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# Standardization of Antibiotic Management and Reduction of Opioid Prescribing in Pediatric Complicated Appendicitis: A Quality Improvement Initiative

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ABSTRACT

*Background:* Appendicitis is one of the most common pediatric surgical procedures in the United States. However, wide variation remains in antibiotic prescribing and pain management across and within institutions. We aimed to minimize variation in antibiotic usage and decrease opioid prescribing at discharge for children with complicated appendicitis by implementation of a quality improvement (QI) initiative.

*Methods:* On December 1st, 2021, a QI initiative standardizing postoperative care for complicated appendicitis was implemented across a tertiary pediatric healthcare system with two main surgical centers. QI initiative focused on antibiotic and pain management. An extensive literature search was performed and a total of 20 articles matching our patient population were critically appraised to determine the best evidence-based interventions to implement. Antibiotic regimen included: IV or PO ceftriaxone/metronidazole immediately post-operatively and transition to PO amoxicillin-clavulanic acid for completion of 7-day total course at discharge. Discharge pain control regimen included acetaminophen, ibuprofen, as needed gabapentin, and no opioid prescription. Guideline compliance were closely monitored for the first six months following implementation.

*Results:* In the first 6-months post-implementation, compliance with use of ceftriaxone/metronidazole as initial post-operative antibiotics was 75.6 %. Transition to PO amoxicillin-clavulanic acid prior to discharge increased from 13.7 % pre-implementation to 73.7 % 6-months post-implementation ($p < 0.001$). Compliance with a 7-day course of antibiotics within the first 6-months post-implementation was 60 % across both sites. After QI intervention, overall opioid prescribing remained at 0 % at one surgical site and decreased from 17.6 % to 0 % at the second surgical site over the study timeframe ($p < 0.001$).

*Conclusion:* Antibiotic use can be standardized and opioid prescribing minimized in children with complicated appendicitis using QI principles. Continued monitoring of the complicated appendicitis guideline is needed to assess for further progress in the standardization of post-operative care.

*Study Type:* Quality improvement.

*Level of Evidence:* Level III.



## 1. Introduction

Appendicitis is the most common pediatric abdominal surgical condition [1–6]. Approximately 20–40 % of pediatric patients present with perforated or complicated appendicitis [1–6]. Complicated appendicitis accounts for most of the morbidity associated with appendicitis and has been shown to significantly increase length of stay, readmissions, organ space infections, and healthcare utilization and cost [1,6–9]. Despite appendicitis being the most common abdominal surgical condition affecting children and adolescents in the United States, wide variation remains in management of patients with complicated appendicitis. Specifically, postoperative antibiotic prescribing strategies in pediatric

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complicated appendicitis vary substantially across and within institutions [9–12]. Recent retrospective reviews have reported improved outcomes and decreased resource utilization with simplified antibiotic regimens consisting of ceftriaxone and metronidazole [9,11,12]. Thus, complicated appendicitis management remains an important topic of continued research.

Prior to 2021, significant variation of postoperative management of complicated appendicitis existed within our institution, as management was at the discretion of each operating surgeon. Development of quality improvement (QI) initiatives in the diagnosis and management of pediatric appendicitis have led to decreased computed tomography (CT) usage, improved outcomes, and decreased costs [13–17]. Though less robust, single-center literature detailing QI processes standardizing management of pediatric patients with complicated appendicitis have also shown improved outcomes [3,18–20]. Through the implementation of a standardized guideline and the use of quality improvement (QI) methodology, we aimed to minimize variation in post-operative antibiotic usage and decrease opioid prescribing at discharge for children and adolescents with complicated appendicitis across a large pediatric healthcare system with two surgical centers.

