

A Quality Improvement Project to Reduce Combination Acetaminophen-opioid Prescriptions to Pediatric Orthopedic Patients

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Abstract

Background: Acetaminophen-opioid analgesics are among the most commonly prescribed pain medications in pediatric orthopedic patients. However, these combined opioid analgesics do not allow for individual medication titration, which can increase the risk of opioid misuse and hepatotoxicity from acetaminophen. The primary aim of this quality improvement project was to alter the prescribing habits of pediatric orthopedic providers at our institution from postoperative acetaminophen-opioid analgesics to independent acetaminophen and opioids. **Methods:** The study took place in a level 1 trauma center at a children's hospital. A multidisciplinary team of health professionals utilized lean methodology to develop a project plan. Guided by a key driver diagram, we removed acetaminophen-oxycodone products from hospital formulary, implemented a revised inpatient and outpatient electronic order set, and conducted multiple education efforts. Outcomes included inpatient and outpatient percent combined acetaminophen-opioid orders by surgical providers over 27 months. **Results:** Before the intervention, inpatient acetaminophen-opioid products accounted for an average of 46% of all opioid prescriptions for orthopedic patients. After the intervention and multiple educational efforts, we reported a reduction in the acetaminophen-opioid products to 2.9%. For outpatient prescriptions, combined analgesics accounted for 88% before the intervention, and we reported a reduction to 15% after the intervention. **Conclusions:** By removing acetaminophen-oxycodone products from hospital formulary, educating the medical staff, and employing revised electronic order sets, the prescribing practice of pediatric orthopedic surgeons changed from the routine use of acetaminophen-opioid analgesics to independent medications. (*Pediatr Qual Saf* 2020;3:e291; doi: 10.1097/pq9.000000000000291; Published online April 28, 2020.)

INTRODUCTION

Pain control after pediatric orthopedic procedures is challenging due to the inability of children to

express the presence or severity of pain adequately.¹

Nationally, combination analgesics, such as acetaminophen-hydrocodone, were the most commonly prescribed medication in pediatric orthopedic patients between 2002 and 2010.²

However, acetaminophen-opioid analgesics do not allow for individual medication titration, which can increase the risk of opioid overdose, opioid dependence, and suboptimal pain control.^{3,4}

Combination analgesics with acetaminophen may also increase the risk of hepatotoxicity, prompting a 2009 FDA advisory committee recommendation against acetaminophen combination products.^{5,6}

Pediatric patients are particularly vulnerable to the risks associated with combined opioid medications. Postoperative medications are the most common source of opioid misuse, with hydrocodone being one of the most commonly abused.⁷ Hospitalizations from opioid poisoning in pediatrics increased 2-fold from 1997 to 2012, and the pediatric mortality rate from opioid poisoning increased 3-fold from 1999 to 2016.^{8,9}

Some providers believe that combining opioids with acetaminophen reduces the risk of opioid abuse due to the risk of hepatotoxicity from the acetaminophen. However, concerns that opioid consumption increases when not combined with acetaminophen may be unfounded, and

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hydrocodone, the most commonly abused opioid, is only available in combination form in America.^{7,10} For pediatric patients, the American Pain Society recommends multimodal pain management strategies that include non-steroidal anti-inflammatory drugs, and acetaminophen.¹¹ Multimodal analgesia reduces opioid use, minimizes unwanted side effects, and improves pain control after surgery.^{12,13} Administration of these modalities individually rather than in combination provides titratability to optimize pharmacological effects while reducing adverse events.^{14,15} Around-the-clock (ATC) administration of acetaminophen alone is associated with a 30% reduction in opioid consumption.¹⁶ Given the potential for unnecessary opioid use when combined with ATC acetaminophen, consideration should be made for independent, as needed (pro re nata [PRN]), administration of opioids combined with ATC acetaminophen.

The primary aim of this quality improvement project was to alter the habits of pediatric orthopedic providers from prescribing combined acetaminophen-opioid products to prescribing opioids and acetaminophen as separate, independent medications. The secondary aim was to explore the prescribing habits of other surgical specialties. As a balancing measure, we recorded total morphine equivalents consumed per orthopedic patient to investigate whether morphine consumption increased when not combined with acetaminophen as a potential dissuader to overuse.

