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Successful emergency department interventions that reduce time to antibiotics in febrile pediatric cancer patients

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ABSTRACT

Children with cancer and fever are at high risk for sepsis related death. Rapid antibiotic delivery (< 60 minutes) has been shown to reduce mortality.

We compared patient outcomes and describe interventions from three separate quality improvement (QI) projects conducted in three United States (US) tertiary care pediatric emergency departments (EDs) with the shared aim to reduce time to antibiotic (TTA) to < 60 minutes in febrile pediatric oncology patients (Temperature > 38.0 C). A secondary objective was to identify interventions amenable to translation to other centers.

We conducted a post project analysis of prospectively collected observational data from children < 18 years visiting these EDs during independently conducted QI projects. Comparisons were made pre to post intervention periods within each institution.

All interventions were derived independently using QI methods by each institution. Successful as well as unsuccessful interventions were described and common interventions adopted by all sites identified.

A total of 1032 ED patient visits were identified from the three projects. Improvement in median TTA delivery (min) pre to post intervention(s) was 118.5–57.0 at site 1, 163.0–97.5 at site 2, and 188.0–111.5 at site 3 (p<.001 all sites). The eight common interventions were 1) Triage application of topical anesthetic 2) Rapid room placement & triage 3) Resuscitation room placement of ill appearing children 4) Close proximity to central line equipment 5) Antibiotic administration before laboratory analyses 6) Consensus clinical practice guideline establishment 7) Family pre-ED education for fever and 8) Staff project updates.

This core set of eight low cost, high yield QI interventions were developed independently by the three ED's which led to substantial reduction in time to antibiotic delivery in children with cancer presenting with fever. These interventions may inform future QI initiatives in other settings caring for febrile pediatric oncology patients.

PROBLEM

In a recent retrospective study of the Nationwide Emergency Department Sample dataset in the US there were 294,289 ED visits by pediatric patients with cancer from 2006-2010. Fever and fever with neutropenia (FN) were the two most common diagnoses in this population, accounting for almost 20% of these visits.[1]

At each institution in this project, providers noted significant delays in antibiotic delivery to children visiting their emergency department (ED) with cancer and fever. As a group, these sites noted a paucity of detailed intervention resources to direct this improvement work.

In this project we explored the approach of three regional children's hospital EDs sharing a similar Specific, Measurable, Achievable, Relevant, Timely (SMART) Quality Improvement (QI) aim of reducing time to antibiotics for a collectively large number of febrile pediatric cancer patients. We sought to compare outcomes as well as identify and describe best practice intervention strategies that led to rapid antibiotic delivery in these patients so as to inform future QI efforts, including the potential for creating a common "bundle" of interventions to improve care in this high risk population.

Characteristics of the participating US children's tertiary care EDs included one suburban and two urban settings with annual ED visits ranging from 25,000-100,000. Each institutional QI project reported use of the Model for Improvement methodology.[2] Quality improvement team composition at minimum included input from nursing, pharmacy and faculty from both ED and pediatric hematology/oncology subspecialists.

BACKGROUND

In pediatric oncology patients with neutropenia, fever may represent the first sign of life threatening infection and is the most common cause of admission to the hospital in this patient population.[1] As these patients are at high risk for sepsis, severe sepsis and septic shock, especially when their absolute neutrophil count (ANC) is < 500 cells/mm, current recommendations by both oncology and infectious disease experts suggest prompt antibiotic delivery within 60 minutes of presentation.[3–5] This sixty minute window led to improved clinical outcomes with reductions in morbidity and mortality in multiple adult studies and in pediatric studies, although prospective studies are limited.[6–8]

In order to achieve the goal of rapid antibiotic delivery, many institutions have employed QI strategies to decrease their time to antibiotic delivery. Several studies have shown that QI projects can improve time to antibiotics for pediatric neutropenic patients on inpatient and intensive care units.[9–11] Furthermore, studies demonstrated that QI initiatives can improve time to antibiotics in the pediatric emergency department (ED).[12–15]

