by the National Institute on Drug Abuse (R01DA042859).

Disclaimer No funder or sponsor had any role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

Competing interests JS, YL, and VG have no disclosures. CMB, MJE, JFW, and MCB receive funding from the Michigan Department of Health and Human Services and the National Institute on Drug Abuse (R01DA042859). CMB is a consultant for Heron Therapeutics, Vertex Pharmaceuticals, Alosa Health and the Benter Foundation, not related to this work. JS had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Patient consent for publication Not applicable.

Ethics approval The Institutional Review Board at the University of Michigan classified this investigation as exempt from regulation due to secondary analysis of deidentified data.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Data may be obtained from the Michigan Surgical Quality Collaborative.

ORCID iDs
Jiyeon Song http://orcid.org/0000-0002-2180-3625
Mark C Bicket http://orcid.org/0000-0001-9406-5953

REFERENCES

1 Barth RJ, Waljee JF. Classification of opioid dependence, abuse, or overdose in opioid-naive patients as a "never event" *JAMA Surg* 2020;155:543–4.
2 Hooten WM, Brummett CM, Sullivan MD, *et al*. A conceptual framework for understanding unintended prolonged opioid use. *Mayo Clin Proc* 2017;92:1822–30.
3 Bicket MC, Brat GA, Hutfless S, *et al*. Optimizing opioid Prescribing and pain treatment for surgery: review and conceptual framework. *Am J Health Syst Pharm* 2019;76:1403–12.
4 Committee on Evidence-Based Clinical Practice Guidelines for Prescribing Opioids for Acute Pain, Board on Health Care Services, Health and Medicine Division. Framing opioid Prescribing guidelines for acute pain. In: *Framing Opioid Prescribing Guidelines for Acute Pain*. Washington, D.C: National Academies Press, 2019.

5 Porter ED, Bessen SY, Molloy IB, *et al*. Guidelines for patient-centered opioid Prescribing and optimal FDA-Compliant disposal of excess pills after inpatient operation. *J Am Coll Surg* 2021;232:823–35.
6 Robinson KA, Thiels CA, Stokes S, *et al*. Comparing clinician consensus recommendations to patient-reported opioid use across multiple hospital systems. *Ann Surg* 2022;275:e361–5.
7 Thiels CA, Ubl DS, Yost KJ, *et al*. Results of a prospective, multicenter initiative aimed at developing opioid-Prescribing guidelines after surgery. *Ann Surg* 2018;268:457–68.
8 Thiels CA, Anderson SS, Ubl DS, *et al*. Wide variation and overprescription of opioids after elective surgery. *Ann Surg* 2017;266:564–73.
9 Howard R, Fry B, Gunaseelan V, *et al*. Association of opioid Prescribing with opioid consumption after surgery in Michigan. *JAMA Surg* 2019;154:e184234.
10 Howard R, Waljee J, Brummett C, *et al*. Reduction in opioid Prescribing through evidence-based Prescribing guidelines. *JAMA Surg* 2018;153:285–7.
11 Vu JV, Howard RA, Gunaseelan V, *et al*. Statewide implementation of postoperative opioid Prescribing guidelines. *N Engl J Med* 2019;381:680–2.
12 Howard R, Brown CS, Lai Y-L, *et al*. The Association of postoperative opioid prescriptions with patient outcomes. *Ann Surg* 2022;276:e1076–82.
13 Centers for disease control and prevention. CDC file of national drug codes for selected benzodiazepines, muscle Relaxants, stimulants, opioid Analgesics, and linked oral morphine milligram equivalent conversion factors for opioids, 2019 version. *Published* 2020. Available: https://www.cdc.gov/drugoverdose/resources/data.html
14 Cheung KY, Lee SMS. Variance estimation for sample Quantiles using them out of N Bootstrap. *Ann Inst Stat Math* 2005;57:279–90.
15 Qian W, Yang Y, Zou H. Tweedie's compound Poisson model with grouped elastic net. *Journal of Computational and Graphical Statistics* 2016;25:606–25.
16 Jørgensen B. Exponential dispersion models. *Journal of the Royal Statistical Society: Series B (Methodological)* 1987;49:127–45. 10.1111/j.2517-6161.1987.tb01685.x Available: http://doi.wiley.com/10.1111/rssb.1987.49.issue-2
17 Lee AH, Wang K, Scott JA, *et al*. Multi-level zero-inflated Poisson regression Modelling of correlated count data with excess zeros. *Stat Methods Med Res* 2006;15:47–61.
18 Mugenyi A, Muhanguzi D, Hendrickx G, *et al*. Spatial analysis of G.F.Fuscipes abundance in Uganda using Poisson and zero-inflated Poisson regression models. *PLoS Negl Trop Dis* 2021;15:e0009820.
19 Läuter H. Density estimation for statistics and data analysis. *Biometrical J* 1988;30:876–7.
20 Massey FJ. The Kolmogorov-Smirnov test for goodness of fit. *Journal of the American Statistical Association* 1951;46:68–78.
21 Brown CS, Vu JV, Howard RA, *et al*. Assessment of a quality improvement intervention to decrease opioid Prescribing in a regional health system. *BMJ Qual Saf* 2021;30:251–9.
22 Bicket MC, Long JJ, Pronovost PJ, *et al*. Prescription opioid Analgesics commonly unused after surgery: A systematic review. *JAMA Surg* 2017;152:1066–71.
23 Schirle L, Stone AL, Morris MC, *et al*. Leftover opioids following adult surgical procedures: a systematic review and meta-analysis. *Syst Rev* 2020;9:139.
24 Overton HN, Hanna MN, Bruhn WE, *et al*. Opioid-Prescribing guidelines for common surgical procedures: an expert panel consensus. *J Am Coll Surg* 2018;227:411–8.
25 Hill MV, Stucke RS, Billmeier SE, *et al*. Guideline for discharge opioid prescriptions after inpatient general surgical procedures. *J Am Coll Surg* 2018;226:996–1003.
26 Fujii MH, Hodges AC, Russell RL, *et al*. Post-discharge opioid Prescribing and use after common surgical procedure. *J Am Coll Surg* 2018;226:1004–12.
27 Moore RA, Derry S, Aldington D, *et al*. Single dose oral Analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database Syst Rev* 2015;2015:CD008659.

Appendix for:

Song J, Li Y, Waljee JF, Gunaseelan V, Brummett CM, Englesbe M, Bicket, MD. What Evidence is Needed to Inform Postoperative Opioid Consumption Guidelines? A Cohort Study of the Michigan Surgical Quality Collaborative. *Reg Anesth Pain Med* 2023. DOI: rapm-2023-104581

eMethods. Additional methods explanation with equations

We determined the necessary sample size of the desired percentile by utilizing the asymptotic normality method. Let ξ_p be the unique p-th quantile and $\widehat{\xi_p}$ be its sample counterpart. Denote f to be the density function. Then, we can derive the asymptotic distribution:

$$\sqrt{n}\left(\widehat{\xi_p} - \xi_p\right) \to N\left(0, \frac{p(1-p)}{f\left(\xi_p\right)^2}\right),$$

and therefore, the 95% confidence interval of ξ_p is written as

$$\widehat{\xi_p} \pm 1.96\sqrt{\frac{p(1-p)}{n \times \hat{f}\left(\widehat{\xi_p}\right)^2}}.$$

By specifying the interval length d such that $1.96\sqrt{\frac{p(1-p)}{n \times \hat{f}\left(\widehat{\xi_p}\right)^2}} = d/2$, the formula for the sample size is given as follows:

$$n \geq \frac{p(1-p)}{\left[\frac{d}{2 \times 1.96} \times \hat{f}\left(\widehat{\xi_p}\right)\right]^2} \dots\dots\dots (1)$$

In practice, it is essential to estimate appropriate density $\hat{f}$ for the sample size determination. Our sample, in particular, had a significantly right-skewed distribution with excess zeros, making it critical to choose a suitable approach to account for these features. As a result, we looked at both parametric and nonparametric approaches: Tweedie and zero-inflated Poisson model for parametric fitting candidates, and a kernel density method for nonparametric fitting method.

Tweedie Model

The Tweedie model is used to model data with highly right-skewed distribution, which has probability mass at zero and nonnegative support and it is also known to be a special case of exponential dispersion models. The density of the Tweedie model is defined by

$$f_\rho(y; \mu, \sigma^2) = a(y, \sigma^2)\ exp\left[\frac{1}{\sigma^2}\left(\frac{y\mu^{1-\rho}}{1-\rho} - \frac{\mu^{2-\rho}}{2-\rho}\right)\right]$$

where the normalizing functions a is known, μ is a mean parameter, $\sigma^2 > 0$ is a dispersion parameter, and ρ is an additional shape parameter called a Tweedie power parameter. The mean and variance of the family of distributions are characterized by $E(y) = \mu$ and $Var(y) = \sigma^2\mu^p$. Note that the Tweedie family includes numerous familiar distributions by assigning different values of ρ.

ρ (Tweedie Power Parameter)	Distribution
0	Normal Distribution
1	Poisson Distribution
1<ρ<2	Compound Poisson/gamma distribution,
2	Gamma distribution
3	Inverse Gaussian distribution

Song J, *et al. Reg Anesth Pain Med* 2023;0:1–7. doi: 10.1136/rapm-2023-104581

In modeling opioid consumption, we particularly consider the case where the Tweedie power is between 1 and 2, which is the primary interest of this article and hence $\hat{f}$ in Equation (1) is replaced with $\widehat{f_{\hat{\rho}}}(\widehat{\xi_p}; \hat{\mu}, \hat{\sigma}^2)$ where $\hat{\rho}, \hat{\mu}$ and $\hat{\sigma}^2$ are estimated by maximum likelihood estimator.

Zero-inflated Poisson Model

A ZIP distribution is also commonly used for count variables to accommodate many zeroes and extreme outliers. The ZIP distribution consists of two parts: Poisson count model and the (zero) logit model for predicting excess zeros. This is designed to account for zeroes on the assumption that zero and nonzero counts are modeled separately. Under the zero-inflated Poisson model assumptions, the density can be written as

$$f(y;\ \lambda, \pi) = \{\pi + (1-\pi)e^{-\lambda}, if\ y = 0, (1-\pi)\frac{\lambda^y e^{-\lambda}}{y!}, if\ y = 1, 2, \ldots$$

where the outcome variable y_i has non-negative integer values, λ is the expected Poisson count for the$i$the individual, and π is the probability of extra zeros. We derived the maximum likelihood estimates of the two parameters, $\hat{\lambda}$ and $\hat{\pi}$, and obtained the sample size using the substitution of $\hat{f}(\widehat{\xi_p};\ \hat{\lambda}, \hat{\pi})$ for $\hat{f}$ in Equation (1). The result of parameter estimations is presented in **eTable 1**.

