JPPT | Single-Center Retrospective Study

# Reduction in Antibiotic Delivery Time Following Improving Pediatric Sepsis Outcomes Quality Improvement Initiative at a Major Children's Hospital

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**OBJECTIVE** Sepsis causes morbidity and mortality in pediatric patients, but timely antibiotic administration can improve sepsis outcomes. The pharmacy department can affect the time from order to delivery of antibiotics. By evaluating the pharmacy process, this study aimed to decrease the time from antibiotic order to delivery to within 45 minutes.

**METHODS** All antibiotic orders placed following a positive sepsis screen for acute care patients at a freestanding children's hospital from April 1, 2019, to December 31, 2019, were reviewed. Lean Six Sigma methodology including process mapping was used to identify and implement improvements, including educational interventions for providers. Outcome measures included time from antibiotic order placement to delivery and to administration. Additional assessment of process measures included evaluation of order priority, PowerPlan (an internally created order set) use, and delivery method.

**RESULTS** Ninety-eight antibiotic orders for 85 patients were evaluated. In an individual chart of antibiotic delivery time, a trend towards faster delivery time was observed after interventions. Stat orders (40.5 minutes [IQR, 19.5–48]) were delivered more quickly than routine orders (51 minutes [IQR, 45–65]; $p < 0.001$). Orders using the PowerPlan (20.5 minutes [IQR, 18.5–38]) were delivered more quickly than those that did not (47 minutes [IQR, 34–64]; $p < 0.01$). Shorter time to administration was observed with pneumatic tube delivery (41 minutes [IQR, 20–50]) than with direct delivery to a health care provider (51 minutes [IQR, 31–83]; $p < 0.05$) or to the automated dispensing cabinet's refrigerator (47 minutes [IQR, 41–62]; $p < 0.0001$).

**CONCLUSIONS** Multifactorial coordinated interventions within the pharmacy department improve medication delivery time for pediatric sepsis antibiotic orders.

**ABBREVIATIONS** ADC, automated dispensing cabinet; APPs, advanced practice providers; CHA, Children's Hospital Association; CPOE, computerized physician order entry; FMEA, Failure Modes and Effects Analysis; IPSO, Improving Pediatric Sepsis Outcomes

**KEYWORDS** antibiotic; pediatric; pharmacy; sepsis; turnaround time

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## Introduction

*Sepsis*, defined as "life-threatening organ dysfunction caused by a severe infection," continues to be recognized as a significant cause of morbidity and mortality within the pediatric population.[1–5] In the United States, an estimated 80,000 pediatric patients are hospitalized annually for sepsis with an associated mortality rate of 6.25%.[6] These statistics highlight the critical nature of timely recognition and management of pediatric sepsis.[2,5] As a result, national efforts are being made to streamline processes associated with the recognition and treatment of pediatric sepsis to reduce morbidity and mortality with an emphasis on development and implementation of sepsis bundles.[1,2]

The Children's Hospital Association (CHA) established a national collaborative entitled Improving Pediatric Sepsis Outcomes (IPSO). IPSO includes 57 children's hospitals working together to improve pediatric sepsis management. Our hospital joined the collaborative and specifically targeted recognition and management of sepsis on acute care floors. Among IPSO's "5 Key Processes to Affect Outcomes" were pharmacy initiatives, including reducing the time to antibiotic administration.[6]

The 2020 "Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children" recommends initiation of antimicrobial therapy within 1