METHODS

Context

We conducted this improvement project in a level one, academic children's hospital in Northern California between January 2017 and April 2019. The pediatric orthopedic surgery division consists of 13 attending surgeons, 2 nonoperative attending physicians, 1 fellow physician, 4 nurse practitioners, and 2 physician assistants. The pediatric orthopedic surgeons perform approximately 950 operations annually. The providers serve a heterogeneous population from neonates to young adults. The Stanford University Institutional Review Board approved a waiver of consent for this quality improvement project.

Intervention

A multidisciplinary perioperative improvement team of anesthesiologists, orthopedic surgeons, nurses, pharmacists, and quality managers initiated efforts to transform the standard postoperative practice of using acetaminophen-opioid products to the administration of medications independently. The team utilized lean methodology to develop an A3 project plan, which included an exploration into the background and current state, problem analysis, aims, and countermeasures.^{17,18}

Key drivers included (1) optimization of the electronic medical record; (2) reliable access to liquid opioids; (3) education of prescribing providers; and (4) patient education

(Fig. 1). Countermeasures included multiple electronic medical record practice alerts, formulary removal of acetaminophen-oxycodone, postoperative electronic order set (EOS) modifications, training for inpatient pharmacists, physician, and nurse education, and increased patient access to liquid oxycodone (Fig. 1). Because community pharmacies do not reliably maintain liquid oxycodone, patients' preferred pharmacies were changed to the hospital's pharmacy upon admission to facilitate access. In addition to the pediatric orthopedic service, other surgical services expressed interest in the project; therefore, all surgical specialties incorporated the EOS modifications.

Before revising the EOS, we obtained approval from each surgical service. Members of the perioperative improvement team first presented to the chief of pediatric orthopedic surgery and then to the entire division. At the division meeting, the team reviewed current orthopedic prescribing habits and described the rationale for prescribing the medicines independently. The surgeons were concerned that standalone liquid oxycodone should be avoided because it was more potent than hydrocodone. Hydrocodone, as a standalone opioid, is not available in America in an immediate release form. However, after a further explanation that oxycodone and hydrocodone were nearly equipotent and that the EOS would reflect a similar morphine equivalency, a consensus was achieved. Also, we discussed the heterogeneity in the dosing guidelines of other analgesics such as acetaminophen. As we discussed the initiative at perioperative chief meetings, other specialties expressed interest.

Consequently, the improvement team presented similarly to the remaining surgical service lines. As a result of these efforts, we modified the EOS to reflect the new recommended dosing guidelines. Beyond avoiding the use of combined analgesics, many surgical teams elected to have acetaminophen preselected as a standing routine postoperative analgesic on the modified EOS.

In addition to splitting acetaminophen-hydrocodone on the revised EOS, we reviewed all acetaminophen-opioid products at the hospital. Acetaminophen-codeine had previously been removed from the hospital formulary after the FDA 2013 black box warning against the administration of codeine in posttonsillectomy patients. Acetaminophen-oxycodone was the only other acetaminophen-opioid still on the formulary, and to minimize ordering variability, we removed the oxycodone containing combination medications from the pharmacy formulary. This action was done in partnership with the Medical Executive Committee and Pharmaceuticals and Therapeutics Committee at our institution, and the Chief Patient Safety Officer championed it. After presenting at each of these committees, they approved the removal. Although acetaminophen-hydrocodone was revised on the EOS to acetaminophen and oxycodone, it was not removed from the formulary. We elected to keep acetaminophen-hydrocodone on the formulary to maintain an alternative medication option for patients with adverse reactions to oxycodone. After the revisions were