Kernel Density Estimation

The kernel density estimation (KDE) is one of the most popular nonparametric methods for density estimation. To calculate the final density estimate, the KDE smooths each data point X_i into little density bumps and then adds all of these small bumps together. The estimated probability density function is calculated by

$$\hat{f}_n(x) = \frac{1}{nb} K(\frac{X_i - x}{b}),$$

where $K(\cdot)$ is a kernel function which is commonly chosen from a symmetric function such as Gaussian function, and b is a bandwidth that controls the level of smoothness, and we chose the bandwidth through a biased cross validation. To cope with mass zeros, we estimated the spike using the proportion of zeros, and the density of the others is estimated via log transformation.

Examination of distributions

We employed both testing and illustrative approaches to determine the model assumptions. For testing, the Kolmogorov-Smirnov test is used to decide if a sample comes from a population with estimated Tweedie or ZIP distributions. The test statistics are reported in **eTable 1** and we see that the test statistic for Tweedie is smaller than the ZIP, implying that the Tweedie is more appropriate for each procedure.

For an illustrative approach, we employed density plots and Q-Q plots to illustrate the model assumption determination (**eTable 2**). We plotted the densities of sample distributions overlaid with the estimated distributions, with the latter plotted in the red line. For all surgical procedures, the Tweedie model's estimated distribution much more closely aligns with the sample data compared to the zero-inflated Poisson model. This result is also consistent with Q-Q plots, which is created by plotting two sets of quantiles against one another. If both sets of quantiles came from the same distribution, we should see the points forming a roughly straight line. The QQ plot for the Tweedie model has straighter lines than the zero-inflated Poisson model.

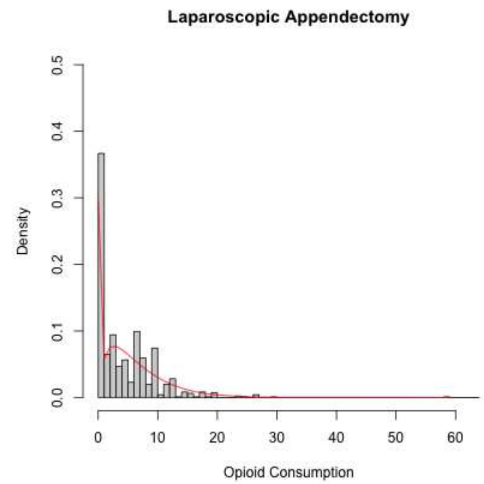
Moreover, in comparison to parametric and nonparametric methods, we evaluate the variability using the bootstrap resampling method. We first drew 100 bootstrap samples with replacement with the original sample size. Here we added noise generated from the uniform distribution within a range between 0 and 1 to the bootstrap sample because the data is discrete; therefore, employing generic bootstrap samples results in little change in sample quantiles. Then, we calculate a sample size for each bootstrap applying both parametric and nonparametric approaches. Lastly, we determined the standard deviation of the calculated sample sizes. In our experiment, the Tweedie model has a smaller variability for the sample sizes of smaller percentiles (50% and 75%) while the kernel density estimation method shows a smaller variability for large percentile (90%) sample sizes. However, the gap is small and thus we can conclude that they are comparable.

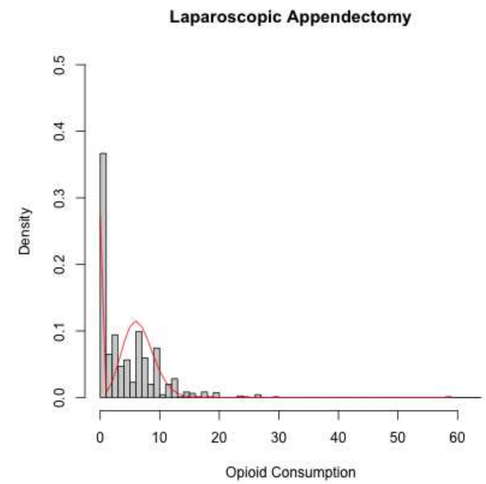
eTable 1. Parameter estimates for distribution models

Procedure type	Distribution model						
	Tweedie				Zero-inflated Poisson		
	Parameter estimates			Kolmogorov-Smirov statistic	Parameter estimates		Kolmogorov-Smirov statistics
	Tweedie power	mu	phi		lambda	phi	
Laparoscopic Appendectomy	1.324	4.714	3.505	0.082	6.471	0.272	0.171
Open Small Bowel Resection or Enterolysis	1.349	5.922	4.245	0.100	9.517	0.378	0.144
Open Appendectomy	1.355	4.892	3.741	0.108	7.222	0.323	0.169
Creation, Re-siting, or Closure of Ileostomy or Colostomy	1.361	7.082	4.882	0.059	10.750	0.341	0.165
Open Cholecystectomy	1.361	6.906	3.737	0.078	9.403	0.266	0.172
Laparoscopic Cholecystectomy	1.367	4.497	3.887	0.111	6.206	0.275	0.188
Abdominal Hysterectomy	1.380	8.642	3.989	0.075	10.758	0.197	0.243
Minor Hernia	1.386	5.132	4.165	0.106	7.077	0.275	0.210
Major Hernia	1.392	5.905	4.242	0.075	8.170	0.277	0.224
Open Colectomy	1.392	7.741	6.003	0.105	11.045	0.299	0.219
Laparoscopic Hysterectomy	1.398	6.021	4.297	0.109	7.983	0.246	0.218
Vaginal Hysterectomy	1.398	6.120	3.538	0.078	8.180	0.252	0.210
Laparoscopic Anti-Reflux	1.435	3.954	4.397	0.115	6.129	0.355	0.184
Thyroidectomy	1.435	3.252	6.346	0.213	5.395	0.397	0.206
Laparoscopic Colectomy	1.441	5.792	6.235	0.104	9.515	0.391	0.203

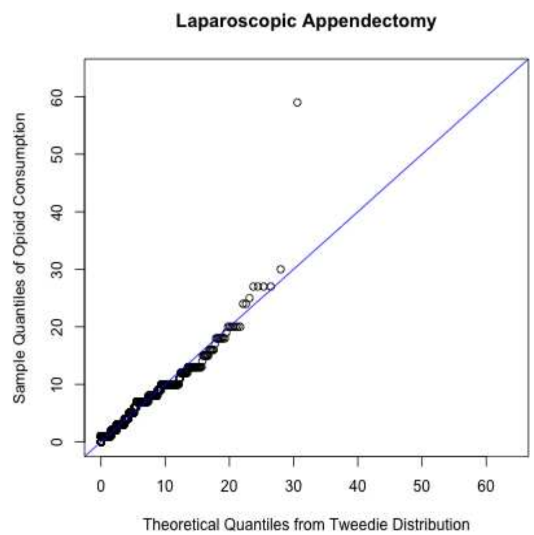
eTable 2. Comparison of density distributions and quantile-quantile plots for surgical procedures

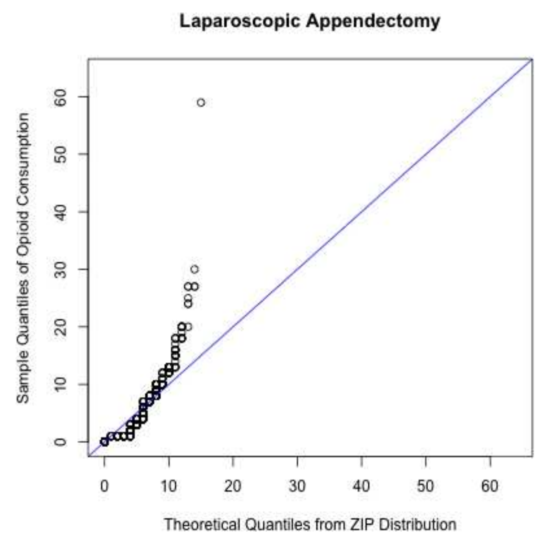
Procedure	Tweedie Model	Zero-inflated Poisson Model
Laparoscopic Appendectomy	Density Distributions	



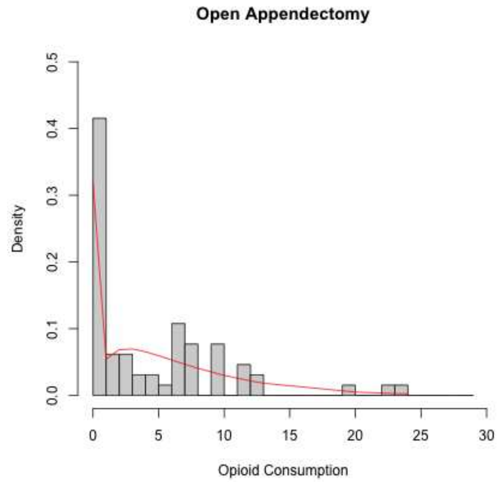


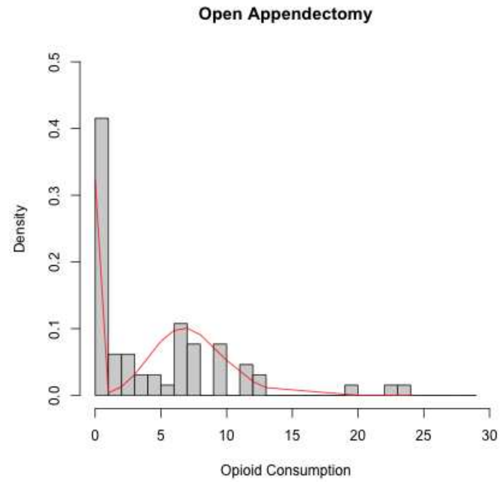
Q-Q Plots



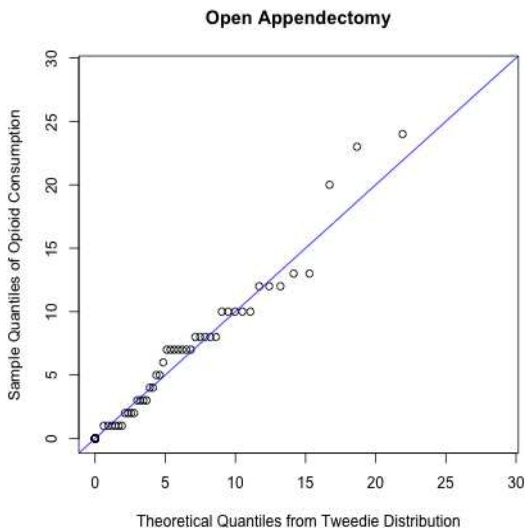


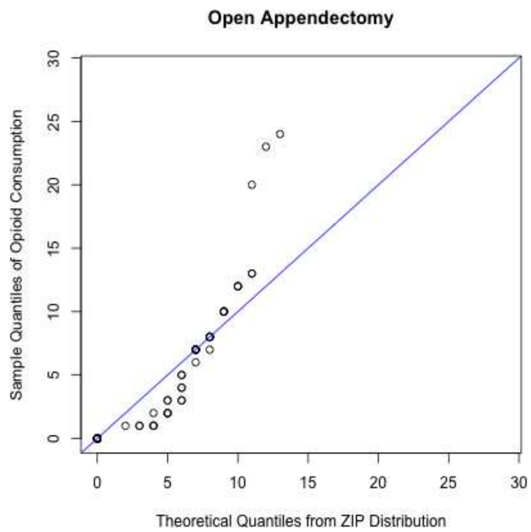
Procedure	Tweedie Model	Zero-inflated Poisson Model
Open Appendectomy	Density Distributions	