**Table 1.** Failure Mode and Effects Analysis*

| Potential Failure Mode | Potential Failure Effects | Severity | Potential Causes | Occurrence | Detection | Overall |
|---|---|---|---|---|---|---|
| Pharmacists do not see the order | Delayed preparation | 6 | No phone call, no alert to the pharmacist, other checks that should be avoided in the case of sepsis | 9 | 9 | 486 |
| No communication about delivery | Medication delivered to the wrong location or via wrong system | 9 | No time for communication, no standard to when communication occurs | 6 | 5 | 270 |
| Patient not on the floor | Cannot administer medication | 9 | Transferred to ICU, getting testing | 7 | 3 | 189 |
| Untrained nurses | Does not know role in sepsis pathway | 7 | New staff, not enough education | 6 | 4 | 168 |
| Unavailable nurses | Not able to perform steps | 9 | Not enough nurses, other duties to perform, nursing ratio | 2 | 8 | 144 |
| No IV access | Cannot administer medication | 9 | Using IV for other things or lost IV access | 5 | 3 | 135 |
| Phone call does not occur | Order is not expedited | 9 | Busy with other tasks, no education | 5 | 2 | 90 |
| Unavailable pharmacists | Not able to perform steps | 9 | Not enough pharmacists, working on other medications | 1 | 8 | 72 |
| Unavailable delivery assistant | Not able to deliver medication | 9 | Not enough assistants | 2 | 3 | 54 |
| Untrained delivery assistants | Will not know where to deliver or priority of delivery | 6 | Frequent turnover | 4 | 1 | 24 |
| Untrained pharmacists | Does not know role in sepsis pathway | 5 | New staff, not enough education | 4 | 1 | 20 |

*ICU, intensive care unit; IV, intravenous*

* Scores represent a unanimously derived score from the stakeholder team. Severity: how strongly a failure would affect the outcome, with 10 being the strongest effect. Occurrence: how frequently a failure occurs, with 10 being most frequently. Detection: how easy it would be to tell if a failure occurred, with 10 being easiest to detect.

hour of recognition of septic shock and within 3 hours of sepsis identification.[1] Previous literature supports the use of sepsis tools to aid in early recognition of sepsis.[1,2,6] However, there is a lack of guidance regarding successful pharmacy processes that affect time to first antibiotic administration in the pediatric setting. The need for weight-based dosing makes it critical to perform this work in a pediatric setting rather than relying on adult-based efforts.

Lean and Six Sigma are complementary quality improvement techniques for processes. Lean focuses on the elimination of waste, or steps in the process that do not add value. Six Sigma involves a systematic analysis of a process to ensure that mistakes would be rare (i.e., the probability of a mistake would be more than 6 standard deviations from the mean). The principles of Lean and Six Sigma can be combined to form a powerful framework for addressing hospital processes; they have previously been used to reduce time to antibiotic administration in adult sepsis.[7] This study aimed to use the concepts of Lean and Six Sigma to improve time to antibiotic administration, focusing on pharmacy processes to reduce time from antibiotic order to delivery of the antibiotic to the care team.

## Materials and Methods

**Overview**. In this study, techniques based on quality improvement from the Lean Six Sigma framework were used to achieve a primary objective of decreasing time from antibiotic order to antibiotic delivery. As a collaborating member of the CHA IPSO initiative, UPMC Child ren's Hospital of Pittsburgh initiated a large quality improvement project with the aim to reduce mortality related to sepsis. The initiative to improve time to

**Table 2.** Education Interventions Performed by Pharmacy Staff

| Date | Education Intervention | Description |
|---|---|---|
| May 31, 2019 | Rxpharmacy assistant phone logs | Guidance for pharmacy assistant phone log documentation process |
| June 12, 2019 | IPSO team Rx process presentation | Analysis of pharmacy order processing to identify department process improvements and education needs to improve dispensing time |
| July 16, 2019 | Pharmacy staff education presentation | Same presentation at a pharmacy staff meeting as to the IPSO team; elicited input from pharmacy staff |
| August 8, 2019 | Resident education, “Sepsis-Inpatient” | Discussion of the CPOE PowerPlan |
| October 30, 2019 | Resident education, “Sepsis PowerPlan” Update, “Pharmacy Sepsis Pager” | Announcement of the pager activation addition to the CPOE PowerPlan |

*CPOE, computerized physician order entry; IPSO, Improving Pediatric Sepsis Outcomes*

antibiotic delivery and administration represented a subset of the larger initiative, which involved improved recognition of sepsis through the development of an automated screening tool and standardized huddle process developed in July 2017. These were supplemented by a written clinical guideline in April 2018 and a sepsis PowerPlan in September 2018 (Figure 1). A PowerPlan is a type of order set created in the computerized physician order entry (CPOE) software to implement clinical guidelines by assisting antibiotic decision-making, including recommended doses of antibiotics and defaulting of antibiotic priority status to one-time stat doses.