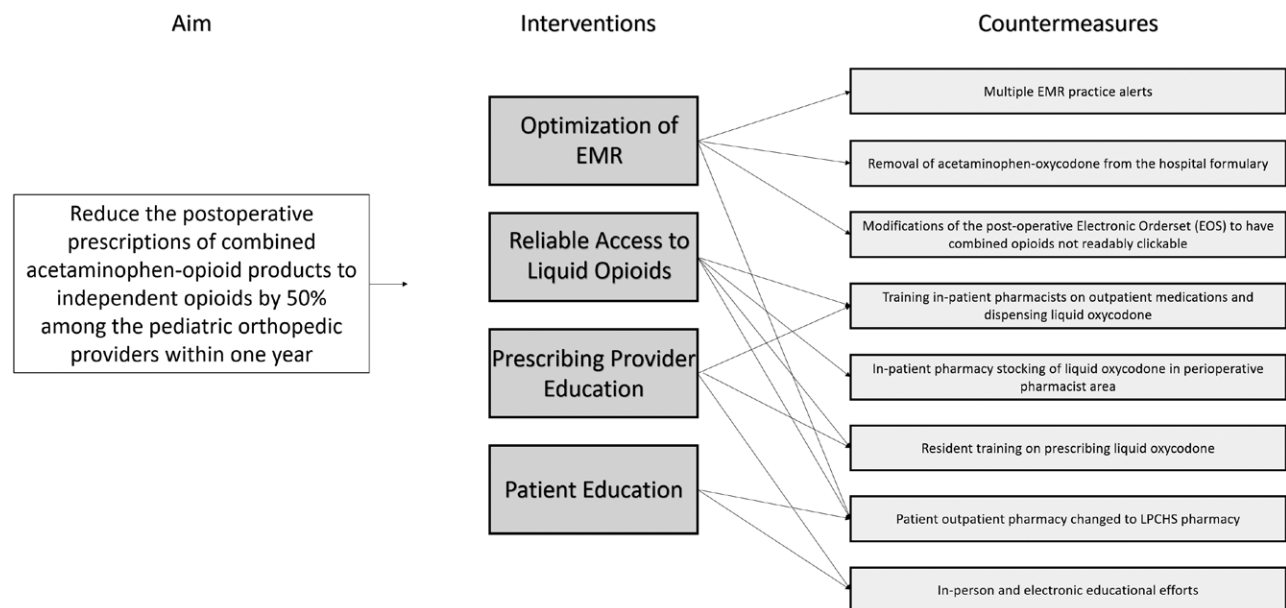


Fig. 1. Key drivers diagram. EMR, electronic medical record; LPCHS, Lucile Packard Children Children's Hospital Stanford.

made to the EOS and formulary changed, we distributed educational material to the Program Directors of each service to be included in resident and fellow orientation. Because the residents frequently rotated off their pediatric surgery rotations, we targeted the pediatric surgical fellows, advanced practice providers, and attending faculty to optimize the longitudinal benefits of our efforts.

The orthopedic and subsequent other surgical providers educated patients and their families during their preoperative appointments. On the day of surgery, immediately postoperatively, the recovery room nurses provided patients with an "After Visit Summary" that described the postoperative analgesic plan, which typically included ATC acetaminophen and as needed oxycodone. Patients received extended postoperative visits from surgical providers to ensure appropriate pain control.

Outcomes

The primary outcome was to reduce the postoperative prescriptions of combined acetaminophen-opioid products to independent opioids by 50% among the pediatric orthopedic providers within 1 year after implementation. We recorded total morphine equivalents of opioids per patient ordered by orthopedic providers as a balancing measure to ensure that the project did not result in increased opioid consumption. The secondary outcome was to describe changes in prescribing habits of other surgical specialties, which included neurosurgery, plastic surgery, otolaryngology (ENT), urology, and general surgery.

Measures

We measured the primary outcome through the electronic capture of the inpatient and outpatient percent combined

acetaminophen-opioid versus independent orders by orthopedic providers. To control for variations in the number of prescriptions per month, we recorded monthly pediatric orthopedic case volume. We collected data using a custom electronic report that displayed the total enteral opioid doses administered to patients as measured by morphine equivalents. Inpatient enteral administration of morphine, hydromorphone, oxycodone, and hydrocodone was converted to total morphine equivalents using the conversion factors of 1:1, 1:4, 1:1.5, and 1:1, respectively.¹⁹ We also collected via a custom electronic report the inpatient and outpatient combined acetaminophen-opioid administration of the other pediatric surgical services. We recorded these data as the percent combination administered, stratified by inpatients and outpatients.