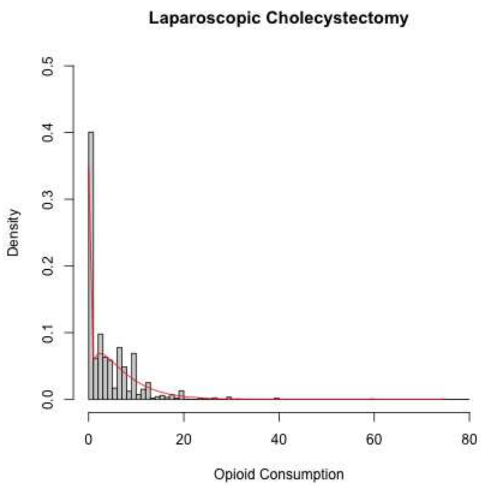


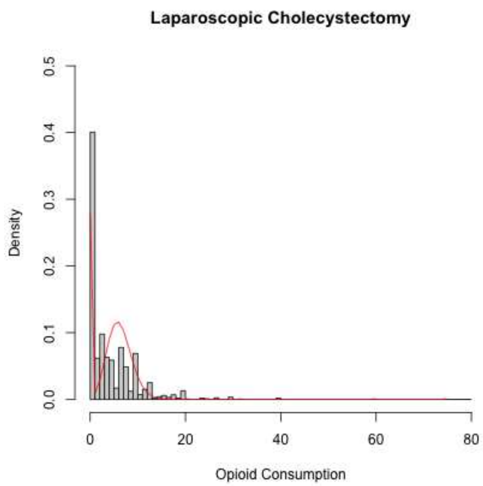
Q-Q Plots



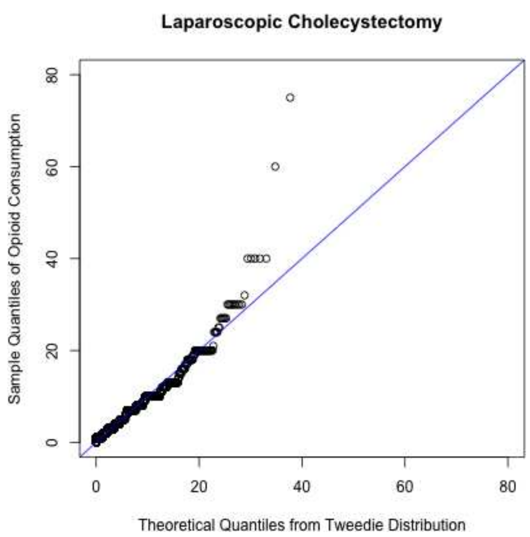


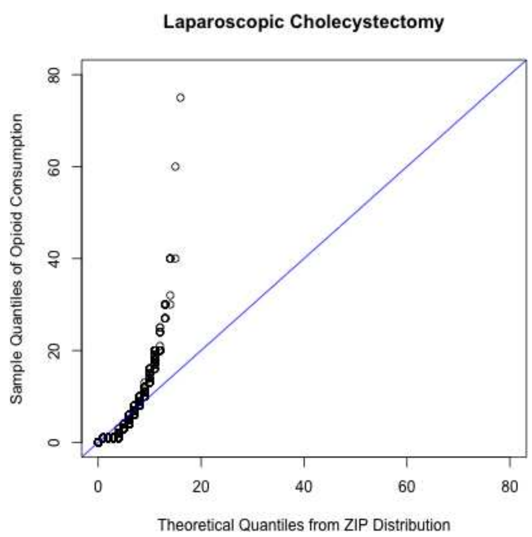
Procedure	Tweedie Model	Zero-inflated Poisson Model
Laparoscopic Cholecystectomy	Density Distributions	

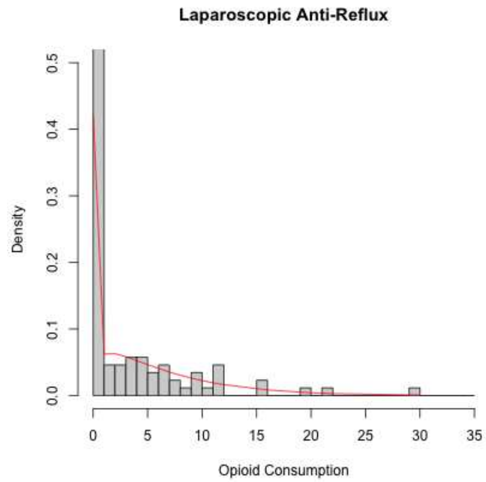
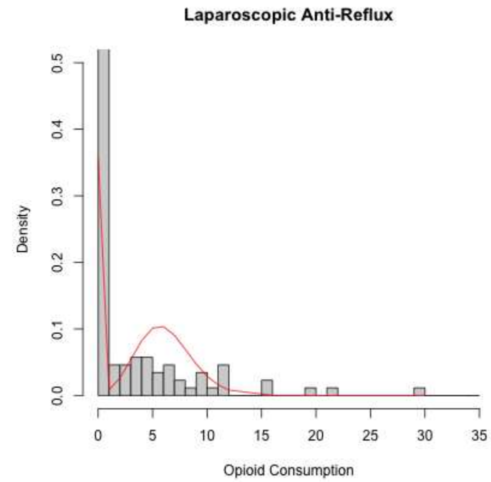
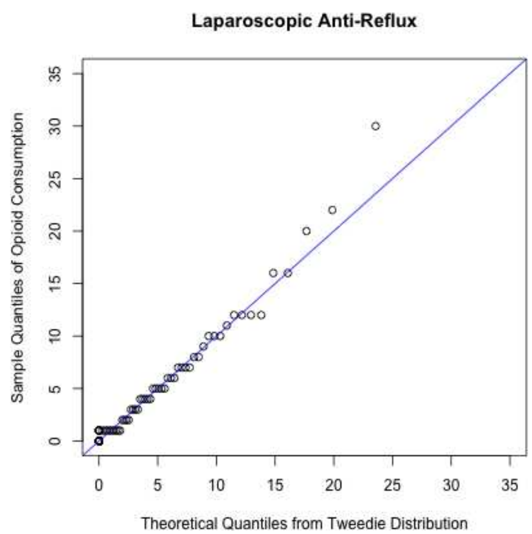
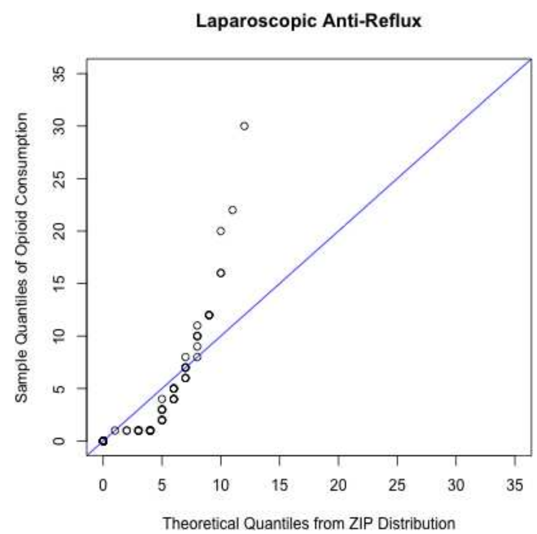




Q-Q Plots



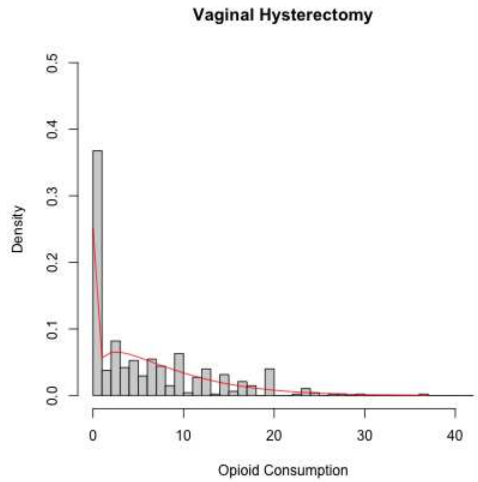


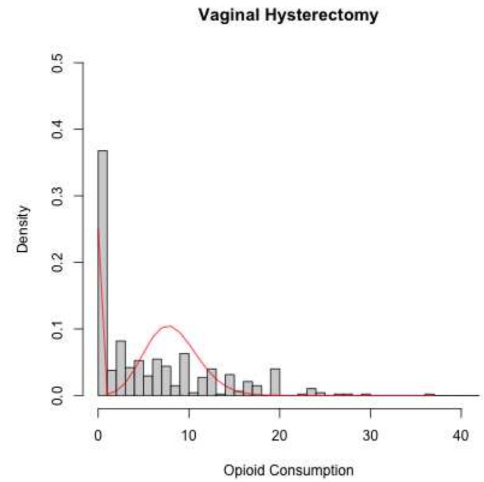
Procedure	Tweedie Model	Zero-inflated Poisson Model
Laparoscopic Anti-Reflux	Density Distributions	
		
	Q-Q Plots	
		

9

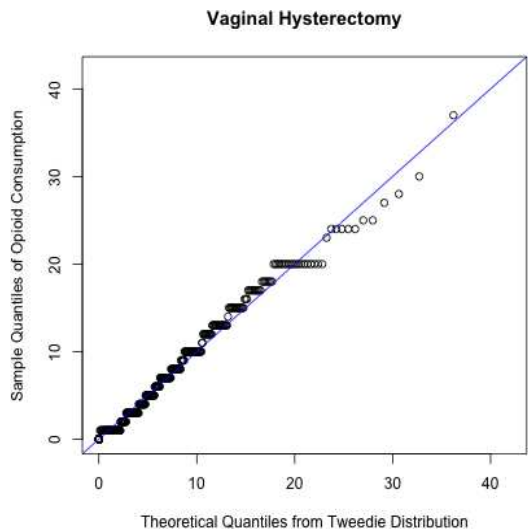
Procedure	Tweedie Model	Zero-inflated Poisson Model
Vaginal Hysterectomy		