**Quality Improvement Overview**. The local IPSO committee assembled a team of stakeholders that included physicians, advanced practice providers (APPs), bedside nurses, pharmacists, and informatics staff. The team (n = 21) included representatives from various settings in the hospital, including multiple acute care floors, the intensive care unit, and emergency department, in order to maximize diversity of opinion and minimize bias from a single unit. Data collection included a review of all antibiotic orders placed following a positive sepsis screen (see Supplemental Figure S2) for acute care patients from April 1, 2019, through December 31, 2019. The aim of this pharmacy effort was to identify areas for pharmacy process improvements and education needs that could result in reducing the time from antibiotic order to delivery and subsequently administration.

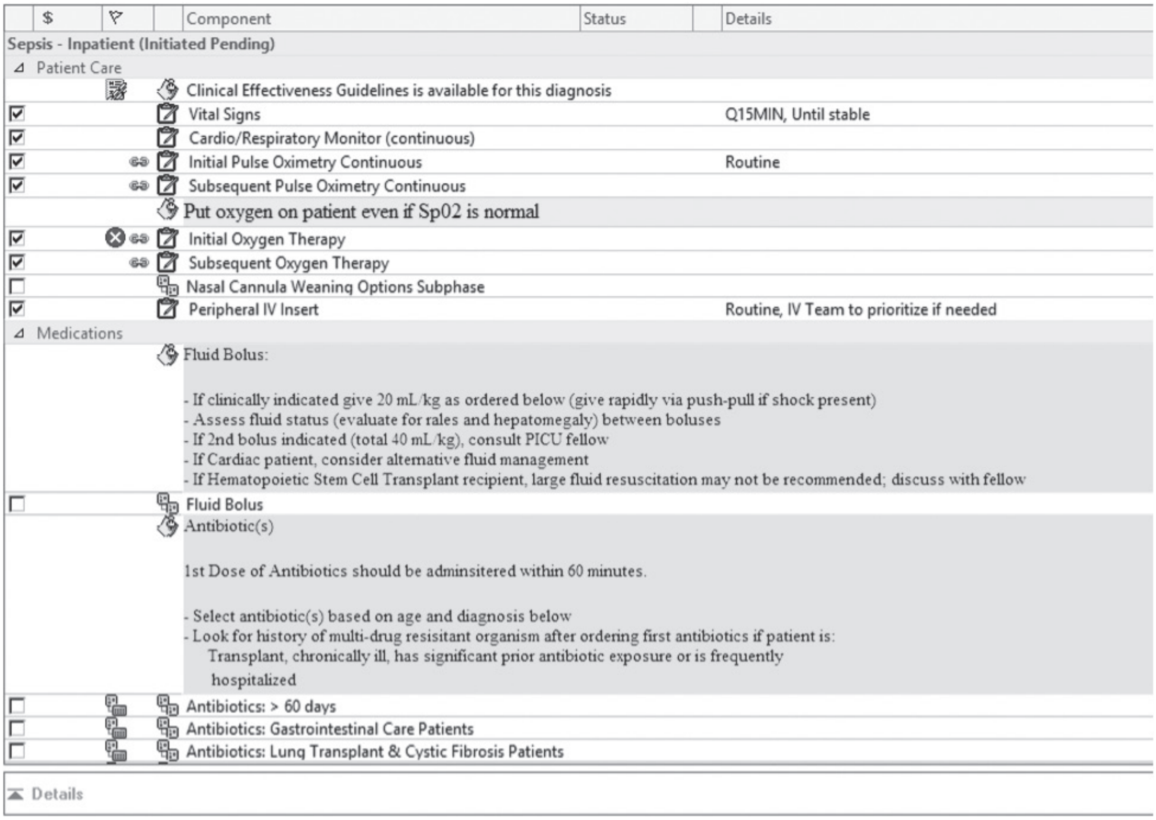
**Intervention Development**. Intervention development followed the Six Sigma framework of Define, Measure, Analyze, Improve, and Control (DMAIC). The stakeholder team defined time to antibiotic administration <60 minutes and time to antibiotic delivery <45 minutes as our targets.