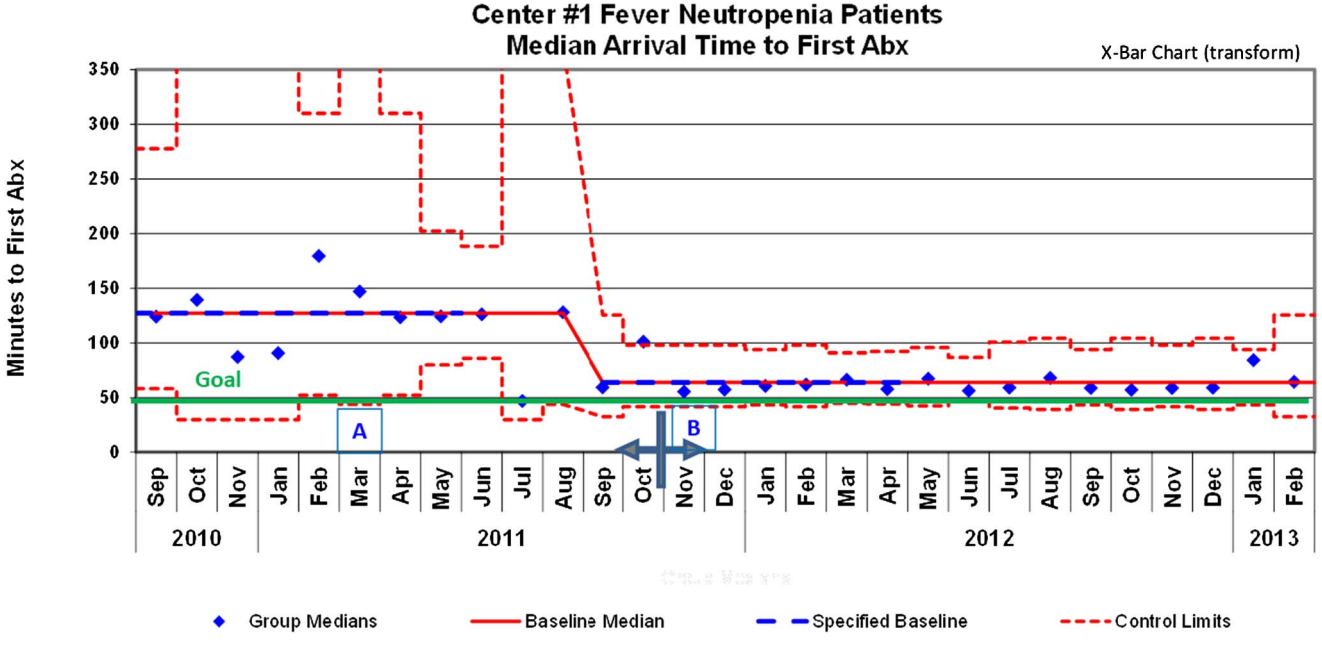
Although it is known that QI efforts can improve the time to antibiotics for these patients, there is limited information regarding specific interventions that did or did not lead to reduced time to antibiotic delivery. Lessons learned from unsuccessful strategies are often underreported but may be helpful to direct other institutions before valuable resources are consumed during attempts to replicate this work. QI strategies isolated to individual institutions may limit their generalizability. [9–15]

BASELINE MEASUREMENT

Data from the medical records of children with all types of cancer presenting to the ED for evaluation of fever were collated from the three separately conducted prospective observational QI projects regardless of ED disposition. All sites excluded children who received any antibiotics prior to arrival at the respective institution. Time to antibiotic (TTA) delivery was defined as the difference in time from ED nurse documentation of first antibiotic administration time and ED arrival time (in minutes), a standard US ED metric.[16] The baseline mean TTA were 118.5 minutes, 163.0 minutes, and 188.0 for Centers 1, 2, and 3 respectively (Figs. 1, 2 and 3). The total mean baseline TTA was 156.5 min for all three hospitals combined.