## 2. Methods

### 2.1. Context

Our pediatric healthcare system is a free-standing, university-affiliated, tertiary children's hospital in a large urban metropolitan area and is made up of two hospital centers where surgical procedures are performed. Approximately 1200 pediatric appendectomies are performed annually across our healthcare system, and approximately 28 % of cases are complicated appendicitis. For this institutional quality improvement initiative, complicated appendicitis was defined by intraoperative findings of perforation with or without abscess. Prior to 2021, there was great variation in the management of complicated appendicitis. Postoperative management of complicated appendicitis, including antibiotic therapy and pain control, within our healthcare system was at the discretion of each operating surgeon and members of the pediatric surgical provider team including surgical trainees (residents and pediatric surgery fellows) and advanced practice providers (APPs). Choice of antibiotic and treatment course length varied across providers. The variation in duration of postoperative antibiotic course length ranged from 7 to 14 days prior to protocol implementation. Discharge PO antibiotics used prior to protocol implementation included: ciprofloxacin/metronidazole or amoxicillin-clavulanic acid. Initial post-operative IV antibiotics used prior to protocol implementation included: piperacillin-tazobactam, ceftriaxone/metronidazole, and meropenem.

Additionally, practice patterns regarding postoperative pain control varied across the healthcare system with one surgical center still prescribing opioids at time of discharge. At least four of the surgeons at one of the two institutions would prescribe opioids at time of discharge, but not for every patient and instead on a patient-by-patient basis. Furthermore, some surgeons made post-operative opioid prescribing decisions based on asking parents if they wanted an opioid prescription for home for their child, indicating that standardization and a larger cultural shift was needed. A multidisciplinary and interprofessional workgroup composed of pediatric surgeons, advanced practice providers, nursing administrators, data analysts, and quality improvement specialists was formed to address this variation in care across our institution. On December 1st, 2021, a QI initiative standardizing postoperative care for complicated appendicitis was implemented across two surgical centers within our tertiary children's healthcare system. The QI initiative streamlined and protocolized the postoperative care of patients with complicated appendicitis.

This study followed the Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) reporting guidelines. The study was determined to be a quality improvement project and therefore was exempt from approval by the Institutional Review Board.

### 2.2. Intervention

One prong of the quality improvement initiative focused on postoperative antibiotic and pain management of complicated appendicitis (Fig. 1). An extensive literature search was performed via PubMed and OVID search engines with the assistance of a medical librarian. A total of 83 articles were reviewed and 20 matching our patient population were critically appraised to determine the best evidence-based interventions to implement. A table of evidence reviewed and used for protocol development is included as Supplemental 1. The guideline involved 4 main aims: ceftriaxone/metronidazole as first line post-operative antibiotic therapy, transitioning to oral antibiotics prior to discharge, discharge home on amoxicillin-clavulanic acid, and 7-day total course of antibiotics. Antibiotic therapy included IV ceftriaxone (75 mg/kg q24hr) and IV metronidazole (30 mg/kg q24hr) immediately post-operatively and transition to per os (PO) amoxicillin-clavulanic acid (45 mg/kg/day BID) for completion of 7-day total course at discharge. Notably, a “step-up” to piperacillin-tazobactam was advised within our protocol if a patient failed ceftriaxone/metronidazole therapy indicated by fever, emesis, and/or poor PO intake at 72-hrs postoperatively or if signs of sepsis develop. This “step-up” with piperacillin-tazobactam approach was guided by our institution's infectious disease providers and the antibiotic stewardship team who consulted and utilized the institutional antibiogram for decision-making.

Seven-day antibiotic course was from the time of source control, either appendectomy or interventional radiology drainage procedure, and combined inpatient and home/post-discharge doses. Additionally, tolerance of at least one dose of PO antibiotic prior to discharge was required. Though not evidence-based, choice to include tolerance of PO antibiotic dose in the QI protocol was made by our team based on collective clinical experience and anecdotal evidence from our institution that observed lack of tolerance as leading to reduced compliance with antibiotic course completion and increased post-discharge “encounters” with the healthcare system. Lack of tolerance was often cited to be secondary to antibiotic side effects such as nausea and/or taste and palatability [21–23]. Therefore, this step was included in our protocol to help anticipate any issues with tolerance and ensure completion of 7-day total antibiotic course once a patient was discharged.