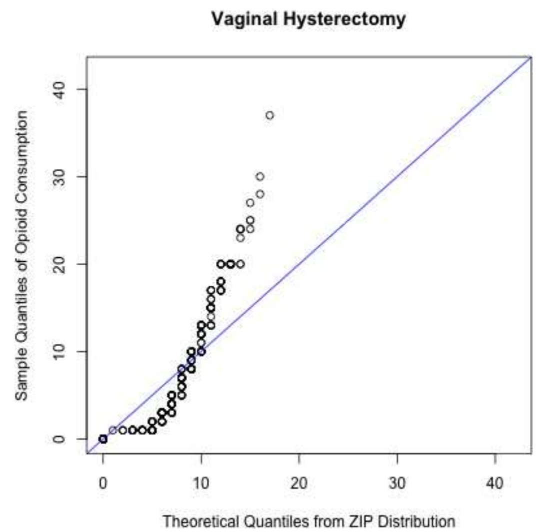
Density Distributions





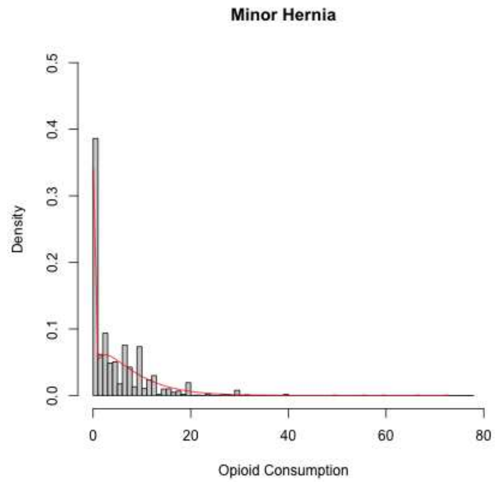
Q-Q Plots

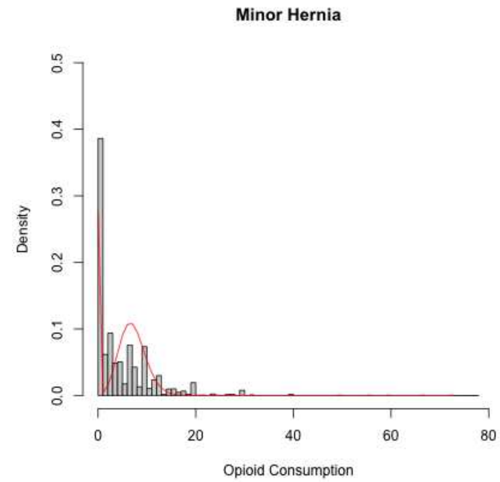




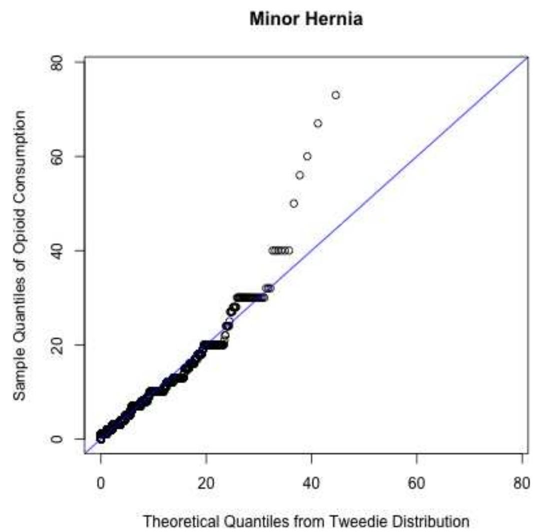
Procedure	Tweedie Model	Zero-inflated Poisson Model
Minor Hernia		

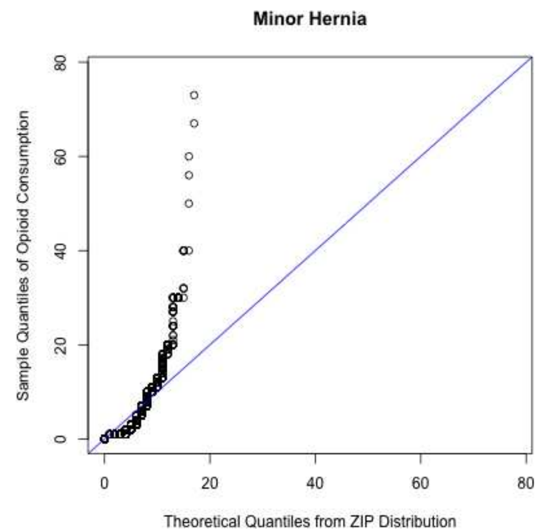
Density Distributions





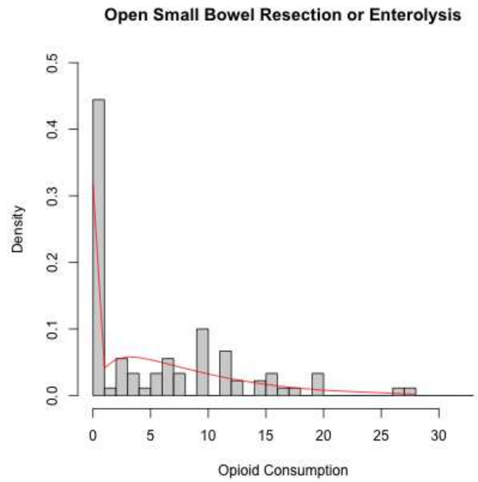
Q-Q Plots

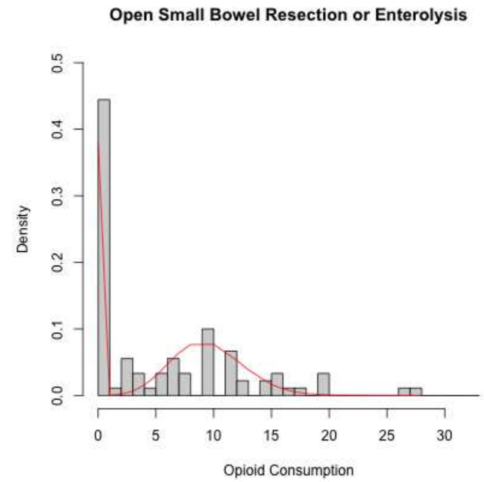




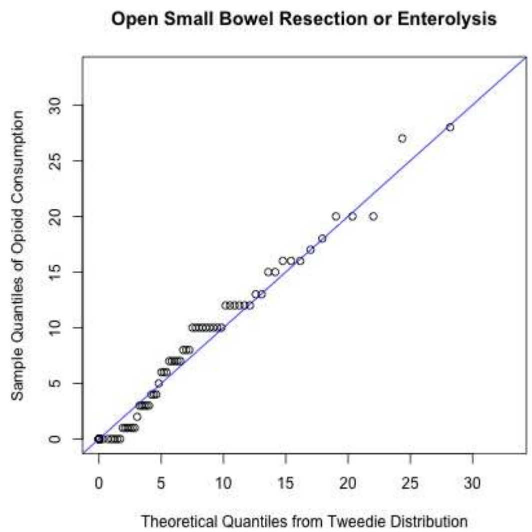
Procedure	Tweedie Model	Zero-inflated Poisson Model
Open Small Bowel Resection or Enterolysis		

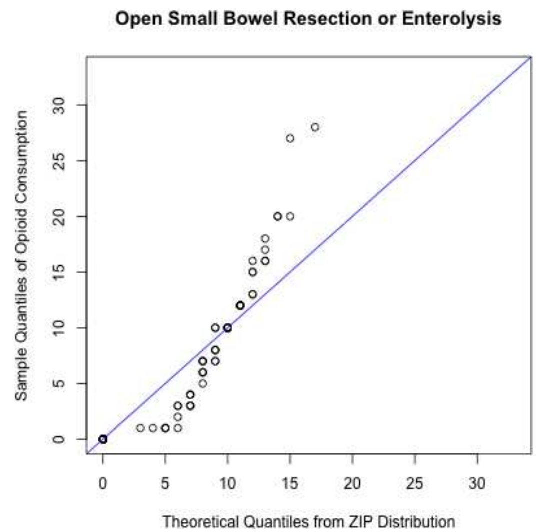
Density Distributions





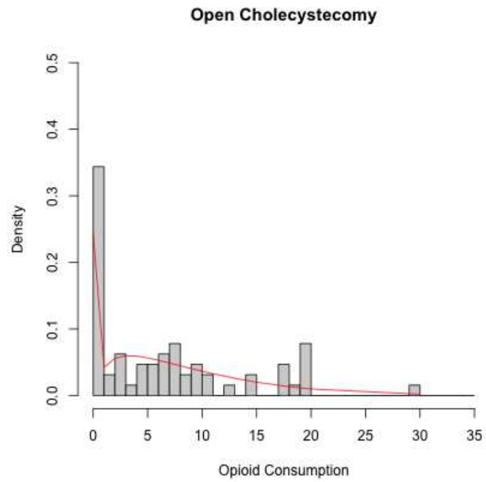
Q-Q Plots

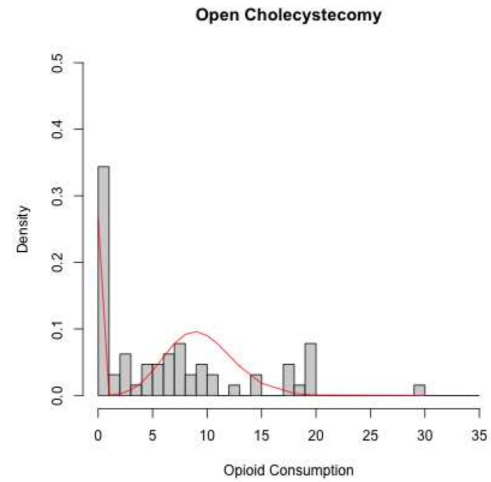




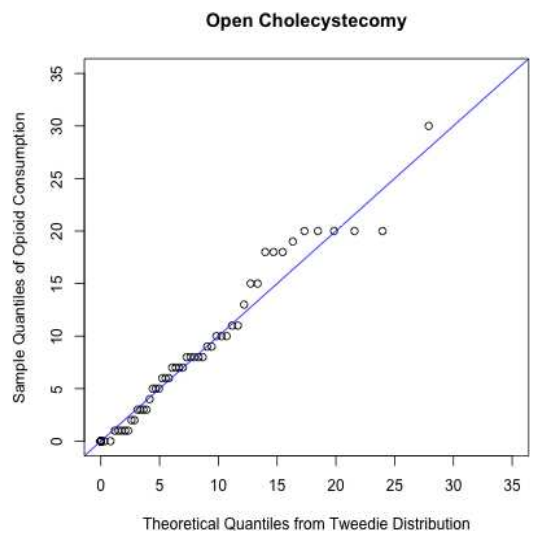
Song J, *et al. Reg Anesth Pain Med* 2023;0:1–7. doi: 10.1136/rapm-2023-104581