DESIGN

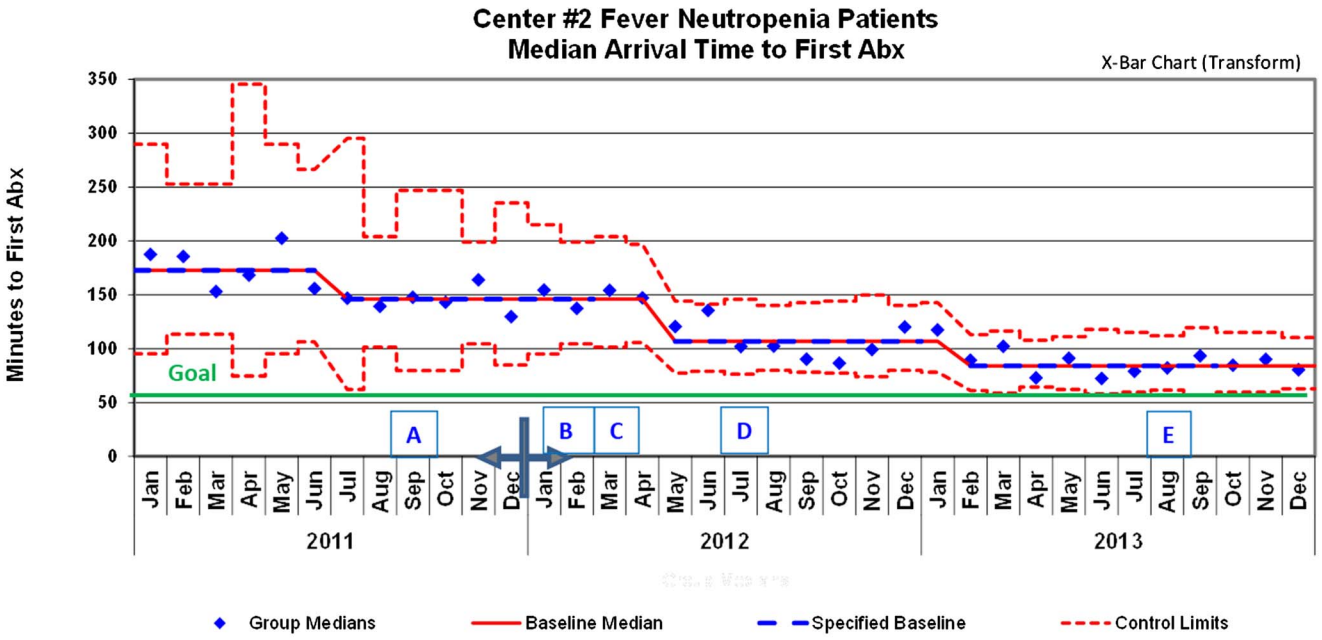
This report is a post project analysis of prospectively collected observational data collected from separately conducted QI projects in three US tertiary care pediatric emergency departments. In each project data from



Group Means (Not Plotted)	140	143	88	91	183	153	152	146	142	55	131	71	110	65	58	63	68	71	61	69	60	69	72	61	63	64	64	98	65
Group Size	5	2	2	2	4	3	4	13	18	2	3	4	9	9	9	11	9	13	12	10	17	8	7	11	7	9	7	11	4

NOTE: A ln(x) transformation was used to determine control limits. Baseline / Group Medians reflect underlying data distributions, not the data itself.

Figure 1 Center 1 Time (min) to Antibiotic Administration SPC Chart. Letters represent interventions A) 1, 2, 3 B) 3, 5, 6, 7, 8, 9, 12, 13, 15 (see intervention detail Table 1). Double arrow indicates statistical transition point for intervention group analysis.



Group Means (Not Plotted)	189	193	163	173	206	171	150	147	158	153	174	134	157	147	163	159	127	140	105	112	95	90	102	127	124	96	108	77	94	76	84	85	106	90	92	83
Group Size	5	9	9	3	5	7	3	12	5	5	14	6	9	14	12	15	14	16	13	17	15	14	11	17	15	17	14	24	19	13	15	18	12	15	15	20

NOTE: A x^1/4 transformation was used to determine control limits. Baseline / Group Medians reflect underlying data distributions, not the data itself.