The second focus of the QI initiative was to reduce discharge/outpatient opioid prescriptions at one of the two surgical centers via non-opioid pain control methods. Pain control regimen included scheduled acetaminophen and ibuprofen, as needed gabapentin, and no opioid prescription. Gabapentin was utilized inpatient and prescriptions were provided at discharge on a case-by-case basis if the surgeon and surgical team caring for the patient post-operatively felt that a patient's pain was not well enough controlled with acetaminophen and ibuprofen alone [24,25].

Notably, discharge criteria did not change with the development of this guideline. Discharge criteria includes: afebrile for 24 h, tolerating a regular diet, adequate pain control with oral medications (pain score is a 3 or less within 1hr of PO medication

## Appendectomy with a Complicated Appendix (Category 2b & 2c)

**2B: Focal perforation** – holecle arly in the appendix, focal collection of pus in the right gutter or pelvis, small perf created during extraction, etc.

**2C: Gross contamination** - purulence throughout abdomen/pelvis, fecal contamination, grossly perforated. Pus outside of RLQ. Diffuse peritonitis. Floating fecalith.

### Initial Post-operative Management

**Antibiotic Therapy**
See table on pg. 2 for dosing schedule
- **Ceftriaxone**
- **Metronidazole**

**IF PCN ALLERGY USE**
Ciprofloxacin & Metronidazole

**Antibiotic Step up Therapy**
- 72hrs post op if febrile, vomiting, poor po intake

***D/C Ceftriaxone &Metronidazole***
- ***Start Zosyn*** unless pt. has a PCN Allergy (See table on pg. 2 for dosing schedule)

**Nutrition/GI**
*(NG not recommended)*
- Clears and advance as tolerated
- When tolerating regular diet start **Miralax** PO (max 17 gm) prn no stool for 24 hours *(see dosing pg.2)*
- Advance to oral pain medications* once tolerating reg. diet

**Pain Control***
- **Acetaminophen:** 10mg/kg/dose po q4hr (max 500mg) for pain
- **Toradol:** 0.5mg/kg/dose IV q 6hrs (max 30 mg/dose) Max 20 doses
- **Morphine:** 0.1mg/kg/dose IV q 3hr PRN pain if acetaminophen or toradol is not effective (max 5mg/dose)
- **Gabapentin** 10 mg/kg/dose po TID (max 300mg)

**Activity/Consults**
*(Routine Labs not recommended)*
- OOB on surgical day X1 minimally & ambulate 3x qd

### Empiric IV Therapy for Appendicitis

| Indication | Antibiotics | Dose & Schedule | Max Single Dose |
|---|---|---|---|
| Complicated Appendicitis (CA) | Ceftriaxone And Metronidazole | 75mg/kg q 24h IV | 2000mg |
| | | 30 mg/kg q 24h IV | 1500mg |
| Complicated Appendicitis with severe penicillin allergy[1] | Ciprofloxacin And Metronidazole | 15 mg/kg q 12hr IV | 400mg |
| | | 30 mg/kg q 24h IV | 1500mg |
| **Complicated Appendicitis Step UP Therapy** | | | |
| Complicated Appendicitis with sepsis | Piperacillin/tazobactam[2] | 100mg/kg q8h IV | 4000mg |

[1]Type 1 allergy defined by urticaria or anaphylaxis

[2]Metronidazole does not need to be added to a regimen with piperacillin/tazobactam since anaerobic coverage is adequate with piperacillin/tazobactam