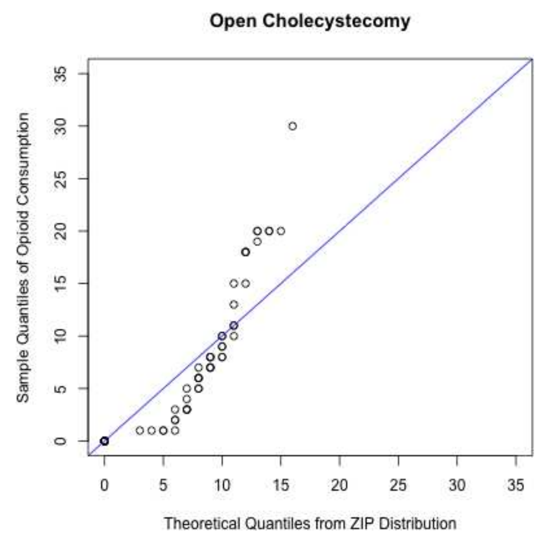
Procedure	Tweedie Model	Zero-inflated Poisson Model
Open Cholecystectomy	Density Distributions	



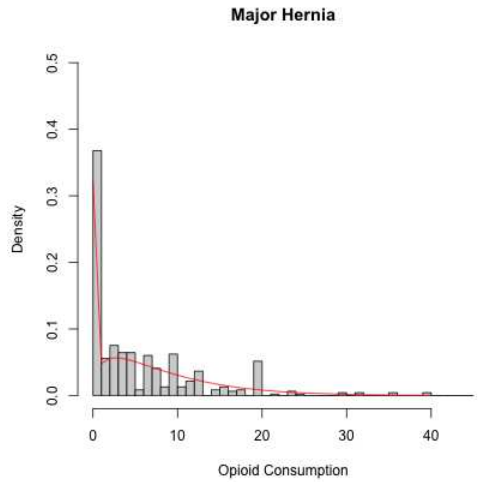


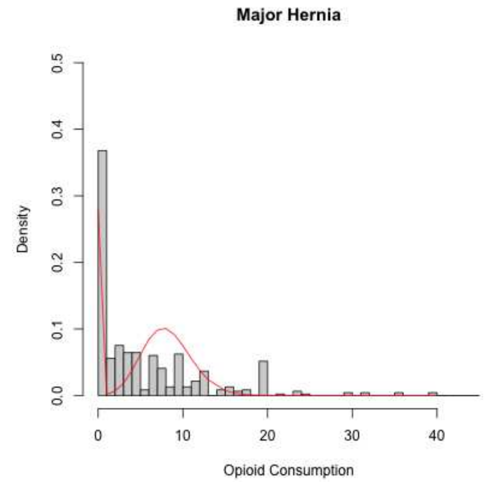
Q-Q Plots



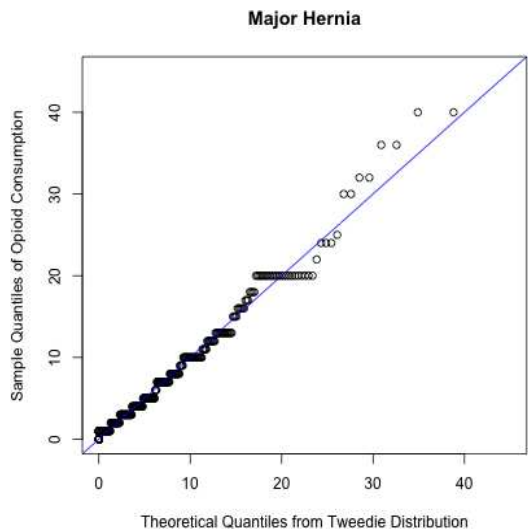


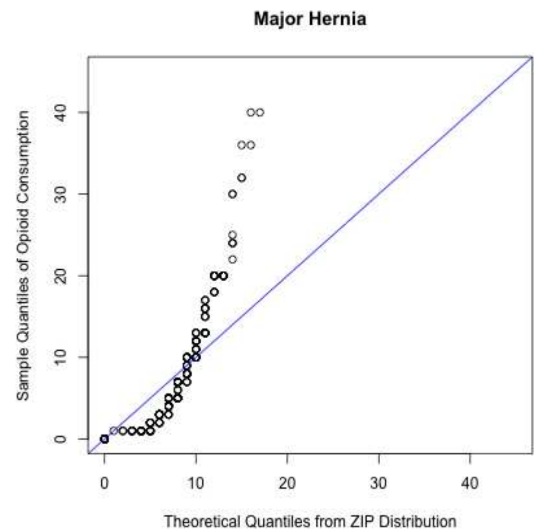
Procedure	Tweedie Model	Zero-inflated Poisson Model
Major Hernia	Density Distributions	





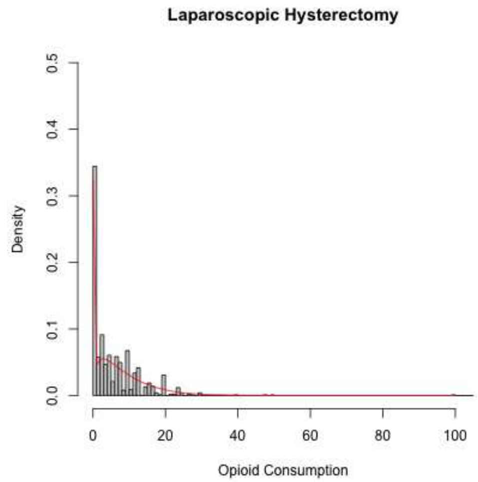
Q-Q Plots

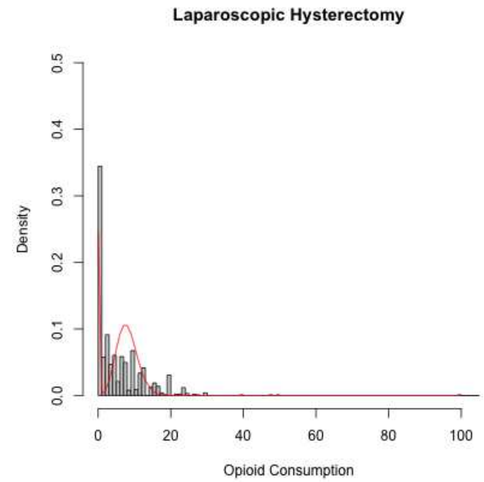




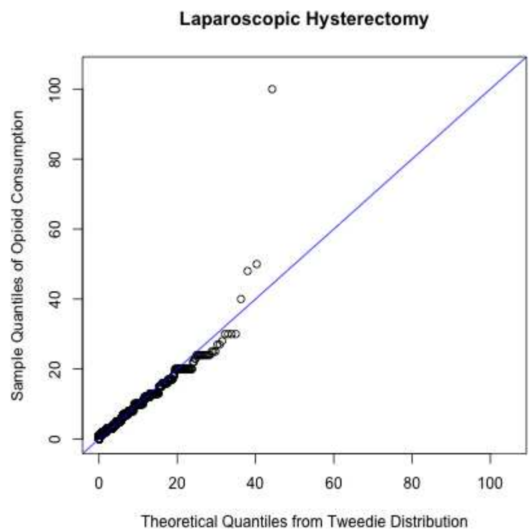
Song J, *et al. Reg Anesth Pain Med* 2023;0:1–7. doi: 10.1136/rapm-2023-104581

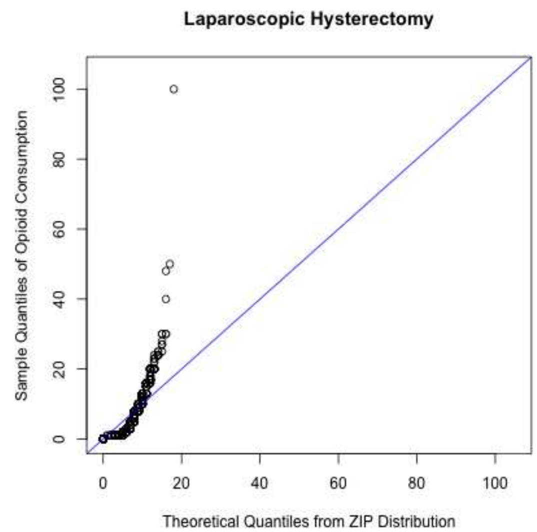
Procedure	Tweedie Model	Zero-inflated Poisson Model
Laparoscopic Hysterectomy	Density Distributions	





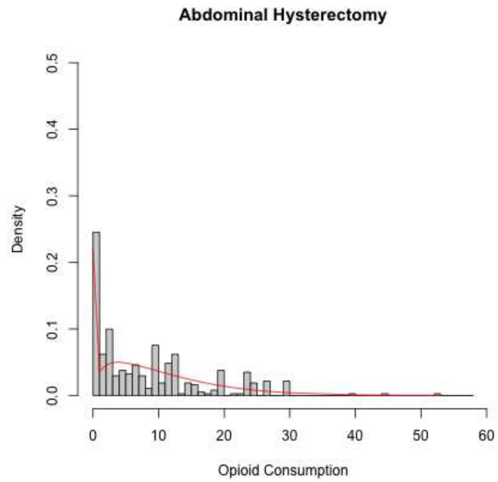
Q-Q Plots

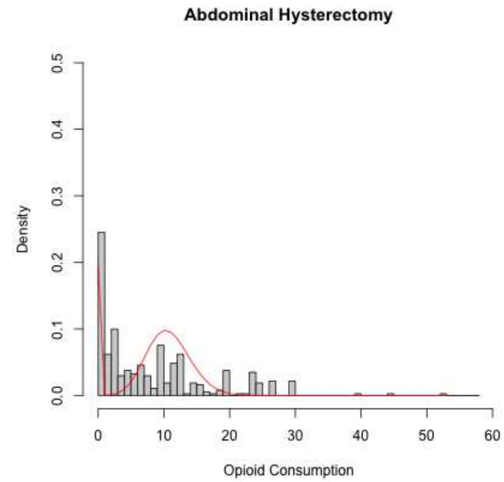




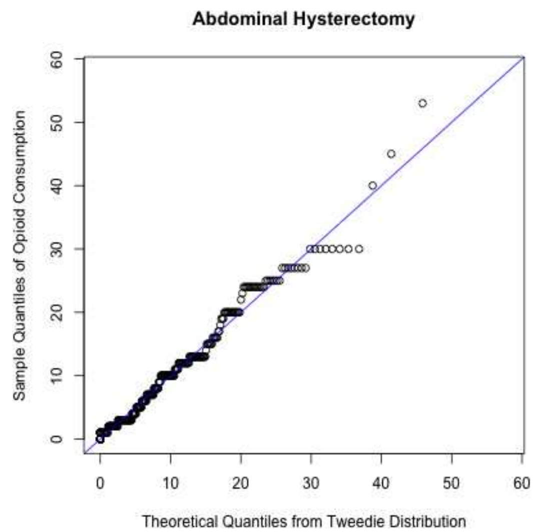
Song J, *et al. Reg Anesth Pain Med* 2023;0:1–7. doi: 10.1136/rapm-2023-104581