Figure 2 Center 2 Time (min) to Antibiotic Administration Baseline to Final Analysis. Letters represent interventions A) 2 B) 1,4 C) 3 D) 5, 6, 7, 8, 10, 11, 13 E) 9 (see intervention detail Table 1). Double arrow indicates statistical transition point for intervention group analysis.

enrolled children < 18 years visiting these ED's with a diagnosis of cancer and fever were analyzed.

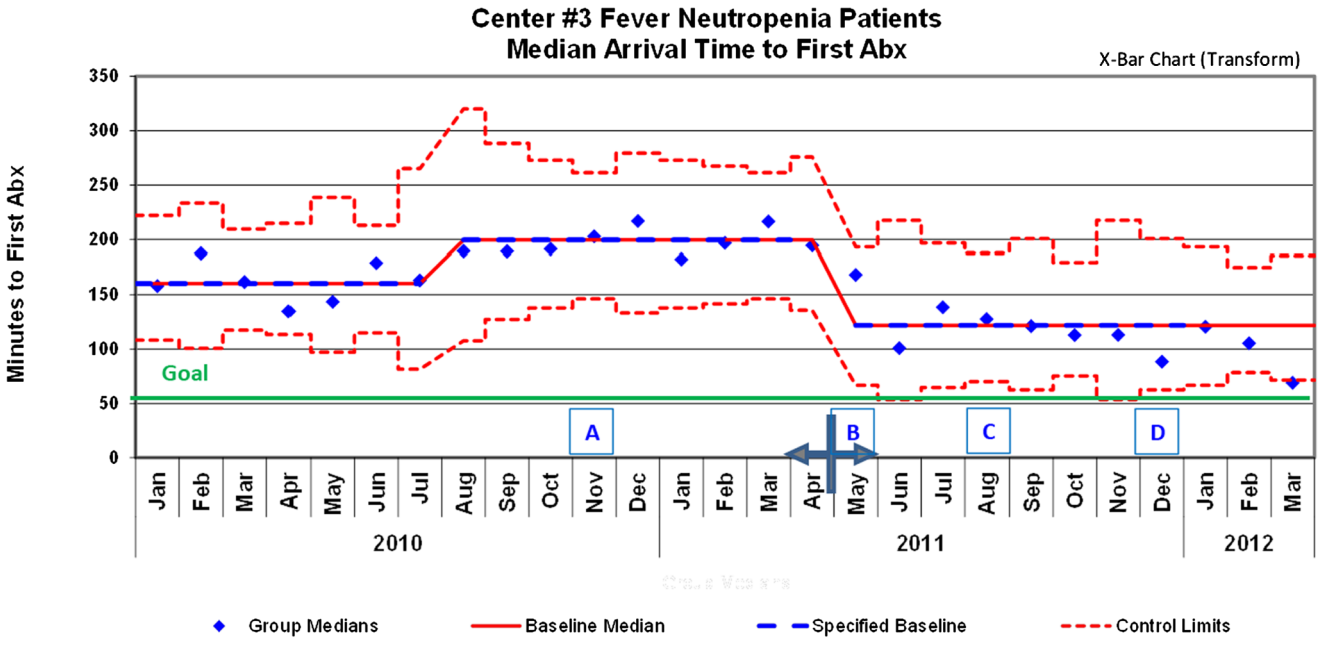
Each QI project was conceived locally within the respective institution. Each institution designed their own interventions which were then implemented independently by that site's authors during their respective study periods. All sites used traditional QI process analysis methodology to identify process inputs (pareto charts, value stream mapping). All institutional projects were completed using a traditional method of defined baseline data collection period followed by subsequent periods in a traditional plan-do-study-act (PDSA) cycle of activity. Multidisciplinary teams met regularly at intervals determined by their respective institutions to analyze data, update clinical providers and monitor outcomes over the project period from baseline to final state.