The initial process map that was created by the stakeholder team is shown in Supplemental Figure S3. The team identified each step taken by physicians and APPs, bedside nurses, and pharmacists in the process from order entry to administration. Key steps identified during process map creation included a phone call from the nurse to the pharmacist to prioritize sepsis-related antibiotic orders and medication delivery. On the basis of this process map, the team performed a Failure Modes and Effects Analysis (FMEA; Table 1). In this tool, the team generated a list of potential ways the process could fail and then asked the stakeholder team to collaboratively score these from 1 to 10 on severity (how strongly a failure would affect the outcome with 10 being the strongest effect), occurrence (how frequently a failure occurs with 10 being most frequently), and detection (how easy it would be to tell if a failure occurred with 10 being easiest to detect). The score for each category was multiplied together to get a final FMEA score for each failure. The highest scoring failures became targets for intervention.

Delayed order verification and inconsistencies in medication delivery method were identified from the FMEA. For the former, the pharmacy team performed a series of educational interventions (Table 2) for physicians and APPs to emphasize PowerPlan use, for nurses to emphasize calling the pharmacy for order verification, and for pharmacy staff to emphasize the priority of sepsis antibiotic orders. For the latter, stakeholder meetings with pharmacy staff and bedside nurses led to standardization of pneumatic tube for delivery of sepsis-related antibiotic orders, which was included in the educational offerings presented to pharmacy and nursing. Educational interventions were completed by the end of July 2019. Monthly audit and feedback was performed for physicians in the form of positive feedback for those that used the PowerPlan at the monthly house staff meeting.

In October 2019, the phone call from the nurse to pharmacy was replaced by a pager linked to the PowerPlan such that when an antibiotic order was placed by using the PowerPlan, a pager in the pharmacy would alert the pharmacist of an impending order for sepsis (pager intervention).

**Figure 1.** Sepsis PowerPlan. The sepsis PowerPlan contains orders immediately recommended for a child with presumed sepsis.