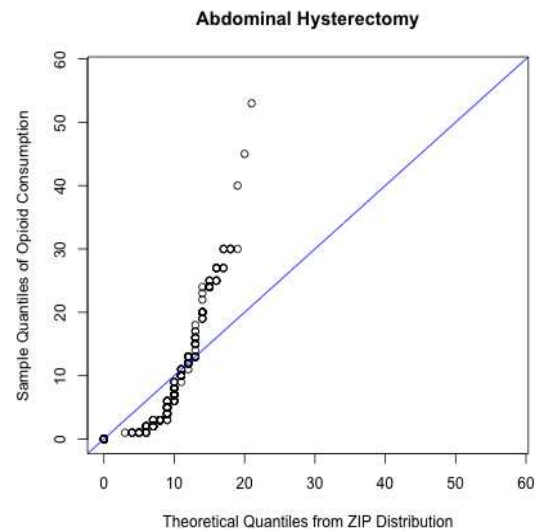
Procedure	Tweedie Model	Zero-inflated Poisson Model
Abdominal Hysterectomy	Density Distributions	





Q-Q Plots

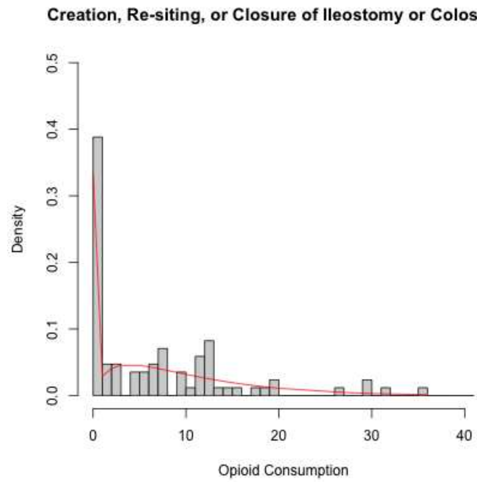


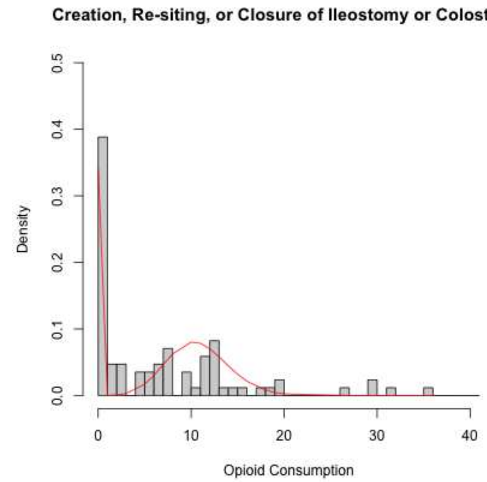


16

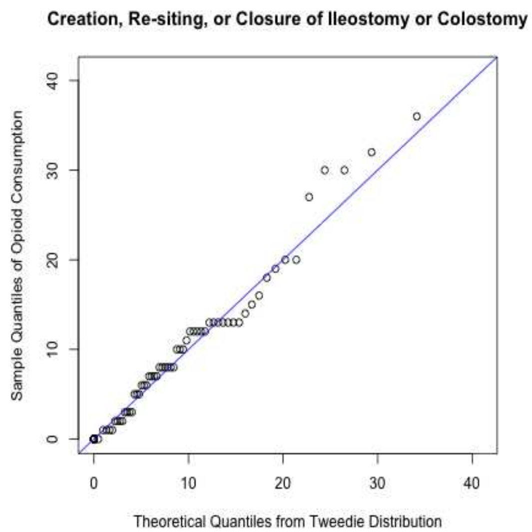
Procedure	Tweedie Model	Zero-inflated Poisson Model
Creation, Re-siting, or Closure of Ileostomy or Colostomy	Density Distributions	

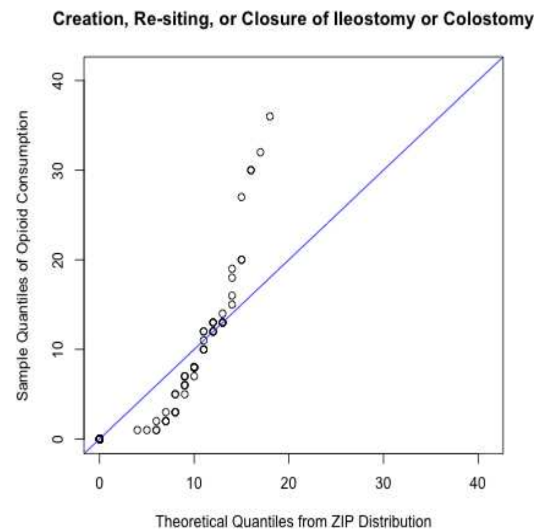
Density Distributions



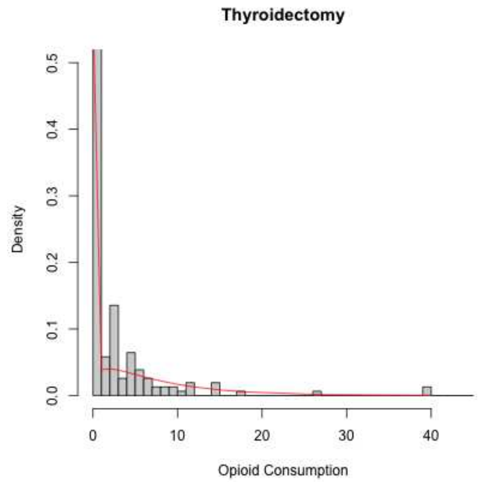


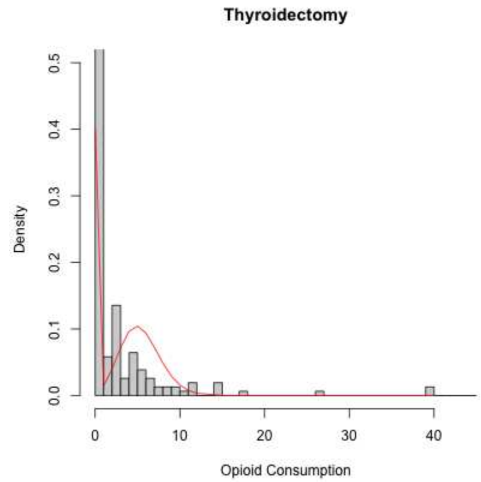
Q-Q Plots



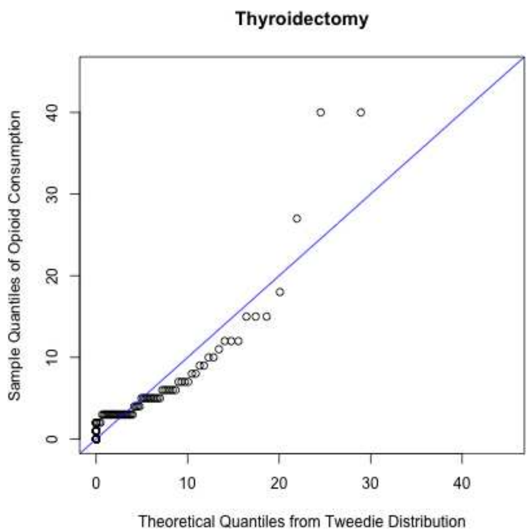


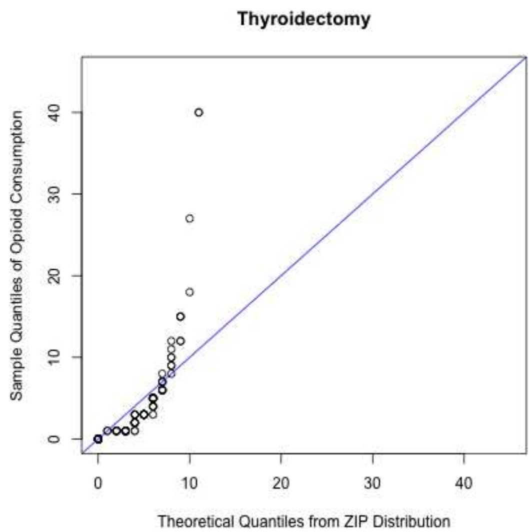
Procedure	Tweedie Model	Zero-inflated Poisson Model
Thyroidectomy	Density Distributions	



