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# A Quality Initiative to Decrease Time to Antibiotics in Children with Sickle Cell Disease and Fever

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## Abstract

Introduction: Children with sickle cell disease (SCD) are at increased risk for sepsis secondary to functional asplenia. Timely administration of antibiotics, within 60 minutes of triage, is a national indicator of guality SCD care in the United States. However, there are no reports demonstrating the feasibility of doing so in the outpatient hematology-oncology clinic setting. Local Problem: At baseline, in our pediatric hematology-oncology outpatient center, just 10% of children with SCD and fever received timely antibiotics. Methods: We implemented a process improvement initiative for children with SCD and fever with the aim of ≥90% receiving timely antibiotics. We enacted interventions focused on general clinic processes from check-in to antibiotics and population-specific interventions, including an intravenous access protocol, notification/communication among staff members, and design of an electronic order set. Results: The percentage of children receiving timely antibiotics improved from 10% to 77% with successful maintenance following the interventions. Residual delays are due to nonexpeditious order placement and difficult intravenous access. Conclusion: Improving the timely administration of antibiotics in the outpatient hematology-oncology clinic setting for children with SCD and fever is possible. Achieving at least 90% timely antibiotics for children with SCD and fever in the outpatient clinic setting will require ongoing efforts at expeditious order placement and intravenous access. (Pediatr Qual Saf 2019;1:e245; doi: 10.1097/ pq9.00000000000245; Published online January 10, 2020.)

# INTRODUCTION

Sickle cell disease (SCD) affects over 100,000 individuals in the United States, including up to 1 in 400 African OUALITY . SAFETY

Americans.1 SCD occurs as a consequence of the inheritance of mutations in the  $\beta$ -globin gene, which results in an abnormal hemoglobin variant. The result is small blood vessel occlusion, chronic hemolytic anemia, endothelial cell dysfunction, and end-organ damage. Historically, children with SCD had a mortality rate of 0.5/100

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To cite: McKinney C, Caruso-Brown A, Montgomery K, Gillespie A, Coughlin R, Law D. Brouwer A. Tytler L. Hilden J. Nuss R. Unique Challenges and Feasibility of a Quality Improvement Initiative to Decrease Time to Antibiotics in Children With Sickle Cell Disease and Fever. Pediatr Qual Saf 2019;1:e245.

Received for publication June 12, 2019; Accepted November 18, 2019.

Published online January 10, 2020

DOI: 10.1097/pq9.00000000000245

person-years due to functional asplenia.<sup>2</sup> Mortality has declined to 0.15/100 person-years due to universal newborn screening with the early referral for education, penicillin prophylaxis initiation, and supplementary

immunization for encapsulated organisms. However, bacterial sepsis with encapsulated organisms continues to be a significant , QUALITY concern in children with SCD.<sup>3</sup>

Bacteremia remains a major concern for children with SCD due to functional asplenia and consistently poor adherence to prophylactic antibiotics and supplementary immunizations.<sup>4-10</sup> A recent publication found that only 18% of children with SCD

received prophylactic antibiotics  $\geq$  300 days per year.<sup>11</sup> Neunert et al<sup>12</sup> have reported just 38% of children receive the pneumococcal vaccine by age 3. Additionally, bacteremia may occur due to nonvaccine pneumococcal serotypes.13,14

Although the impact of delayed antibiotics specifically on children with SCD and fever is unknown, delayed antibiotic therapy initiation for a child with bacteremia is associated with increased mortality leading to the adoption of early antibiotic administration within the "Golden Hour" as the standard of care for sepsis management.<sup>15</sup> Pediatric oncology centers now track the percentage of children with febrile neutropenia receiving antibiotics in <60 minutes as a quality of care indicator.<sup>16</sup> The outcome of an initiative at our pediatric hematology/oncology center to decrease the time to antibiotic administration



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for children with febrile neutropenia demonstrated both feasibility and reduced need for critical care.<sup>17</sup>

Until 2011, when a panel with expertise in SCD published 41 indicators, there were no quality indicators of care for children with SCD.<sup>18</sup> The panel identified 8 indicators as "most likely to have a large effect on improving quality of life and health outcome" including, "Children with SCD who have a fever  $\geq 38.5$ °C should receive parenteral broad-spectrum antibiotic treatment within 60 min of triage." In 2014, an National Heart Lung Blood Institute (NHLBI)-endorsed sickle cell consensus expert panel similarly endorsed timely antibiotics for febrile children with SCD and was more specific about the antibiotics.<sup>19</sup> The NHLBI panel rated their recommendation importance as 9 out of 9, their highest ranking.