We collected preintervention data from January 2017 to March 2018. We recorded data during the intervention period with countermeasure deployment from April 2018 to October 2018, and sustainment data from November 2018 to April 2019.

Analysis

We used statistical process control charts to measure combination acetaminophen-opioid prescribing practices for orthopedic and other surgical specialties. We displayed centerlines to represent the average percent acetaminophen-opioid. We included 3 SDs of upper and lower control limits centerline breaks at times of special cause variation attributed to nonrandom conditions.²⁰ We visualized the data using Microsoft Excel (Redmond, Wash.) and analyzed the data using R version 3.5.1 (Vienna, Austria). To determine the statistical significance of group differences before and after the implementation

of the interventions and countermeasures, we used the Chi-square test with $P < 0.05$ considered significant.

RESULTS

Primary Aim: Orthopedic Prescribing Habits

The mean percentage of inpatient acetaminophen-opioid doses in the historical period was 46% (Fig. 2). During the intervention period, the mean percentage of combined doses was 31%, and the mean percentage of combined doses was 2.9% in the sustainment period. The difference in inpatient combined doses percentage between the historical and sustainment periods was significant ($P < 0.001$).

The mean percentage of outpatient acetaminophen-opioid prescriptions in the historical period was 88% (Fig. 3). The mean percentage of combined prescriptions was 47% in the interventional period and 15% in the sustainment period. The difference in outpatient combined prescriptions percentage between the historical and sustainment periods was significant ($P < 0.001$).

Balancing Measure: Morphine Equivalent Doses

Inpatient, enteric morphine equivalent doses per patient ordered by orthopedic providers averaged 3.3 in the historical period (Fig. 4). During the intervention period, morphine equivalent doses per patient were averaged at 2.5, and during the sustainment period, 3.2. The difference in morphine equivalent doses between historical and sustainment periods was statistically insignificant.

Secondary Aim: Prescribing Habits of Other Surgical Providers

The mean percentage of inpatient acetaminophen-opioid doses for other surgical specialties was historically 20% (Fig. 5). In the interventional period, the mean percentage of inpatient combined doses was 12% and 0.1% during

the sustainment period. The difference in inpatient combined prescriptions percentage between historical and sustainment periods was significant ($P < 0.001$).

The mean percentage of outpatient acetaminophen-opioid prescriptions was 30% historically (Fig. 6). In the interventional period, the mean percentage of combined prescriptions was 14% and 25% during the sustainment period. The difference in outpatient combined prescriptions percentage between historical and sustainment periods was significant ($P < 0.001$).

DISCUSSION

The project presents a reliable method to transform the practice of prescribing acetaminophen-opioid combination products to independently prescribed opioids and acetaminophen to optimize pediatric pain control. Pediatric orthopedic prescriptions of acetaminophen-opioid combination products significantly reduced over 2 years. Despite theoretical concerns that splitting the opioid from acetaminophen would result in increased opioid consumption, the average enteric morphine equivalents per patient were unchanged after the intervention. The prescribing habits of other surgical specialties were also significantly altered to the independent ordering of opioids and acetaminophen.

The independent administration of opioids and acetaminophen may be advantageous for several reasons. Acetaminophen is a dose-dependent toxin, and opioids have several harmful effects, including gastroparesis, nausea, pruritus, and respiratory depression. Moreover, opioids can be addictive after even minor exposure.²¹⁻²³ An independent titration of each medication allows greater control when managing escalating doses. The separate titration approach may be ideal given the difficulty associated with managing pediatric pain and the risks associated with the use of combination products. Also, the