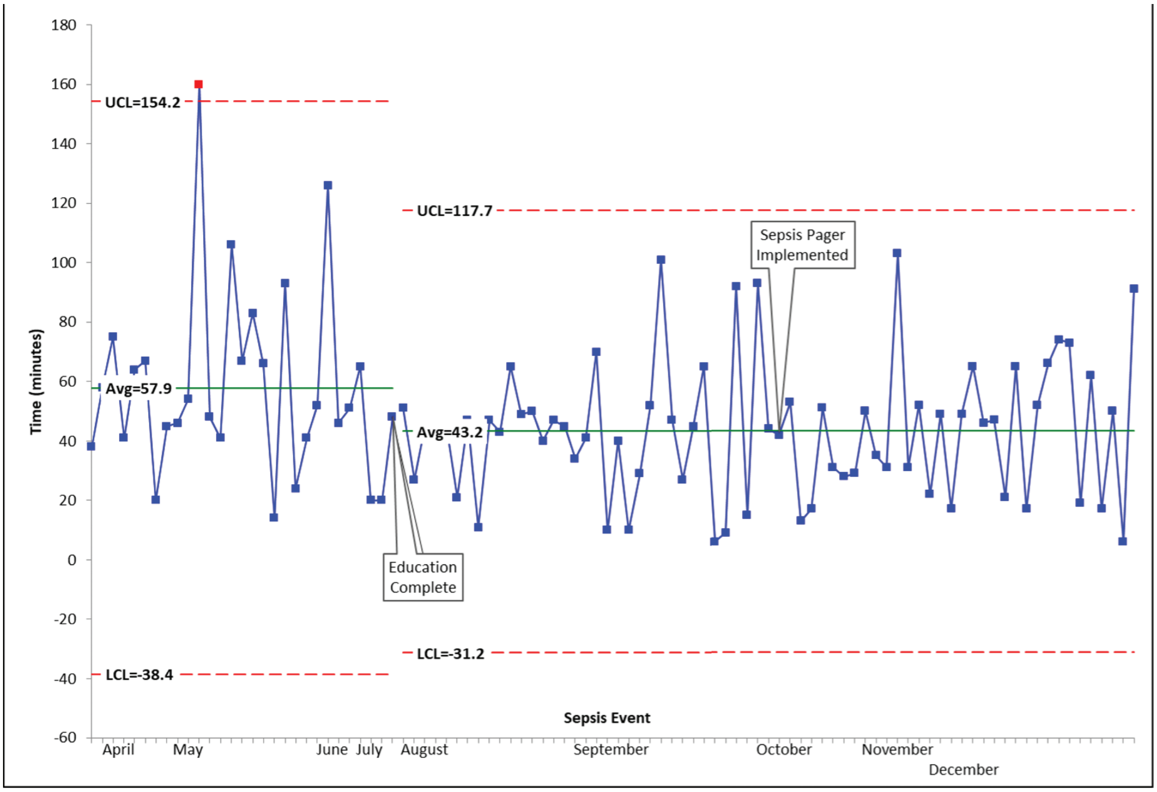

*IV, intravenous; PICU, pediatric intensive care unit; $SpO_2$, oxygen saturation*

**Time to First Antibiotic Administration**. All antibiotic orders temporally associated with a positive sepsis screen were identified for inclusion in the analysis. Initially, order identification required directed queries to search an institutional data warehouse for antibiotic orders associated with positive sepsis screens. Beginning June 1, 2019, the queries were automated as part of the sepsis QlikView (Qlik Software Company, King of Prussia, PA) dashboard providing real-time graphical analytics using the institutional data warehouse. The sepsis dashboard supplied sepsis alert time, medication(s), pharmacy verification time, and administration time. Additional information collected through chart review from the Cerner electronic record (Cerner, Kansas City, MO) included location of patient, use of PowerPlan, and order priority. Delivery details were retrieved from the pharmacy's medication delivery scanning and tracking records. Antibiotic doses were included if ordered within an *a priori* defined time frame of 2 hours before and 4 hours after a positive sepsis alert to avoid capturing antibiotics ordered beyond the context of sepsis identification. Only the first antibiotic administered for a particular alert was included. Orders were excluded after careful review by our clinical pharmacy team if they were deemed to be not ordered for sepsis or if they were ordered as a continuation of a previously prescribed antibiotic. Repeated antibiotic orders for the same admission were included if a new antibiotic order was placed, because this was considered a new sepsis episode.

The medication delivery scanning and tracking system was queried so that the final location and delivery time of the medication could be assessed. The antibiotics are delivered to the unit in 1 of 3 ways: 1) pneumatic tube system; 2) hand delivered to nurse or other health care professional; or 3) placed inside the refrigerator unit within the automated dispensing cabinet (ADC).

**Statistical Analysis**. The primary outcome was time from order placement to order delivery, because this was the most direct measurement of the pharmacy process. Secondary outcomes included time from order to antibiotic administration. Only the first antibiotic for each sepsis alert was included. A control chart was created by using the SPC for Excel package (BPI Consulting, LLC, Katy, TX) in Microsoft Excel (Microsoft Corporation, Redmond, WA). Additional pre- and post-

**Figure 2.** Individual chart of time from antibiotic order to delivery for each sepsis event. Each point represents a single antibiotic order. After the education interventions, there was a decrease in time from antibiotic order to delivery, which was sustained after sepsis pager implementation.