### PO Stepdown Therapy

| Indication | Antibiotic | Dose & Schedule | Max Single Dose |
|---|---|---|---|
| Complicated Appendicitis (CA) | Amoxicillin/Clavulanate Liquid 400mg/5mg for < 40kg | 45/mg/kg/day divided BID | 875 mg |
| | Amoxicillin/Clavulanate Tablet (875mg) for > 40kg | 1 tablet BID | 875mg |
| Complicated Appendicitis (CA) with Severe PCN Allergy | Ciprofloxacin And Metronidazole | 15mg/kg q 12h po | 500mg |
| | | 10mg/kg q 8h po | 500mg |

**Fig. 1.** Complicated appendicitis postoperative care management guideline.

administration), benign abdominal exam by surgeon, and ambulation without assistance (at least 250 feet).

### 2.3. Implementation

A key driver analysis was performed which guided the guideline implementation (Fig. 2). The aim was for at least 70 % compliance with the postoperative complicated appendicitis antibiotic guideline. To achieve this goal, we first secured provider buy-in by engaging the surgeons in protocol development and encouraging feedback during QI workgroup meetings. Before implementation, the guideline was presented to the entire surgical provider care team to allow for questions, input, and discussion. Once accepted and finalized, the new complicated appendicitis guideline was communicated via email to the entire pediatric surgical team and nurse educators on surgical floors. The guideline was posted throughout the surgical provider team offices including in trainee and advanced practice provider (APP) offices where order placement and electronic medical record (EMR) documentation occurs (Supplemental 2). Importantly, an order-set within the EMR was created to reflect the guideline, and advertised to the provider team to reduce errors and friction with implementation. Email reminders to the surgical provider team regarding the guideline were sent each month. Data was reviewed by the quality improvement workgroup monthly. Additional email reminders to the surgeons, APPs, and surgical floor nurse educators regarding the guideline were sent on an as needed basis depending on compliance noted during data review.

### 2.4. Monitoring & study of the intervention

Guideline compliance and clinical outcomes were closely monitored for the first six months following implementation: December 1st, 2021 to June 1st, 2022. Notably, there was a shortage of metronidazole at our institution in the first month of implementation (December 2021) and thus post-implementation data for initial postoperative antibiotic use excluded December 2021 and instead was examined from January 1st, 2022–June 30th, 2022. During the first six months, compliance and outcomes data was manually extracted from the EMR by study team members and stored within Research Electronic Data Capture (REDCap)-based database. REDCap is a secure web-based application which provides an intuitive interface for collection of research data and offers access via secure authentication (user ID and password). Auditing in the form of manual chart review extraction was performed on all patients with complicated appendicitis admitted to both surgical centers every 2-weeks by the multidisciplinary quality team. Two week intervals were chosen to allow for patients to be discharged, allow for frequent check-ins, and ability to quickly detect and address lags in compliance. When compliance issues were identified, the quality team would provide feedback in the form of personal conversations with the operative surgeon. Notably, the manual chart review served a dual purpose of also validating the Qlikview electronic application dashboard. The Qlikview electronic application dashboard was developed which automated a limited data capture for continued monitoring beyond 6 months that does not require substantial human capital. This application allows for automated database building and check-ins on protocol compliance, granting opportunities for early triage and intervention if a decrease in protocol compliance is observed.

### 2.5. Outcome measures

Primary outcome of interest was compliance with antibiotic guideline including: use of ceftriaxone plus metronidazole as initial post-operative antibiotics, transition to PO amoxicillin-clavulanic acid prior to discharge, and 7-day total postoperative antibiotic course. Secondary outcomes of interest included opioid prescription at discharge, hospital length of stay (LOS), and 30-day readmissions.