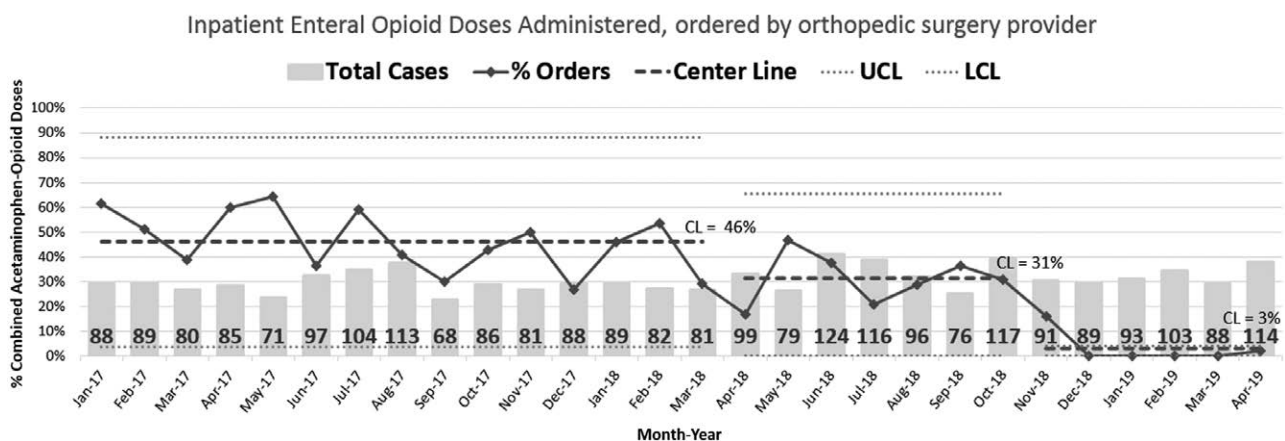


Fig. 2. Statistical process control (SPC) chart for the monthly inpatient percentage combined acetaminophen-opioid doses ordered relative to total enteral opioid doses ordered by orthopedic surgery providers as represented by the centerline (CL). Three SD upper control (UCL) and lower control limits (LCL) are displayed. The monthly volume of orthopedic cases is represented by the bars over a period from January 2017 to April 2019.

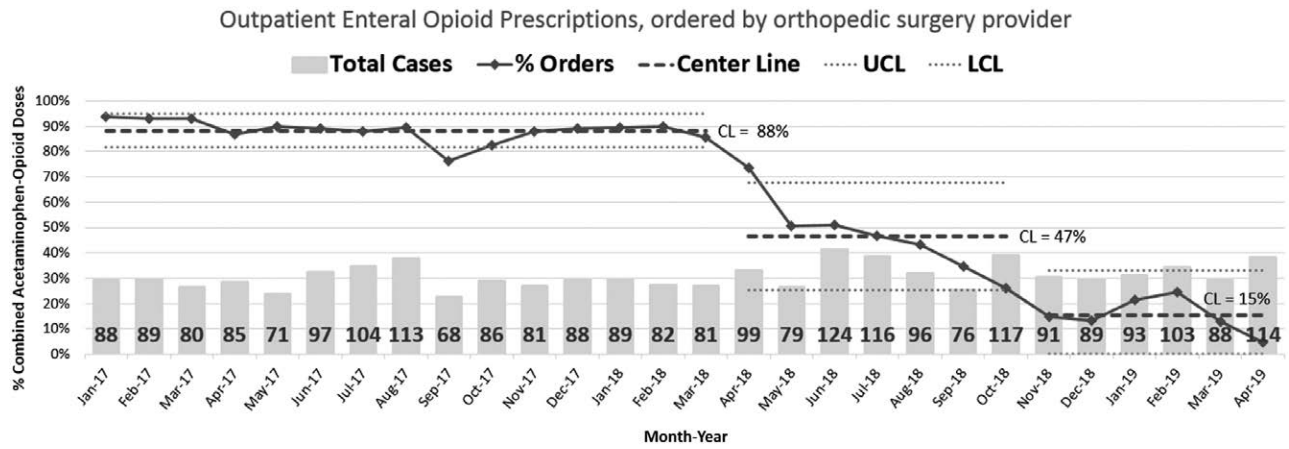


Fig. 3. Statistical process control (SPC) chart for a monthly percentage of outpatient combined acetaminophen-opioid prescriptions relative to total enteral opioid prescriptions ordered by orthopedic surgery providers as represented by the centerline (CL). The 3 SDs for upper control (UCL) and lower control limits (LCL) are displayed. The monthly volume of orthopedic cases is represented by the bars over a period from January 2017 to April 2019.