The rationale of the quality improvement (QI) initiative reported here was to improve the percentage of febrile children with SCD who receive a parenteral broad-spectrum antibiotic within 60 minutes of triage from 10% or 90% or greater as a step toward meeting the quality indicator. To date, there have been no prior reports on initiatives to do so in a pediatric hematology–oncology outpatient clinic setting.

## **METHODS**

#### Approval

The Organizational Research Risk and Quality Improvement Review Panel affiliated with the Institutional Review Board at the University of Colorado Denver reviewed and approved the QI initiative. Initiative completion occurred at the Center for Cancer and Blood Disorders (CCBD) at the Children's Hospital Colorado, following multidisciplinary team formation. The rationale was to meet the quality initiative with a goal of >90% of children with SCD receiving antibiotics within 60 minutes of the triage.

## Multidisciplinary Team

We organized a multidisciplinary team including stakeholders from scheduling, pediatric hematology, nursing, and medical assistants. Each stakeholder was tasked to champion the initiative as it related to their functional domain by educating their colleagues. The CCBD QI officer provided leadership and support. Although not included on the multidisciplinary team, we discussed the project with a convenience sample of affected families, who supported an intervention that could theoretically reduce the time spent in the outpatient center. The team frequently met to review data and develop intervention strategies.

## Improvement Population and Setting

For context, children with SCD and fever and those with cancer and febrile neutropenia are treated in the CCBD outpatient clinic during business hours so that they can be evaluated and treated more promptly than in the emergency department (ED) by physicians with expertise in their conditions. Management of children presenting after-hours occurred in the ED. There are approximately 23,000 visits to the CCBD outpatient clinic annually, including scheduled and add-on ill visits. Eighty percent of the visits are for oncologic care. The approximately 200 children with SCD followed at the CCBD have an average of 920 visits annually; this incudes scheduled and add-on ill visits.

There are discrete teams for children with solid, liquid, and brain tumors. There is also a team for experimental therapeutics. The oncologic teams have multiple physicians and mid-level practitioners present for each session. The hematology team functions independently of the oncologic teams and includes a scheduler, a medical assistant, 2–3 nurses, and a single physician in clinic per session.

The CCBD outpatient clinic also has an infusion center where specifically designated infusion nurses care for both children with oncologic and hematologic disorders as needed. The process improvement project conducted for the febrile neutropenia population with cancer conducted by the oncologists from CCBD is published.<sup>17</sup>

Electronic medical record (EMR) data were reviewed to identify children who met the following operational definition: laboratory-proven SCD and reported temperature at home or on arrival at the clinic  $\geq$ 38.3°C without prior antibiotic treatment. We excluded children who developed a fever during blood transfusion in the clinic.

#### Improvement Strategy

We evaluated the clinic flow process through a quantitative time-series study design and determined the time between specific processes by analyzing timestamps in the EMR. We performed process mapping and defined check-in as the time the child was registered as arrived at the receptionist's desk and triage as the time vital signs were first recorded in real-time by the medical assistant. We employed Lean Methodology and assessed a series of process changes and interventions to assess outcome. Subprocess measures included check-in time to triage, triage time to provider order placement, check-in to order placement, and triage to antibiotic administration.

At the time the project began, approximately 10 children presented per six-month time period with fever. We gathered a baseline performance assessment before initiating the improvement work. For baseline performance, therefore, we chose to review the process data and the percent of children who received timely antibiotics for the 6 months from January to June 2012.