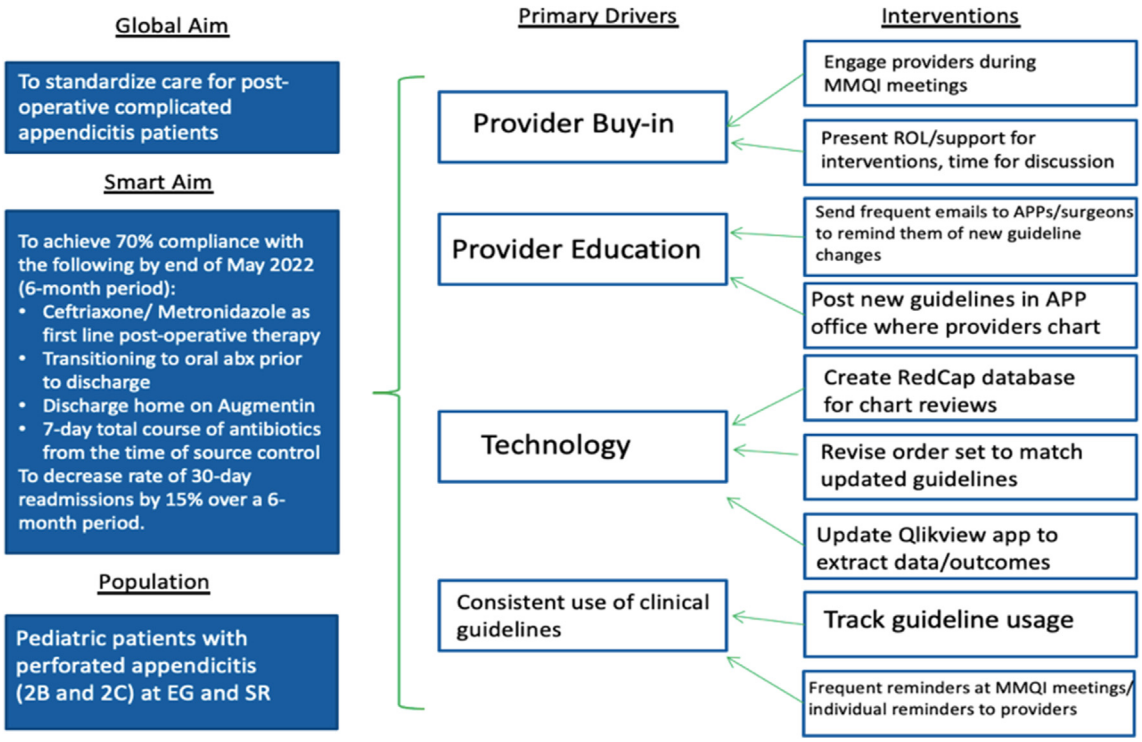


**Fig. 2.** Key driver analysis for complicated appendicitis postoperative guideline.

### 2.6. Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences Version 28. Differences between groups were explored using chi-squared tests or Fischer's exact test for categorical data. P-values less than 0.05 were considered statistically significant.

## 3. Results

From December 1st, 2021 to June 1st, 2022, 179 patients underwent appendectomy for complicated appendicitis at one of the two inpatient surgical centers. In the first 6-months of implementation, compliance with initial use of ceftriaxone and metronidazole as initial post-operative antibiotics was 75.6 % across both surgical sites. In the 6 months prior to guideline implementation (from June 1st, 2021 to December 1st, 2021), transition to PO amoxicillin-clavulanic acid prior to discharge occurred in only 13.7 % of patients with complicated appendicitis. Across the 6 months following protocol implementation, transition to PO amoxicillin-clavulanic acid prior to discharge occurred in 73.7 % of patients ($p < 0.001$) and compliance was up to 86.7 % by June of 2022 (Fig. 3). In the 6-months post-implementation, compliance with a 7-day course of antibiotics was 60 % across both sites.

After QI intervention, opioid prescribing at discharge remained at 0 % at one surgical site that was already practicing opioid stewardship. At the second surgical site, opioid prescribing at discharge decreased from 17.6 % in December 2021 to 0 % by April 2022 and remained at 0 % through the remainder of the study timeframe ($p < 0.001$, Fig. 4). Length of stay was stable across the study timeframe with median LOS of 4.5 days pre-implementation and 4.5 days post-implementation ($p = 0.102$). Readmissions within 30-days decreased by 34.4 %, from an average of 0.64 per month to 0.42 per month ($p < 0.001$).