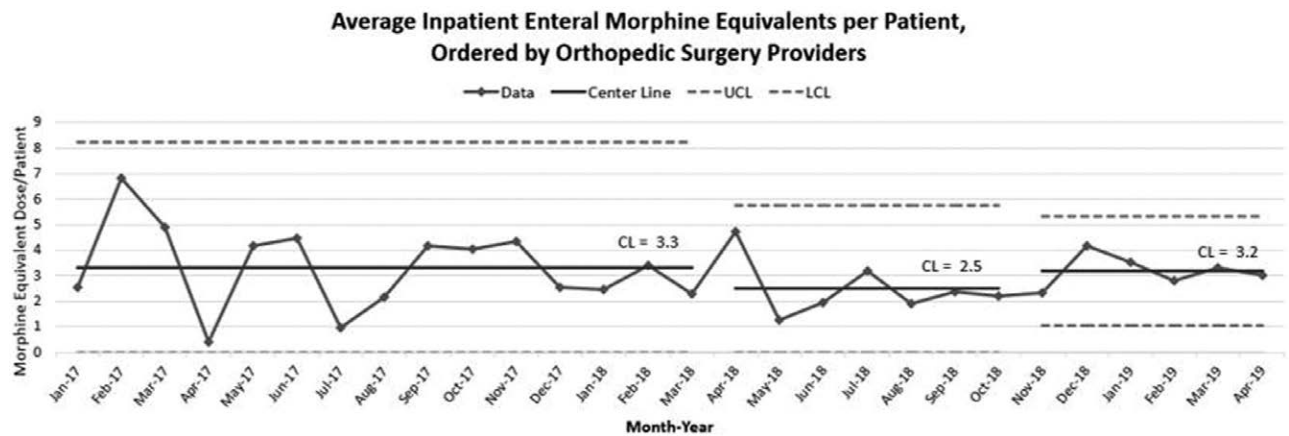


Fig. 4. Statistical process control (SPC) chart showing average morphine equivalent dose of opioids per patient ordered by orthopedic providers from January 2017 to April 2019 as represented by the centerline (CL). The 3 SDs for upper control (UCL) and lower control limits (LCL) are displayed. The monthly volume of orthopedic cases represented by the bars over a period from January 2017 to April 2019.

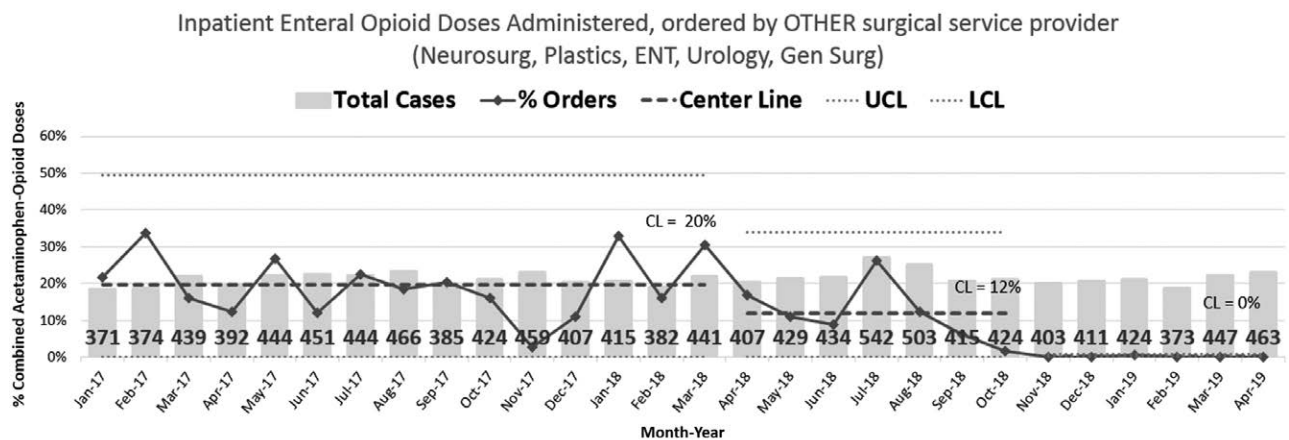


Fig. 5. Statistical process control (SPC) chart showing the monthly percentage of inpatient combined acetaminophen-opioid doses relative to total enteral opioid doses ordered by other surgical providers as represented by the centerline (CL). The 3 SDs for upper control (UCL) and lower control limits (LCL) are displayed. The monthly volume of surgical cases represented by the bars over a period from January 2017 to April 2019.