For the first intervention, we streamlined the check-in and triage process using the most successful elements from the cancer febrile neutropenia initiative.<sup>17</sup> These elements included extensive, repetitive education by email, meetings, and informally to staff about fever urgency, creation of a new encounter type in the EMR designated "SCD Fever" which designated an infusion room placement rather than in a standard clinic room by the medical assistant triaging the child. Antibiotics were already available locally due to prior work with the cancer febrile neutropenia initiative.

The second intervention focused on decreasing delays in antibiotic administration related to difficulty obtaining venous access. We implemented a protocol that quickly escalated care if the designated treatment center nurse was unsuccessful at obtaining quick access. If the primary treatment center nurse was unable to obtain access after 2 attempts and the child had stable vital signs, the treatment center charge nurse would then attempt up to twice, then discuss the situation with the doctor. A decision was then made to give the antibiotic orally or intramuscularly if a blood culture had been obtained or to await ultrasound guidance by the flight team staff or hospital peripherally inserted central catheter (PICC) service. We made notations in the hospital chart for children with known difficult venous access and the more experienced nurses, or ultrasound guidance was used earlier in the process for these children.

The third intervention focused on the prearrival process triggered by the clinic nurse receiving a patient phone call about an impending fever visit. The goal was to improve communication to support proactive tasks in parallel: nurses notified the scheduler to create the patient encounter in the EMR to avoid delays at check-in, the medical assistant, the clinic charge nurse to identify an available fever infusion room and nurse, and the clinician for antibiotic order placement. The primary role fell to the clinic nurse to communicate with all involved.

For the fourth intervention, an author (R.N.) developed an EMR order set designed specifically for SCD and fever. Other hematology physicians modified, and then endorsed the order set. The order set was readily available, and use was repetitively encouraged at meetings, one-on-one discussions with the hematologists, and recurrent email messages. The clinic nurses and infusion nurses were also informed and asked to encourage physicians to use the order set.

## Analysis

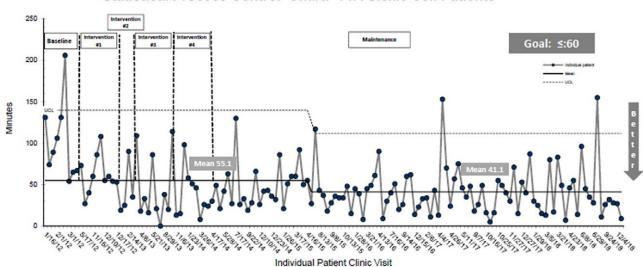
An analyst (D.L.) ran reports quarterly through an automated system to determine case frequency. The EMR was then reviewed by an author to verify the identified cases met criteria. We reviewed the time to antibiotics from triage outcome metric and the subprocess measure quarterly. We defined antibiotic administration time as the antibiotic start time.

To evaluate the intervention impact on time to antibiotics, we employed a statistical process control chart (Fig. 1). We evaluated these data for special cause, to link interventions to outcomes. We gathered the baseline performance assessment before initiating the improvement initiatives. We continued to collect data in the maintenance phase.

# RESULTS

At baseline, caregivers of children with SCD were asked to call in if their child had a fever  $\geq$ 38.3 (our institutional threshold for fever). However, the clinic arrival process was the same whether prenotification was given or not (Fig. 2A).

At baseline, just 1 of 10 children seen over the 6 months received timely antibiotics. Lack of recognition that fever was a time-sensitive issue for children with SCD by schedulers, medical assistants, and nursing contributed to delays



Statistical Process Control Chart: TTA Sickle Cell Patients

Fig. 1. The statistical process control chart shows improvement in time to antibiotic administration with successive interventions. Baseline data were obtained from January to June 2012 which identified delays at many stages of complex process. Intervention #1: revision to check-in process and designation of fever infusion room. Intervention #2: development of protocol for IV access. Intervention #3: Revision of process for notification/communication. Intervention #4: Availability of order set in electronic medical records.