## 4. Discussion

This study reports the successful implementation of a QI initiative standardizing postoperative antibiotic use for complicated appendicitis across a large pediatric healthcare system. Prior to implementation of the guideline, substantial variation in postoperative antibiotic use existed within our institution with many patients exposed to piperacillin-tazobactam and carbapenems as initial postoperative antibiotic. Studies have shown that a combination of ceftriaxone and metronidazole has similar efficacy to broader-spectrum regimens such as piperacillin-tazobactam for the treatment of perforated appendicitis without an increase in complications [9,12,26–28]. In addition to concerns for antibiotic stewardship and preventing emergence of resistant organisms, judicious use of broad-spectrum antibiotics such as piperacillin-tazobactam reduces risk of opportunistic infections such as *Clostridium difficile*, possibility of side effects such as nephrotoxicity, and healthcare costs [12,29–31]. Therefore, while practice differences across the United States exist, most recent literature has been aimed at reducing use of piperacillin-tazobactam for pediatric perforated appendicitis [9,11]. Our study reports compliance with the use of ceftriaxone and metronidazole as initial postoperative antibiotic up to 75.6 %, though further efforts for continued improvements with compliance are needed.

Beyond antibiotic selection, there are also no standardized guidelines for the length of antibiotic treatment for perforated appendicitis and thus wide variation in care exists. Historically, perforated appendicitis management included 10–14 days of treatment with IV antibiotic therapy often in addition to peritoneal irrigation and universal drain placement [32]. However, more recent literature has shown benefits to shorter duration of therapy and earlier transition to PO antibiotics [3,33–36]. A randomized controlled trial by Fraser et al. found success with earlier discharge with PO amoxicillin-clavulanic acid to a total of 7 days of antibiotic therapy without increased adverse events [33]. Unique to our protocol is the insurance that the patient tolerates at least one dose of PO antibiotics prior to discharge in effort to reduce post-discharge nursing phone calls and return to the healthcare system. We report successful implementation of transition to PO amoxicillin-clavulanic acid prior to discharge with significant increase in compliance up to 86.7 % by June 2022. However, an area identified for continued monitoring and improvement is the duration of