Data collection time periods, including baseline and subsequent stages, were determined by respective institutions (Figures 1, 2 & 3). Within each site, median TTA was calculated monthly and analyzed using statistical process control (SPC) charts.[17 18] After identifying common goals within our region, QI methods and data from each of the three sites were combined to compare strategies and results. All intervention strategies implemented within individual projects were reviewed by project leads (MN, SS, KH) for benefits and limitations. Successful and unsuccessful strategies were described.

STRATEGY

Eight shared interventions were independently derived and implemented in all three sites. Five of these were process changes, three were educational changes. Interventions contributing to reported outcomes are summarized in Table 1 and the site specific intervention time periods are noted in Figures 1, 2 and 3.

Process interventions at each site resulted in fixed changes to standard workflows of providers. First, nurse initiated processes were implemented allowing for application of a topical anesthetic to any child with a port type vascular access device at the time of ED presentation/triage and before physician assessment if the child was hemodynamically stable. Second, nurse triage procedures were modified to identify all children with cancer presenting for evaluation of fever and prioritized these patients for rapid ED room placement and/or in-room triage. Project teams reported slightly lower rates of compliance for patient room placement as this process directly depended on ED census (with availability of rooms) and acuity of other children present in the ED. Site one assigned febrile pediatric cancer patients the



Group Means (Not Plotted)	164	193	164	137	161	186	167	194	195	201	212	222	186	203	231	197	179	106	143	135	139	122	127	104	132	118	81
Group Size	12	9	18	15	8	16	5	6	10	14	19	12	14	16	19	13	13	8	12	15	11	19	8	11	13	22	16

NOTE: A sqrt(x) transformation was used to determine control limits. Baseline / Group Medians reflect underlying data distributions, not the data itself.

Figure 3 Center 3 Time (min) to Antibiotic Administration Baseline to Final Analysis. Letters represent interventions A) 2 B) 1, 3, 4, 5, 6, 7, 9, 14 C) 8,11,12 D) 3 (see intervention detail Table 1). Double arrow indicates statistical transition point for intervention group analysis.

highest level triage classification allowing those children the highest priority ED status (including a dedicated nurse). Third, nurse procedures emphasized movement of any child who appeared ill (regardless of vital signs) or who met that institution's "high acuity" triage assignment to placement in a specific resuscitation bed space if available. Fourth, all sites made improvements to the availability of central line access equipment. Typically, this was moved into or very near patient rooms so that line access could commence simultaneously with triage within a patient bed space. Project teams reported highest compliance with nurse line access changes.

The fifth intervention concerned selection and delivery of the antibiotic. Sites 1 and 3 adopted a process of care change at inception of their QI project that allowed patients to receive an immediate first dose of a single antibiotic (cefipime) following establishment of venous access/initial blood draw without waiting for laboratory results. Site 2 trialed a process whereby staff would search the medical record for the most recent complete blood count (CBC)/absolute neutrophil count (ANC) result to determine likelihood of neutropenia on the date of the current ED visit to direct the antibiotic choice. This process was deemed unreliable, time consuming and was quickly abandoned. Site 2 also utilized a commercially available rapid absolute neutrophil count pathology test to direct antibiotics only to those children found to be neutropenic. However, this was determined to be an unsuccessful intervention as it did not lead to decreased time to antibiotic delivery. Subsequent to these experiences, Site 2 adopted the process of administration of a single antibiotic dose delivered prior to laboratory results regardless of anticipated ANC, similar to the other two sites. Physician compliance with antibiotic order entry prior to or at the time of patient arrival was also reported to be high at each site demonstrated through aggregate upward trend in percent of children receiving antibiotics (that required an early antibiotic order by a physician) in less than sixty minutes

The first of the three educational interventions adopted by all sites was the development of an institutional consensus document or clinical practice guideline (CPG) outlining clear definitions for the target population and procedures for clinical management including process(es) of care which was shared amongst provider stakeholders. Following initial roll out of practice guidelines all projects communicated status updates to provider stakeholders at intervals to inform them of progress toward TTA goal. Second, all three institutions independently adopted cefipime monotherapy for hemodynamically stable children with cancer presenting

Table 1 Quality Improvement Project Interventions & Team Composition (Bolded items included by all 3 centers)