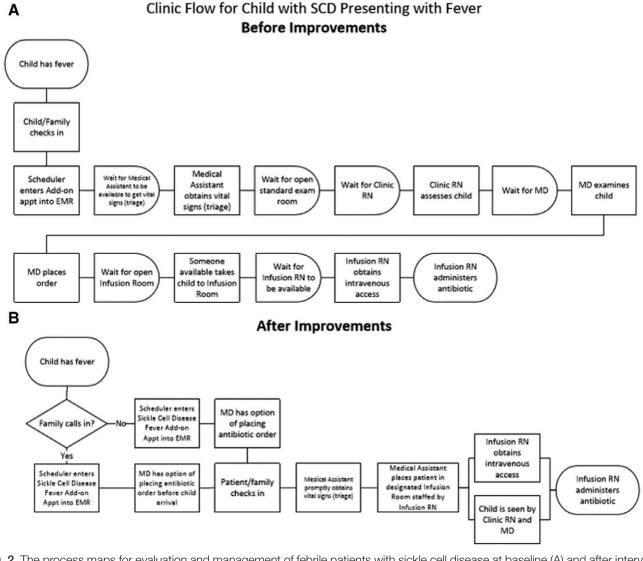


Fig. 2. The process maps for evaluation and management of febrile patients with sickle cell disease at baseline (A) and after interventions 1–3 (B) are presented. Appt, appointment; RN, registered nurse; MD, medical doctor.

in time to antibiotic administration (TTA) at baseline. The unpredictable nature of these add-on visits stressed an already heavily booked clinic without the flexibility of an additional "doctor of the day," as was present in oncology, who was assigned to provide urgent care. Poor communication between staff including: the person who received a call, the scheduler, the medical assistant who took the vital signs and roomed the child, the nurse, the physician placing antibiotic orders, and infusion staff administering the antibiotic also led to delays.

Intervention 1 revised the check-in through the antibiotic process and designated a "fever infusion room." and lasted 6 months. Ten children presented; 6 children received timely antibiotics. The root cause analysis revealed a delay in time from triage to provider antibiotic order placement and successful venous access by nursing.

Intervention 2 addressed intravenous access by introducing a protocol. The intervention was 2 months, and 4 children presented; 2 received timely antibiotics. The delays were again due to suboptimal antibiotic order placement and difficult intravenous access. The intervention period was limited because the team thought better notification and communication were rapidly indicated.

Intervention 3 was 6 months and focused on improved notification/communication as described in the Methods. Six of 9 children seen received timely antibiotics. Delays persisted with order placement and venous access.

Intervention 4 addressed order placement by providing a specific order set to streamline care. Eleven children presented, and 9 received timely antibiotics. Figure 2B shows the process map for intervention 4, which was 6 months and maintenance, which was 55 months.

The root cause analysis in maintenance confirmed delayed order placement, and difficult venous access persisted. However, 77% of the 102 children in maintenance received timely antibiotics. The mean time from check-in to antibiotics fell from 135 minutes at baseline to 46 minutes in maintenance (data not shown). The median time to antibiotics was reduced from 81.5 minutes at baseline to 36 minutes in maintenance, as shown in Figure 3.

# DISCUSSION

# Summary

Although numerous reports demonstrate the feasibility of decreasing delays in antibiotic administration to febrile children with cancer and neutropenia, we are the first to demonstrate the same is feasible for children with SCD and fever. Similar to Hariharan et al,<sup>20</sup> we found that to achieve the same end goal of timely antibiotics, process maps must be population specific. Whereas our goal was 90% timely antibiotics, we were able to improve from 10 to nearly 80% by streamlining care to reduce non–value-added processes. We found that there was some overlap with processes identified as helpful for children with febrile neutropenia, but presumed limited staffing and venous access issues were unique to the SCD population.

## Interpretation

We initially postulated that the febrile neutropenia process for receipt of parenteral antibiotics in the outpatient clinic setting would be effective and perhaps timelier for the children with SCD because there was no need to apply Eutectic Mixture of Local Anesthetic and wait for it to be effective before accessing a central venous catheter (CVC) or to wait for an absolute neutrophil count report from the laboratory to administer antibiotics. Instead, we found that we were able to achieve and maintain 77% timely antibiotics, whereas the febrile neutropenia initiative achieved and maintained at 100%.