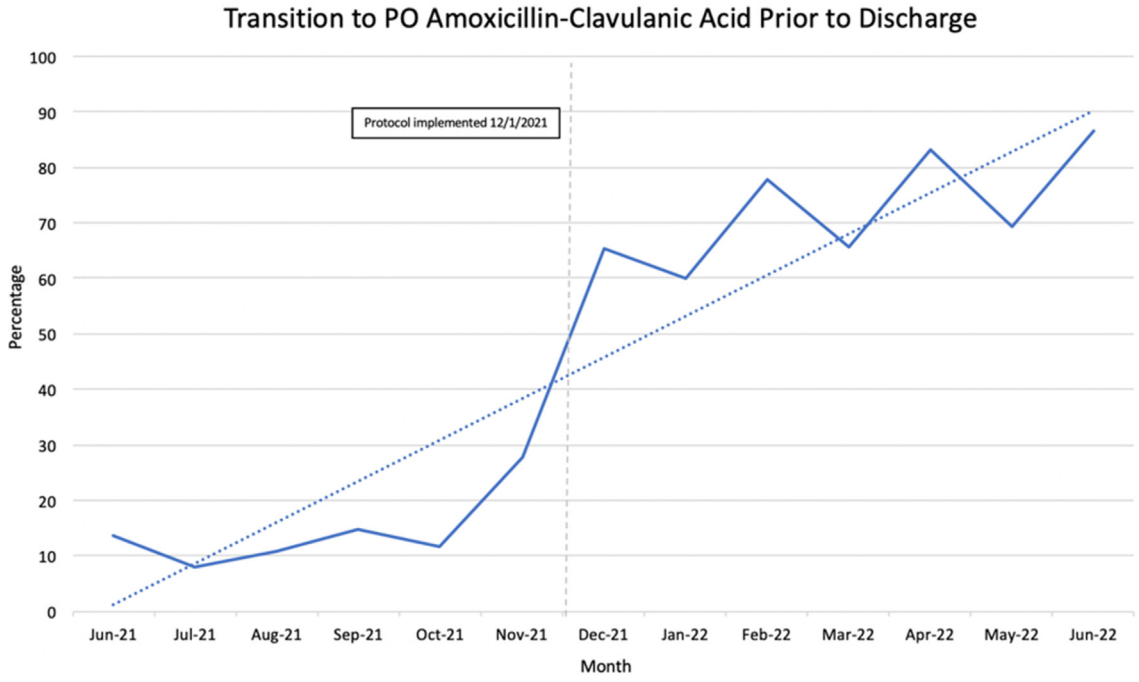


**Fig. 3.** Percentage of patients transitioned to PO amoxicillin-clavulanic acid prior to discharge per month prior to and following guideline implementation.

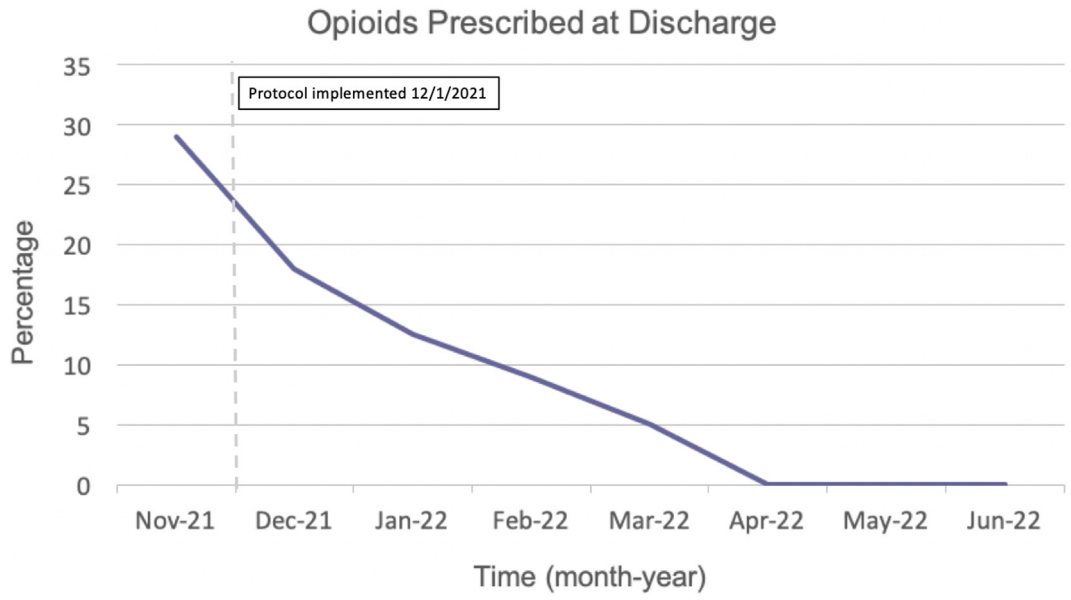


**Fig. 4.** Percentage of opioids prescribed at discharge per month immediately before and 6-months post-guideline implementation.

antibiotic therapy as compliance with a 7-day total treatment course was 60 % in the first 6 months following implementation. Some of the common issues associated with non-compliance that arose during our study timeframe included overcoming individual surgeon preferences and years of practice patterns and training/orienting new team members (new APPs and rotating residents) to the protocol.