	Center 1	Center 2	Center 3
Education Interventions			
1. Patient/Family information for ED experience during fever with neutropenia (FN) episodes	X	X	X
2. Staff/faculty on consensus guidelines for FN care (Time to Antibiotic goal<60 minutes and Antibiotic type)	X	X	X
3. Staff/faculty initial education & update on project progress	X	X	X
4. Standardized RN central line education/training		X	X
Process Change			
5. Topical anesthetic to central line site in triage	X	X	X
6. Rapid rooming for all cancer patients with fever	X	X	X
7. Ill appearing or severe triage category placed in resuscitation room	X	X	X
8. Central line equipment more accessible	X	X	X
9. Antibiotic delivery prior to absolute neutrophil count (ANC) result	X	X	X
10. Rapid ANC testing		X*	
11. Electronic order entry modifications/order set development		X	X
12. Pharmacy assistance for antibiotic readiness/availability	X		X
13. MD notified upon patient arrival	X	X	
14.Direct phone communication (Oncology MD to Emergency MD) of incoming patient prior to arrival (when possible)			X
15. All febrile cancer patients triage level 1(highest acuity)	X		
TEAM Composition			
Emergency Physicians	X	X	X
Emergency Nurses	X	X	X
Pharmacy Representative	X	X	X
Oncology Physicians	X	X	X
Computer Order Entry Representative		X	X
Infectious Disease Physician		X	X
Quality Improvement Representative		X	X

* At site 2, this rapid ANC testing was trialed but determined to be a failed strategy and was stopped.

for fever (with addition of other antibiotics depending on severity of illness and altered hemodynamics on presentation) within their CPG. Finally, all sites provided instructions to their patients with cancer during outpatient visits specifically directing them to report immediately to the ED during episodes of fever and emphasized need for ED providers' timely access to their child's central venous device for rapid antibiotic and fluid delivery.

RESULTS

Data from 1032 pediatric ED de-identified patient visits made by children with cancer and fever from the three institutions contributed to the final data set (Table 2). Mean age of children was 6.9 years (SD 4.6), 45 % were female. Although 78.6% of children were described as Caucasian in the total sample, there was significant variation in race between sites. Forty-six percent of children carried an underlying diagnosis of Acute Lymphoblastic Leukemia, the most common cancer diagnosis of children at each institution. Other cancer diagnoses were significantly different between sites. Type of central venous access device (if present) in children was not significantly different between institutions and subcutaneous implanted ports were most common (76%) followed by tunneled devices such as Broviac catheters (13.4%). Of the 792 children with port central line devices, only 39 % received topical anesthetic prior to ED access and this practice was not significantly different between sites. Overall 118 (11.5%) children developed positive blood cultures drawn from the ED central line at the time of ED evaluation, interpreted by all sites as confirmation of a central line infection.

Time of ED visit was similar across institutions with 29.7% of children arriving for evaluation during daytime hours (8am-4pm), 50.7% arriving between 4pm – midnight and 19.6% between midnight and 8am. Forty-one percent of patient visits were made on weekends (Saturday or Sunday). Seventy percent of children were admitted to the hospital however one of the three sites followed an institutional protocol that required all children with cancer and fever be admitted to the hospital. Admission rates for the two remaining sites were 58% (Site 2) and 69% (Site 3). Overall our balancing measure, mean ED length of stay (LOS) was 265 minutes (range 52 - 1424 minutes) and there was no significant differences between mean ED LOS within or between sites. Hospital mean LOS was 6 days (range 1-188 days) overall.