Although there were some commonalities in the processes, there was also a need for disease-specific modification. Both initiatives included a need for multidisciplinary champions who would provide education and reinforcement to their colleagues to achieve sustainability. Also, in common was the need for education reinforcement and improved communication between disciplines. An add-on fever visit in the EMR indicating immediate placement into a designated infusion room rather than a standard clinic room was beneficial for both initiatives, as was antibiotic storage in the clinic.

Whereas the febrile neutropenia initiative did not develop a specific order set but was able to achieve 100% timely antibiotics, we did develop a specific order set. It does not appear that the availability of the order set facilitated timely order placement since delays persist. The rare add-on nature of the visits to an already heavily scheduled single hematologist who must triage patients may be more the root cause. The NHLBI recognizes that SCD is a rare underserved disease, and implementing the National Institutes of Health guidelines into practice may be difficult, so it has established the SCD Implementation Consortium to assist chosen SCD centers do so.<sup>21</sup> Perhaps, the Consortium will develop effective tools to overcome staffing limitations.

Timely venous access is a second root cause for delayed antibiotics in SCD but not for febrile neutropenia.<sup>17</sup> Children with febrile neutropenia almost universally have indwelling CVCs due to the need for chemotherapy administration and/or frequent blood product transfusion. Children with SCD usually do not have a CVC. Nurses staffing pediatric hematology/oncology outpatient clinics are generally highly skilled at accessing CVCs but, as a consequence, are less skilled at peripheral venous access. A future direction may include a request to house ultrasound equipment in the center to facilitate venous access.

We postulated that more timely antibiotics would be administered in the ED for a child with SCD and fever because scheduled visits are not competing, and potentially the nurses are more skilled at peripheral venous access than in an outpatient hematology/oncology clinic. However, 2 recent publications report that just 81.4%–91% of children with SCD seen in the ED for fever receive antibiotics.<sup>22,23</sup> Eisenbrown et al<sup>24</sup> found that timely antibiotic administration within 60 minutes occurred in only 7.4% of patients. Even following

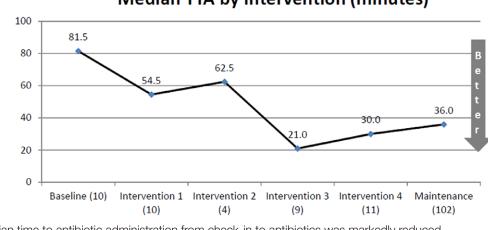




Fig. 3. The median time to antibiotic administration from check-in to antibiotics was markedly reduced.

a quality initiative, the percentage of children receiving timely antibiotics increased to only 37.7% in the ED.

As a consequence of the initiative, there is a benefit to the children and families. The unexpected benefit is an 89-minute or 66% reduction in mean clinic visit time, and median visit time reduction of 56% or 46 minutes. Although we did not survey the families, prior studies document a strong, inverse relationship between wait times in outpatient clinics and patient satisfaction.<sup>25,26</sup> From a management perspective, improving clinic room turnover is financially advantageous.

#### Limitations

The volume of children receiving care at the outpatient center is modest compared with many centers where SCD febrile visits may be more routine. Performance of this initiative at a tertiary children's hospital in a large pediatric hematology/oncology outpatient clinic with an infusion center limits the generalizability of the work. Also, clinic flow processes likely vary at other sites.

# CONCLUSIONS

The initiative implies that a dedicated, multidisciplinary team can significantly improve the percentage of children with fever and SCD who receive timely antibiotics in the outpatient clinic setting and reduce visit duration secondarily. Understaffing and difficult venous access are likely generalizable root causes that must be addressed to meet the quality indicator.

The report employed the Standards for QI Reporting Excellence 2.0 publication guidelines for reporting health care QI research.<sup>27</sup>

## DISCLOSURE

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

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