Notably, our study reports the successful reduction and elimination of postoperative opioid prescription at discharge for patients with complicated appendicitis throughout our healthcare system without an increase in 30-day readmissions. Our system is composed of two main surgical centers, which have historically functioned nearly independently. One of the surgical centers stopped prescribing opioids at discharge for appendicitis following implementation of enhanced recovery protocols in years prior, but the second surgical center had yet to make this transition. Anderson et al. showed that two-thirds of pediatric patients are discharged with an opioid prescription following appendectomy and that significant variation in the total amount prescribed existed across providers [37]. Furthermore, it was shown that patients provided with an opioid prescription had higher complications including constipation requiring a clinical encounter and no reduction in post-discharge ED visits [37]. Similarly, Mahdi et al. reported that early and continued postoperative opioid use increased hospital length of stay in children with perforated appendicitis [38]. There is extensive literature investigating pain management protocols to reduce post-operative opioid prescribing in the pediatric population with overall positive success [38–43]. Specifically, in pediatric appendectomy implementing multimodal, non-opioid pain management protocols have been shown to reduce opioid prescribing [39,41,42]. However, most of these studies are examining cases of acute, uncomplicated appendicitis alone [39,40], with studies examining perforated appendicitis less successful at reducing opioid use [44]. Our study reports elimination of opioid prescribing at discharge for pediatric patients with complicated appendicitis following implementation of a discharge pain management protocol composing of ibuprofen, acetaminophen, and as needed gabapentin, without an increase in return to system for pain control.

This study is not without limitations. First, it is retrospective in nature and data collection was focused on compliance with the QI guideline. Therefore, many clinical factors which may have influenced adherence to or deviation from guideline are unknown within the scope of this study. For example, pain scores were not collected and though documentation within the EMR of pain scores by nursing staff is subjective and not extremely reliable, we acknowledge it as a limitation to our study. Additionally, we did not capture post-discharge ED visits or other touches with the healthcare system apart from 30-day readmissions, which may influence our results reported especially considering the elimination of opioid prescribing at discharge. Furthermore, we did not capture rates of organ space infections (OSI) specifically, which is a limitation. However, 30-day readmissions significantly decreased following guideline implementation without an increase in length of stay, and though imperfect, these findings can be used as a surrogate for post-discharge OSI development. Though limited in scope, the automated form of data collection utilized greatly increases ease of real-time monitoring by decreasing human capital required and allows for early intervention if protocol compliance wanes. As a single-center quality improvement project, our results reported may have been facilitated by institutional culture and thus lack generalizability to other institutions and populations. Furthermore, our institution is a tertiary children's hospital associated with an academic affiliation and postoperative care is delivered by a relatively large team of trainees and advanced practice providers (APPs), which eases burden of implementation away from the operating surgeon. However, reporting on a single-center intervention allows for more granular information regarding the process of implementation of a QI initiative to allow for other institutions to learn from our process. Notably, the trends seen in Figs. 3 and 4 show that shifts in PO antibiotic dose prior to discharge and opioid prescribing at discharge may have started in the month leading up to protocol implementation. We hypothesize the trends seen in November 2021 were a result of the many conversations with the multidisciplinary workgroup leading to protocol development and surgeon anticipation and alteration of their practice to comply. Efforts are needed to continue to improve compliance with all aspects of the postoperative complicated appendicitis guideline specifically duration of postoperative antibiotic treatment course. Additionally, future work is needed to expand quality improvement efforts at standardizing care in the management of acute uncomplicated appendicitis at our institution.

## 5. Conclusion

Postoperative antibiotic choice and treatment length can be successfully standardized in children and adolescents with complicated appendicitis using quality improvement methodology. Additionally, opioid prescribing at discharge can be eliminated without an increase in 30-day readmissions. Continued monitoring and education around the complicated appendicitis guideline is needed to see further progress in the standardization of post-operative care. Compliance with a 7-day course of antibiotics postoperatively is an area for future, targeted improvement.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpedsurg.2023.11.001.

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