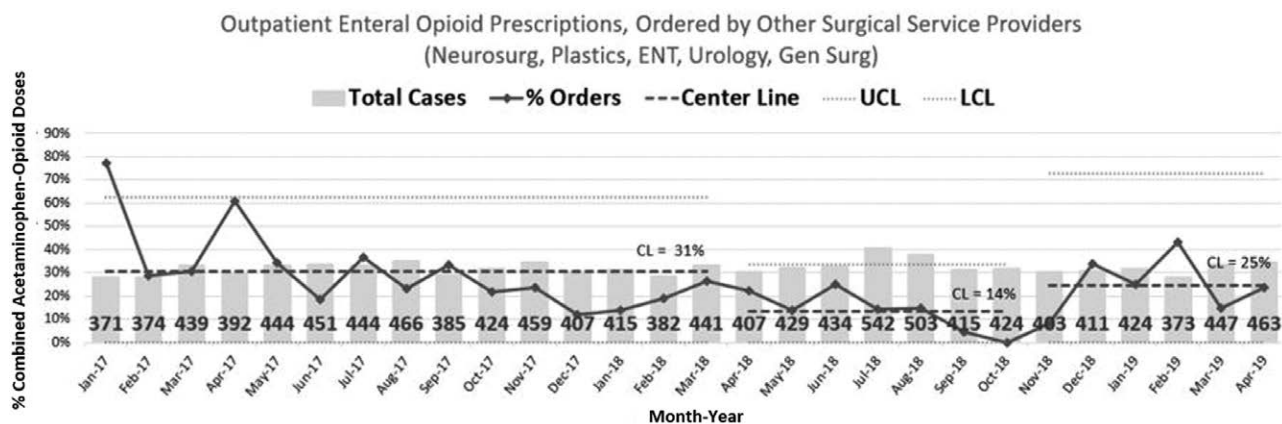


Fig. 6. Statistical process control (SPC) chart for a monthly percentage of outpatient combined acetaminophen-opioid prescriptions ordered by other surgical providers as represented by the centerline (CL) and the monthly volume of surgical cases represented by the bars over a period from January 2017 to April 2019. The 3 SDs for upper control (UCL) and lower control limits (LCL) are displayed.

amount of opioids prescribed to ambulatory patients can be adjusted independently, without making adjustments in opioids that must consider the dose and duration of the acetaminophen prescription. With this foundation, we are well-situated to optimize EOS further to guide prescriber habits toward multimodal therapies, while independently limiting opioid exposure.

The addition of acetaminophen to opioids is sometimes considered a potential dissuader to limit opioid abuse or overdose.²⁴ However, hydrocodone, which is only present in combination form in the United States, accounts for the largest proportion of opioid overdose in children and adolescents in pediatric orthopedic patients.⁷ Given this misuse, the prevalent practice of prescribing hydrocodone as a combination medication may also be increasing the potential for acetaminophen toxicity. Administering the opioid independently from acetaminophen at our site did not increase opioid consumption in inpatients. Many providers chose to include acetaminophen as a preselected postoperative analgesic.

This project has several limitations. Although the countermeasures seemed to evoke a sustainable practice change, as a quality improvement initiative without randomization, we may not have accounted for some confounders. Second, the project took place at an academic institution, which may limit its generalizability to other hospital settings. Third, although the ability to independently titrate opioids may improve pain management, we did not measure this outcome due to the inability to reliably collect pain scores with validated scales from all patients affected by this intervention over the years of data collection. Fourth, we were able to measure the total opioid consumption of inpatients, but due to limitations in tracking outpatient consumption, measurement of outpatient use was outside the scope of this project.

This project describes a quality improvement initiative to transform provider prescribing habits that reduce the risks associated with the use of combined

acetaminophen-opioid products. Future studies will measure patient satisfaction and pain scores in controlled populations.

DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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