Table 2 Patient Demographics

	Center 1	Center 2	Center 3	Total	p-value
N (%)	225 (21.8)	448 (43.4)	359 (34.8)	1032 (100.0)	n/a
Baseline study period	9/8/2010-10/25/2011	1/1/2011-12/31/2011	1/1/2010-4/30/2011		
Final Study period	10/31/2011-2/25/2013	1/1/2012-12/31/2013	5/1/2011-3/30/2012		
Mean Age Years (SD)	6.6 (4.3)	6.4 (4.3)	7.6 (5.0)	6.9 (4.6)	0.002
Female	122 (54.2)	179 (40.0)	163 (45.4)	464 (45.0)	<0.001
Race					<0.001
African American	40 (17.8)	36 (8.0)	21 (5.8)	97 (9.4)	
Caucasian	128 (56.9)	363 (81.0)	320 (89.1)	811 (78.6)	
Hispanic	15 (6.7)	0 (0.0)[1]	0 (0.0)[1]	15 (1.5)	
Asian	5 (2.2)	10 (2.2)	2 (0.6)	17 (1.6)	
Other	37 (16.4)	39 (8.8)[1]	16 (4.5)[1]	92 (8.9)	
Diagnosis					<0.001
ALL[2]	104 (46.2)	240 (53.6)	131 (36.5)	475 (46.0)	
AML[3]	5 (2.2)	6 (1.3)	4 (1.1)	15 (1.5)	
Brain Tumor	23 (10.2)	29 (6.5)	28 (7.8)	80 (7.8)	
Lymphoma	26 (11.6)	24 (5.4)	46 (12.8)	96 (9.3)	
Neuroblastoma	19 (8.4)	22 (4.9)	45 (12.5)	86 (8.3)	
Sarcoma	21 (9.3)	55 (12.3)	44 (12.3)	120 (11.6)	
Wilm's Tumor	8 (3.6)	16 (3.6)	2 (0.6)	26 (2.5)	
Other	19 (8.4)	56 (12.5)	59 (16.4)[2]	134 (13.0)[4]	
Type of Line					<0.001
PICC	14 (6.2)	15 (3.3)	15 (4.2)	44 (4.3)	
Port	172 (76.4)	370 (82.6)	250 (69.6)	792 (76.7)	
Broviac	30 (13.3)	52 (11.6)	56 (15.6)	138 (13.4)	
Other	0 (0.0)	10 (2.2)	38 (10.6)	48 (4.7)	
Multiple	3 (1.3)	1 (0.2)	0 (0.0)	4 (0.4)	
None	6 (2.7)	0 (0.0)	(0.0)	6 (0.6)	
Time of visit					0.547
Weekend	105 (46.7)	182 (40.6)	131 (36.5)	418 (40.5)	
Weekday	120 (53.3)	266 (59.)	228 (63.5)	614 (59.5)	
8AM-4PM	58 (25.8)	132 (29.5)	117 (32.6)	307 (29.7)	
4PM-12AM	121 (53.8)	229 (51.1)	173 (48.2)	523 (50.7)	
12AM-8AM	46 (20.4)	87 (19.4)	69 (19.2)	202 (19.6)	
EMLA/LMX[5] applied in ED on port devices	78/172 (45.3)	143/370 (38.6)	92/250 (36.8)	313/792 (39.5)	0.188
Documented Line Infection	40 (17.9)	24 (5.4)	55 (15.3)	119 (11.5)	<0.001
Admit	224 (100)[6]	259 (57.8)	246 (68.5)	729 (70.7)	<0.001
Admit To PICU	8 (3.6)	20 (7.7)	10 (2.8)	38 (3.7)	0.451

[1]Hispanic included in "other" at these institutions
[2]ALL: Acute Lymphoblastic Leukemia
[3]AML: Acute Myeloid Leukemia
[4]One diagnosis not listed
[5]EMLA=Eutectic mixture of local anesthetics. LMX=Topical lidocaine anesthetic
[6]Site 1 policy to admit all children with fever and cancer

No child died during their ED visit. Eight children expired during subsequent hospitalization from the index ED visit and three of these deaths occurred after prolonged hospital stays (52, 100 and 182 days respectively). Of the eight hospitalized children who expired, only one died within 24 hours of ED visit and admission to the pediatric intensive care unit after presenting in shock during the baseline period of that site's QI project (and received antibiotics within 30 minutes).