*LCL, Lower control limit; UCL, Upper control limit*

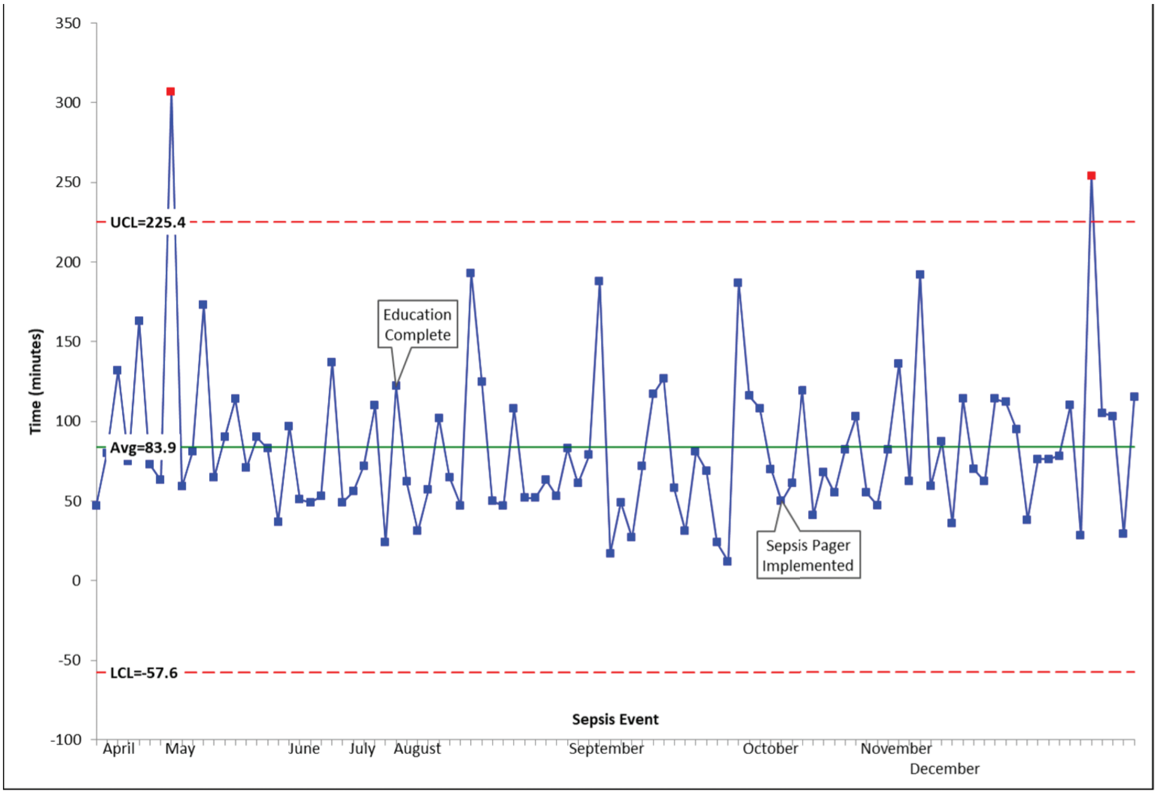
analysis for an overall change in median time from order to verification, delivery, and administration were performed with Mann-Whitney *U* test. The end of education interventions (July 31, 2019) was used as the end of the pre-period and beginning of the post-period for analysis. Based on the results of directed feedback from stakeholders, exploratory analyses were performed to identify the association between order priority and time to delivery, PowerPlan use and time to delivery, and delivery method and time to administration. When a medication is ordered, the priority status can be designated as routine (target delivery within 4 hours) or stat (target delivery within 1 hour). The Mann-Whitney *U* test was used to detect a difference between these 2 priority statuses. Because delivery method involved 3 categories, the Kruskal-Wallis test was performed to detect differences with *post hoc* testing, using the Dunn test with Bonferroni correction for multiple comparisons. These exploratory analyses were performed by using Stata version 15 (StataCorp, College Station, TX).

## Results

A total of 172 antibiotic orders for 108 patients were ordered as a result of a positive sepsis screen. Of these, 98 antibiotic orders for 85 patients met inclusion criteria during the study time frame (see Supplemental Figure S1). For the 98 included antibiotic orders, 20 were identified by using directed queries and 78 were identified by using the dashboard. Sixty-nine orders occurred after the initial interventions. Prior to interventions (April–July 2019), the median times from order to verification, delivery, and administration were 10 minutes, 51 minutes, and 75 minutes, respectively. Following educational interventions (August–December 2019), the median times from order to verification and order to delivery significantly decreased to 5 minutes ($p < 0.05$) and 45 minutes ($p < 0.05$), respectively. The median time from order to administration was unchanged at 70 minutes ($p = 0.42$).