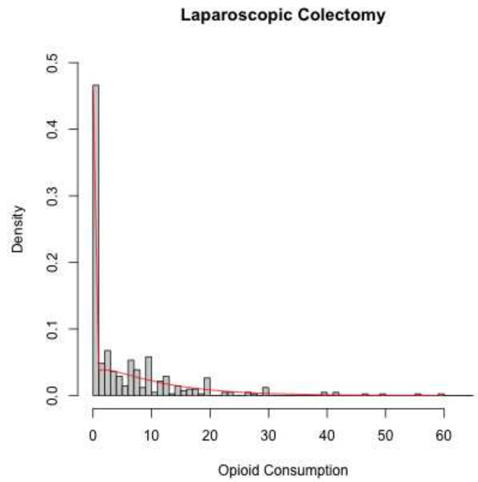


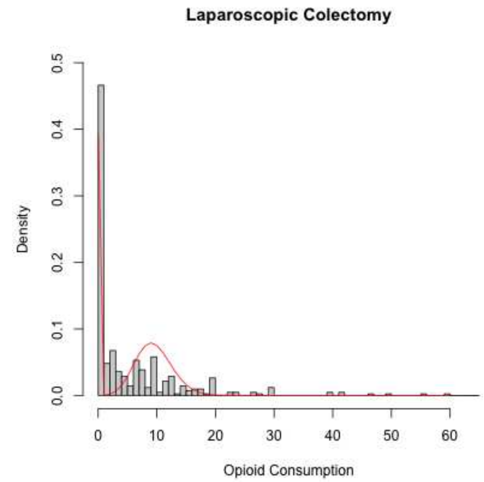
Q-Q Plots



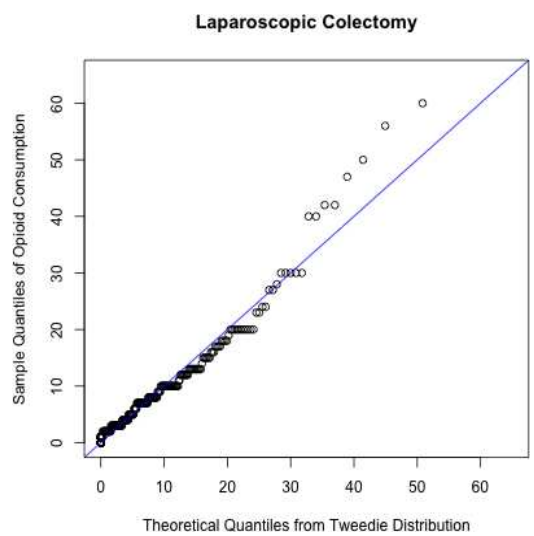


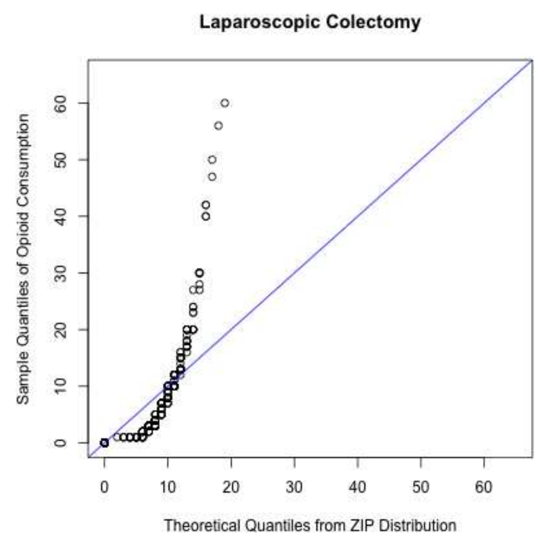
Procedure	Tweedie Model	Zero-inflated Poisson Model
Laparoscopic Colectomy	Density Distributions	





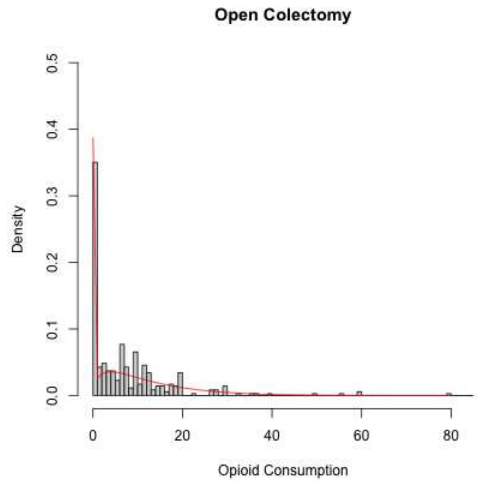
Q-Q Plots

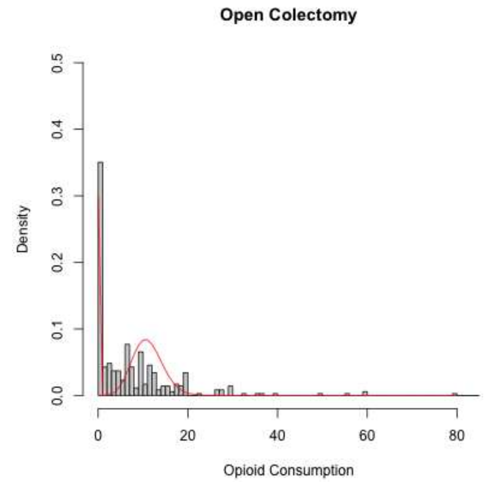




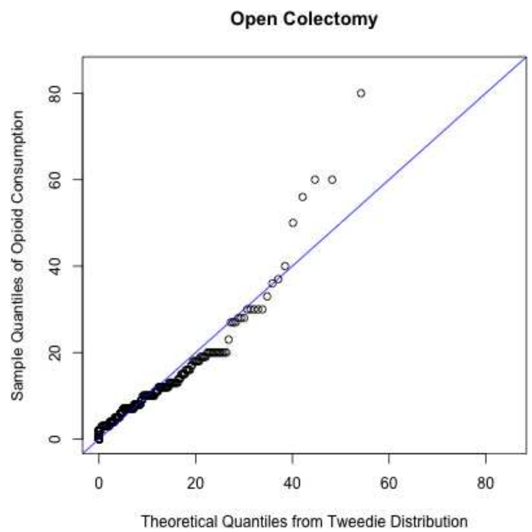
19

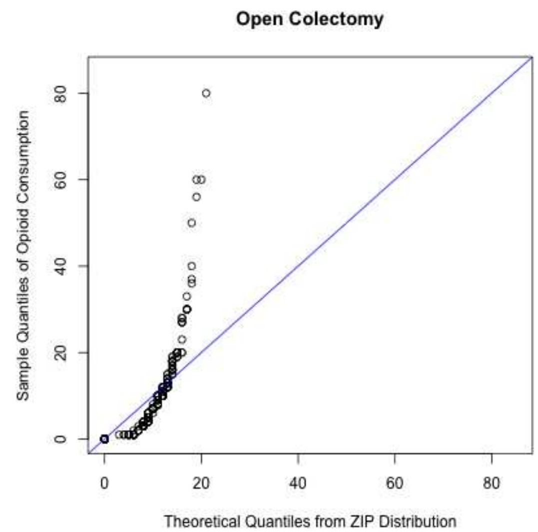
Procedure	Tweedie Model	Zero-inflated Poisson Model
Open Colectomy	Density Distributions	





Q-Q Plots





Song J, *et al. Reg Anesth Pain Med* 2023;0:1–7. doi: 10.1136/rapm-2023-104581

eTable 3. Sample sizes for opioid consumption at the 50th percentile by type of surgical procedure

Procedure type	Width of 95% confidence interval													
	Tweedie							Nonparametric						
	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill
Laparoscopic Appendectomy	3	7	27	41	73	164	653	3	7	27	42	75	168	669
Open Appendectomy	4	8	32	50	88	198	792	6	13	52	81	144	323	1290
Laparoscopic Cholecystectomy	4	9	34	52	93	208	832	3	6	22	34	61	136	544
Laparoscopic Anti-Reflux	5	10	38	60	106	237	948	1	2	7	11	19	41	164
Vaginal Hysterectomy	5	10	40	63	111	249	993	6	14	54	83	148	332	1328
Minor Hernia	5	11	42	66	117	262	1045	3	7	26	41	72	162	647
Open Small Bowel Resection or Enterolysis	6	12	46	72	127	285	1140	13	28	111	173	308	691	2764
Open Cholecystectomy	6	13	52	80	142	319	1276	8	18	70	110	194	437	1745
Major Hernia	6	13	52	81	144	324	1295	5	11	43	68	120	269	1073
Laparoscopic Hysterectomy	7	14	55	85	151	339	1354	5	11	44	69	122	275	1097
Abdominal Hysterectomy	8	18	69	108	192	432	1725	12	26	101	157	278	626	2502
Creation, Re-siting, or Closure of Ileostomy or Colostomy	9	19	75	116	207	464	1855	13	28	112	174	309	695	2779
Thyroidectomy	11	25	98	153	271	609	2433	1	2	7	11	19	42	167
Laparoscopic Colectomy	13	28	109	171	303	681	2724	6	12	47	73	129	289	1154
Open Colectomy	14	32	125	196	347	781	3121	10	22	87	135	240	538	2152

Song J, *et al. Reg Anesth Pain Med* 2023;0:1–7. doi: 10.1136/rapm-2023-104581

eTable 4. Sample sizes for opioid consumption at the 75th percentile by type of surgical procedure

Procedure type	Width of 95% confidence interval						
	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill
Laparoscopic Appendectomy	5	10	40	62	111	248	991
Laparoscopic Cholecystectomy	7	14	55	85	152	340	1360
Laparoscopic Anti-Reflux	11	23	91	142	251	565	2257
Open Appendectomy	10	22	85	133	235	529	2115
Minor Hernia	8	17	67	105	186	418	1672
Open Cholecystectomy	14	32	126	196	349	784	3134
Thyroidectomy	4	9	34	53	94	212	845
Major Hernia	14	31	121	188	334	751	3002
Vaginal Hysterectomy	15	33	131	205	364	818	3271
Open Small Bowel Resection or Enterolysis	15	34	135	211	374	841	3361
Laparoscopic Hysterectomy	14	30	119	186	330	742	2967
Abdominal Hysterectomy	20	44	174	272	484	1087	4348
Laparoscopic Colectomy	16	35	138	215	381	857	3426
Creation, Re-siting, or Closure of Ileostomy or Colostomy	22	49	193	302	536	1205	4817
Open Colectomy	15	33	130	203	360	810	3239

Note: Sample sizes estimates use the nonparametric model.

Song J, *et al. Reg Anesth Pain Med* 2023;0:1–7. doi: 10.1136/rapm-2023-104581

eTable 5. Sample sizes for opioid consumption at the 90th percentile by type of surgical procedure

Procedure type	Width of 95% confidence interval													
	Tweedie							Nonparametric						
	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill
Laparoscopic Appendectomy	7	16	61	95	169	379	1515	6	13	50	77	137	308	1230
Laparoscopic Cholecystectomy	9	19	75	116	206	463	1851	8	16	64	99	176	396	1584
Thyroidectomy	13	29	115	179	319	716	2863	16	36	142	222	394	885	3538
Open Appendectomy	14	30	120	187	331	745	2977	15	34	134	210	372	837	3346
Minor Hernia	18	40	157	246	436	981	3922	20	44	173	270	479	1077	4308
Laparoscopic Anti-Reflux	20	44	173	270	480	1080	4318	28	62	245	383	680	1529	6115
Laparoscopic Hysterectomy	23	51	203	317	563	1265	5059	25	55	217	339	602	1355	5418
Creation, Re-siting, or Closure of Ileostomy or Colostomy	28	61	244	380	676	1520	6078	34	75	298	466	828	1862	7446
Open Small Bowel Resection or Enterolysis	30	67	265	413	735	1652	6607	28	61	244	380	676	1519	6076
Major Hernia	31	69	274	428	760	1710	6838	39	86	344	538	955	2149	8594
Vaginal Hysterectomy	33	75	297	464	825	1856	7422	31	68	272	424	754	1696	6784
Open Colectomy	38	84	336	525	934	2100	8399	52	117	466	728	1294	2911	11643
Laparoscopic Colectomy	39	87	347	543	964	2169	8674	51	115	457	714	1269	2855	11418
Open Cholecystectomy	44	98	391	611	1086	2442	9768	45	102	405	632	1123	2526	10102
Abdominal Hysterectomy	81	183	729	1139	2025	4555	18217	79	177	705	1102	1959	4406	17623

eTable 6. Standard deviations of sample size at the 50th percentile by type of surgical procedure