SPC charts displaying median TTA in the pre- and post-intervention periods in each site are shown in Figures 1–3. As indicated by the downward shifts in the centerlines of the SPC charts, all three institutions achieved significant reductions in TTA from baseline to final study periods as a result of interventions. Site specific improvements in median TTA delivery (min) from baseline to final periods were as follows: 118.5 (interquartile range (IQR) 92.8–167.8) – 57.0 (IQR 48.0–76.0) at site 1, 163.0 (IQR 126.5–200.8) – 97.5 (IQR 76.0–126.5) at site 2, and 188.0 (139.5–228.0) – 111.5 (67.0–160.3) at site 3 ($p< .001$ all sites). Analogously, from each site the percent of children receiving antibiotics within 60 minutes improved significantly.

LESSONS AND LIMITATIONS

In this project we describe the experience and outcome of 1,032 children with cancer presenting for evaluation

of fever compiled from a regional collaboration of tertiary children's emergency department's quality improvement projects spanning approximately 3 years (2010–2013). All three institutions in this project demonstrated ability to significantly reduce time needed to administer a first dose of antibiotic near a target goal of 60 minutes, a metric supported by evidence known to improve patient outcome, through focused multi–disciplinary project improvement methodology designed to address a local need.

To our knowledge, this is the first report highlighting changes to clinical pediatric ED practice affecting children with cancer and fever living within a large regional geographic segment of the US. Consistent with a call for rewarding quality of care by Werner & McNutt,[19] rather than just reporting of metrics, for each site in this project success was largely driven by similar yet independently developed local strategies. These strategies were low cost educational or standardized process changes leading to sustainable improvement in care for this large set of high risk children over a relatively short period of time.

Our data contribute evidence of inter-institutional success achieved through utilization of similar strategies despite site specific differences in geographic and economic settings, racial mix, and large, varied cancer population served. Improvements in care of children with fever and cancer were made despite differences in institutional characteristics such as those with high (> 100K) versus lower (25K) annual ED volumes as well as urban and suburban locations with no significant change in balancing measures. It is also worth noting these improvements were made in each center within the context of most subjects presenting for care during traditionally peak hours of ED census activity (after 4pm and on weekends). These findings add external validity evidence for commonly adopted interventions, independently derived but similar to previous small sample single institution reports from other authors.

Limitations of this project include inability to determine effect of specific interventions on TTA. Due to the nature of this analysis of prospectively collected observational data pooled from three individual sites, we could only assess interventions as a group from baseline to final periods. There may have been a larger effect on TTA for specific interventions that we were unable to measure. We did not include general EDs in this project. This may affect the generalizability of interventions in a non-children's ED setting. However, our purpose in this project was to analyze the experiences of large enough sample of infrequently encountered subjects who typically visit pediatric subspecialty centers to effectively identify interventions that led to reduced TTA. The patient experience of febrile pediatric cancer patients in non-children's hospitals may be different using interventions described here. Because only two of the three sites had procedures in place allowing discharge of some children with cancer presenting for fever, it was not possible to effectively compare outcomes such as re-admission in this project. A larger sample, suggesting national collaborative work would be required to effectively identify strategies that may reduce mortality in this population. Measurement of long term sustainability was not within the scope of this project, however each site reported ongoing use of TTA as an ongoing standard QI metric in their institutional care of children with cancer and fever.

CONCLUSION

We describe the experience of a large sample of children with cancer and fever presenting to three regional children's hospital EDs covering a large geographic catchment area of the US. A core set of eight low cost, high yield quality improvement interventions were developed independently which contributed to significant reduction in time to antibiotic delivery in this high risk population of children at risk for sepsis. These interventions were simple, easy to implement and as a bundle may serve to inform future QI research in other settings. Next steps include ongoing participation by all three sites in national pediatric emergency collaborative work to more accurately identify, treat and improve outcomes in children with sepsis, including children with cancer.

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Declaration of interests The authors have nothing to declare.

Ethical approval Institutional Review Board (IRB) review or exemption was obtained by each of three tertiary care children's hospital members of a regional Midwest United States pediatric research collaborative with common interest in reporting data, intervention strategies, and outcomes from independently conducted QI projects with the aim of reducing time to antibiotic delivery in febrile (T > 38.0 C) pediatric cancer patients presenting to the ED.

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