Antibiotic delivery times are represented by the control chart in Figure 2. Following pharmacy and resident educational intervention in July, special cause variation was identified with a shift of 8 consecutive points below

**Figure 3.** Individual chart of time from antibiotic order to administration for each sepsis event. Each point represents a single antibiotic order. Neither intervention led to a decrease in time from antibiotic order to administration.




*LCL, Lower control limit; UCL, Upper control limit.*

the center line, allowing for a change in control limits after the intervention. No special cause variation was observed after implementation of the pager intervention. Figure 3 shows the control chart for the secondary outcome, time to antibiotic administration after order placement. A similar shift or trend after educational intervention was not observed.

Forty-nine percent of antibiotic orders were placed with a stat priority. Stat orders were delivered at a median time of 40.5 (IQR, 19.5–48) minutes compared with a median time of 51 (IQR, 45–65) minutes for routine orders ($p < 0.001$).

Method of delivery was assessed for the first antibiotic delivery for each alert. One order did not have the method of delivery recorded. Of the other 97 orders, the pneumatic tube system was used to deliver 39% (38/97) of first antibiotic doses, 42% (41/97) of first doses were placed into the refrigerator housed in the ADC, and 19% (18/97) of first antibiotic doses were delivered to the health care provider by hand. The median time to administration when delivered by pneumatic tube (41 minutes [IQR, 20–50]) was significantly less than the median time to administration when delivered by a delivery courier to a health care provider (51 minutes [IQR, 31–83]; $p < 0.05$) or to the ADC refrigerator (47 minutes [IQR, 41–62]; $p < 0.0001$). No significant difference was found between delivery to a health care provider and to the ADC.

Twelve orders used the PowerPlan; all of these occurred after the educational interventions. Orders that used the PowerPlan were delivered faster (20.5 minutes [IQR, 18.5–38]) than those ordered without the PowerPlan (47 minutes [IQR, 34–64]; $p < 0.01$).

## Discussion

Implementation of targeted interventions reduces morbidity and mortality in pediatric sepsis.[8,9] The importance of time to first antibiotic is universally endorsed in institution-derived sepsis bundles and recommendations have been incorporated into evidence-based guidelines.[1] Lean methodology for optimization of antibiotic dispensing workflow has been described in the adult setting, but there is a paucity of data describing the best practices for pediatric pharmacy processes.[7] This study used the methods of Lean and Six Sigma to evaluate pharmacy-specific processes to aid in the overall improvement of antibiotic order time to delivery where the pharmacy department in a pediatric institution can have the most effect. In particular, an education intervention (see Table 2) derived from a multidisciplinary team approach using the techniques of Lean Six Sigma resulted in a reduction in time to antibiotic delivery. While implementation of an automated pager system to alert the pharmacy did not result in further improvement, it likely helped to maintain the existing improvement because education initiatives are known to require periodic updates. The automated pager has also been very well received by both nursing and pharmacy staff. Similarly, the monthly audit and feedback by providing positive reinforcement likely contributed to the sustained improvement seen over the many months after the initial education intervention.

Initiatives targeting patients with presumed or developing sepsis have been instituted at many adult institutions nationally, and specific program descriptions can be found in the literature.[10,11] These initiatives were multidisciplinary with pharmacy participation focused on the antibiotic order and delivery process. Flynn et al[10] describe a sepsis response program in an adult setting. The primary goal was to increase the proportion of patients receiving antimicrobial therapy within 1 hour of onset. The sepsis response team was able to decrease median time to administration from 2.4 hours to 0.65 hours. In 2016, Beardsley et al[11] reported a similar scenario, again in the adult population, with the goal of trimming turnaround time and expediting prompt antibiotic administration on non-critical care units using pager alerts and an electronic order set. The time from page to antibiotic administration was reduced to 51 minutes in the non-critical care setting. These time reductions are similar to our experience.