Procedure type	Standard deviation of sample sizes of 50% percentile													
	Tweedie							Nonparametric						
	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill
Abdominal Hysterectomy	0.7	1.4	5.4	8.4	14.9	33.6	134.5	1.5	3.4	13.7	21.5	38.2	85.9	343.6
Creation, Re-siting, or Closure of Ileostomy or Colostomy	1.3	2.8	10.9	17.0	30.2	68.0	272.0	5.9	13.3	53.2	83.3	148.0	333.0	1332.1
Laparoscopic Anti-Reflux	0.4	1.0	3.8	5.8	10.3	23.1	92.7	0.9	2.0	8.0	12.5	22.2	49.9	199.7
Laparoscopic Appendectomy	0.0	0.5	0.8	1.2	2.3	5.0	19.8	0.6	1.2	4.7	7.3	13.1	29.4	117.7
Laparoscopic Cholecystectomy	0.1	0.1	0.5	0.8	1.3	2.9	11.8	0.3	0.5	2.0	3.2	5.5	12.5	49.9
Laparoscopic Colectomy	0.5	0.9	3.4	5.2	9.2	20.8	83.1	1.6	3.5	13.9	21.6	38.4	86.5	346.1
Laparoscopic Hysterectomy	0.4	0.6	1.8	2.8	5.0	11.2	44.8	0.7	1.4	5.7	8.9	15.7	35.4	141.6
Major Hernia	0.4	0.7	2.4	3.7	6.7	15.0	60.1	0.8	1.7	6.7	10.6	18.7	42.1	168.1
Minor Hernia	0.2	0.5	0.6	0.9	1.5	3.4	13.6	0.5	0.8	2.7	4.1	7.3	16.5	66.1
Open Appendectomy	0.8	1.9	7.3	11.4	20.3	45.8	183.1	2.1	4.6	18.5	28.9	51.4	115.6	462.3
Open Cholecystectomy	1.2	2.7	10.5	16.4	29.3	65.9	263.5	2.6	6.0	23.7	37.0	65.9	148.3	593.1
Open Colectomy	0.9	1.9	7.7	11.9	21.2	47.8	191.2	1.6	3.4	13.7	21.4	38.0	85.5	341.9
Open Small Bowel Resection or Enterolysis	0.9	2.3	9.1	14.3	25.4	57.0	228.1	7.4	16.8	67.1	104.8	186.4	419.5	1677.8
Thyroidectomy	0.3	0.7	2.3	3.4	6.2	13.9	55.5	0.6	1.0	3.9	6.2	11.0	24.6	98.6
Vaginal Hysterectomy	0.4	0.8	2.8	4.3	7.7	17.3	69.0	1.1	2.4	9.4	14.7	26.1	58.8	235.2

Note: Standard deviations derived from bootstrap samples. Estimates expressed in units of pills of oxycodone 5 mg.

Song J, *et al. Reg Anesth Pain Med* 2023;0:1–7. doi: 10.1136/rapm-2023-104581

eTable 7. Standard deviations of sample size at the 75th percentile by type of surgical procedure

Procedure type	Standard deviation of 75% percentile													
	Tweedie							Nonparametric						
	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill
Abdominal Hysterectomy	1.3	2.8	11.3	17.7	31.6	71.0	283.9	3.7	8.3	33.1	51.7	91.9	206.8	827.1
Creation, Re-siting, or Closure of Ileostomy or Colostomy	4.3	9.7	38.6	60.3	107.1	241.0	964.1	12.1	27.2	109.0	170.3	302.7	681.1	2724.5
Laparoscopic Anti-Reflux	3.0	6.8	27.2	42.4	75.5	169.8	679.4	4.7	10.4	41.8	65.4	116.1	261.4	1045.6
Laparoscopic Appendectomy	0.6	1.0	3.8	5.9	10.5	23.5	93.9	0.9	2.2	8.6	13.5	23.9	53.8	215.2
Laparoscopic Cholecystectomy	0.4	0.7	2.3	3.6	6.4	14.3	57.2	0.7	1.4	5.5	8.7	15.6	35.0	139.8
Laparoscopic Colectomy	3.1	6.9	27.8	43.5	77.4	174.1	696.3	4.6	10.3	41.2	64.4	114.5	257.6	1030.6
Laparoscopic Hysterectomy	1.4	3.1	12.5	19.5	34.6	77.9	311.5	1.5	3.3	13.3	20.8	37.0	83.2	332.9
Major Hernia	2.1	4.6	18.6	29.1	51.7	116.3	465.1	2.4	5.4	21.4	33.5	59.6	134.1	536.3
Minor Hernia	0.5	1.0	4.0	6.2	11.1	24.9	99.8	0.9	1.8	7.5	11.6	20.6	46.5	185.7
Open Appendectomy	2.6	5.9	23.4	36.6	65.1	146.5	586.2	5.0	11.3	44.8	70.0	124.5	280.2	1120.7
Open Cholecystectomy	13.1	29.5	118.0	184.5	327.9	737.9	2951.8	10.9	24.5	98.1	153.3	272.6	613.3	2453.3
Open Colectomy	2.3	5.3	21.2	33.0	58.7	132.0	528.2	2.9	6.6	26.6	41.6	73.9	166.4	665.9
Open Small Bowel Resection or Enterolysis	3.8	8.7	34.6	54.1	96.1	216.3	865.2	9.9	22.2	88.6	138.6	246.3	554.1	2216.2
Thyroidectomy	1.7	3.8	15.2	23.8	42.2	95.0	380.1	1.9	4.2	16.6	26.0	46.1	103.7	414.9
Vaginal Hysterectomy	1.7	3.9	15.2	23.8	42.4	95.4	381.7	2.1	4.6	18.6	29.2	51.8	116.6	466.2

Note: Standard deviation derived from bootstrap samples. Estimates expressed in units of pills of oxycodone 5 mg.

Song J, *et al. Reg Anesth Pain Med* 2023;0:1–7. doi: 10.1136/rapm-2023-104581

eTable 8. Standard deviations of sample size at the 90th percentile by type of surgical procedure

Procedure type	Standard deviation of 90% percentile													
	Tweedie							Nonparametric						
	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill	15 pills	10 pills	5 pills	4 pills	3 pills	2 pills	1 pill
Abdominal Hysterectomy	23.9	53.9	215.5	336.6	598.5	1346.5	5385.9	16.4	37.0	148.2	231.6	411.7	926.3	3705.3
Creation, Re-siting, or Closure of Ileostomy or Colostomy	83.8	188.7	754.7	1179.3	2096.6	4717.2	18868.6	32.8	73.8	295.1	461.3	820.0	1845.0	7380.0
Laparoscopic Anti-Reflux	19.4	43.7	174.8	273.2	485.6	1092.6	4370.4	10.0	22.5	89.9	140.5	249.8	561.9	2247.6
Laparoscopic Appendectomy	2.6	5.9	23.5	36.8	65.5	147.3	589.0	2.5	5.5	21.8	34.0	60.4	136.0	544.0
Laparoscopic Cholecystectomy	1.0	2.4	9.4	14.7	26.1	58.9	235.3	1.5	3.2	13.0	20.4	36.2	81.4	325.7
Laparoscopic Colectomy	14.9	33.5	133.7	208.8	371.3	835.4	3341.5	19.2	43.2	172.6	269.8	479.6	1079.1	4316.5
Laparoscopic Hysterectomy	5.8	13.0	51.9	81.2	144.3	324.7	1298.9	5.1	11.6	46.4	72.4	128.7	289.7	1159.0
Major Hernia	21.5	48.5	193.8	302.8	538.2	1210.9	4843.8	14.1	31.7	126.6	197.7	351.5	791.0	3163.8
Minor Hernia	1.2	2.7	10.8	16.8	30.0	67.4	269.5	1.8	4.0	15.8	24.5	43.8	98.3	393.3
Open Appendectomy	123.4	277.6	1110.3	1734.8	3084.1	6939.4	27757.7	17.5	39.4	157.6	246.2	437.6	984.8	3939.1
Open Cholecystectomy	17.4	39.1	156.5	244.4	434.6	977.8	3911.2	17.8	40.1	160.3	250.5	445.3	1002.0	4007.9
Open Colectomy	6.4	14.4	57.6	90.1	160.2	360.4	1441.7	12.4	27.9	111.6	174.3	309.9	697.3	2789.2
Open Small Bowel Resection or Enterolysis	15.1	34.0	135.9	212.4	377.7	849.9	3399.6	12.8	28.9	115.8	181.0	321.8	724.0	2896.0
Thyroidectomy	7.1	16.0	63.8	99.8	177.4	399.2	1596.7	10.4	23.5	93.7	146.4	260.2	585.5	2342.2
Vaginal Hysterectomy	13.0	29.3	117.2	183.2	325.6	732.7	2930.8	5.8	12.9	51.8	81.0	144.0	324.0	1295.7

Note: Standard deviation derived from bootstrap samples. Estimates expressed in units of pills of oxycodone 5 mg.

eTable 9. Estimated 95% confidence intervals by type of surgical procedure

Procedure	95% confidence intervals		
	50th percentile	75th percentile	90th percentile
Creation, Re-siting, or Closure of Ileostomy or Colostomy	4.694	6.996	8.416
Open Cholecystectomy	4.467	5.800	12.312
Open Small Bowel Resection or Enterolysis	3.553	5.535	8.571
Open Appendectomy	3.502	5.200	6.753
Laparoscopic Anti-Reflux	3.369	4.481	7.027
Thyroidectomy	4.074	3.885	4.288
Open Colectomy	2.988	3.651	4.887
Laparoscopic Colectomy	2.482	3.164	4.602
Abdominal Hysterectomy	2.160	3.103	6.989
Vaginal Hysterectomy	1.448	2.293	3.938
Major Hernia	1.670	2.291	3.832
Laparoscopic Hysterectomy	1.164	1.751	2.232
Laparoscopic Appendectomy	0.824	1.115	1.261
Minor Hernia	0.559	0.790	1.091
Laparoscopic Cholecystectomy	0.545	0.740	0.815

Note: Estimates expressed in units of pills of oxycodone 5 mg.

Song J, *et al. Reg Anesth Pain Med* 2023;0:1–7. doi: 10.1136/rapm-2023-104581