Similarities between our initiative and these publications are the assembly of a multidisciplinary team, creation of a guideline-based antibiotic therapy order set, and a pharmacy notification system to alert personnel of imminent orders.[10,11] Some important differences to note are that adult facilities use standard dosing regimens and can facilitate availability of more common medications through addition to ADC stock. In pediatric facilities, medication doses must be weight based, requiring compounding by the pharmacy.

It is undeniable that adding antibiotics to ADCs can significantly reduce time to first dose administration in adult patients where standard doses are broadly suitable.[12] In the pediatric population, weight-based dosing makes eliminating or minimizing manipulation of drugs outside of the sterile products environment problematic. Levine et al[13] state that ADC stock in the pediatric setting typically consists of bulk containers requiring dose calculations and manual preparation of medications, which has been associated with medication errors. In keeping with the recommendations above, our institution chose to explore pharmacy department practice changes that would decrease the order-to-delivery period enough that antibiotic administration within 60 minutes could occur.

It should be noted here that delivery via pneumatic tube system was associated with a significantly shorter time to administration than either of the human courier options ($p < 0.05$). This is compatible with the experience of the Code Sepsis initiative per Beardsley et al[11] which identified the use of pneumatic tube as the preferred mode of delivery. This improvement from pneumatic tube delivery likely highlights several important factors. First, the pneumatic tube represented a more reliable system. Delivery assistants often worked in multiple floors and may have had limited availability. Even if they were available, direct delivery to a nurse was not always possible owing to the number of tasks that they were required to perform for a patient with suspected sepsis. Finally, the pneumatic tube has an alert system, once the antibiotic has been delivered, that would notify those nearby on the floor; this would not be the case for a delivery to the ADC. Unfortunately, only 39% of orders were delivered via pneumatic tube despite attempts to standardize. Further work may examine the limitations in improving pneumatic tube use.

It was thought that more rapid availability of antibiotics would trigger a secondary effect of reduction of time from order-to-administration to occur within 60 minutes, but this was not observed in our study. One reason for this may be that education was offered regarding practical CPOE suggestions for providers and specific process changes for pharmacy personnel, but nursing staff education focused on assuring timely communication and did not discuss timely administration. The next steps in this process for us will be to focus on timely administration once delivery occurs, which will include nursing educational interventions. Combining this with increased PowerPlan use would likely lead to significant improvements in the final steps of the process.

There are several limitations to this quality improvement project. Data collection evolved over time, with an initial set of directed queries eventually transitioning to data collection using a real-time dashboard. Not uncommonly, data collection changes during the course of quality improvement work. In the present work, it is reassuring to note that there was no special cause variation in the control charts, occurring at this change in data collection methodology and only after the intervention. Once data collection was real-time, just-in-time education could be provided to the pharmacy and medical residents as immediate feedback. The inclusion time between sepsis alert and antibiotic ordering was determined *a priori*. This could have led to the exclusion of antibiotic orders that potentially related to a sepsis alert, but should have not biased results because all orders for sepsis should be handled with a similar urgency once placed. While a pharmacy-led initiative resulted in a reduction in antibiotic delivery time at the study institution, these specific interventions may not be generalizable to other institutions or care settings. However, the Lean Six

Sigma methodology can be widely applied to optimize processes tailored for a specific institution.

## Conclusion

Pharmacy involvement in the timely administration of antibiotics in pediatric sepsis is essential. Multifactorial coordinated interventions determined by Lean Six Sigma methodology within the pharmacy department facilitate improved delivery time but not medication administration time for pediatric sepsis antibiotic orders. Future work targeted towards reducing the time from delivery to administration may involve coordinated efforts between pharmacy, nursing, and other disciplines involved in the administration process.

## Article Information

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**Ethical Approval and Informed Consent.** This study was deemed a quality improvement project not subject to review for human subjects research by the University of Pittsburgh Institutional Review Board. The study was conducted under approval for a quality improvement project by the UPMC Quality Improvement Review Committee.

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