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Implementing Pediatric Surviving Sepsis Campaign Guidelines: Improving Compliance With Lactate Measurement in the PICU

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OBJECTIVES: The 2020 pediatric Surviving Sepsis Campaign (pSSC) recommends measuring lactate during the first hour of resuscitation for severe sepsis/shock. We aimed to improve compliance with this recommendation for patients who develop severe sepsis/shock while admitted to the PICU.

DESIGN: Structured, quality improvement initiative.

SETTING: Single-center, 26-bed, quaternary-care PICU.

PATIENTS: All patients with PICU-onset severe sepsis/shock from December 2018 to December 2021.

INTERVENTIONS: Creation of a multidisciplinary local sepsis improvement team, education program targeting frontline providers (nurse practitioners, resident physicians), and peer-to-peer nursing education program with feedback to key stakeholders.

MEASUREMENTS AND MAIN RESULTS: The primary outcome measure was compliance with obtaining a lactate measurement within 60 minutes of the onset of severe sepsis/shock originating in our PICU using a local Improving Pediatric Sepsis Outcomes database and definitions. The process measure was time to first lactate measurement. Secondary outcomes included number of IV antibiotic days, number of vasoactive days, number of ICU days, and number of ventilator days. A total of 166 unique PICU-onset severe sepsis/shock events and 156 unique patients were included. One year after implementation of our first interventions with subsequent Plan-Do-Study-Act cycles, overall compliance increased from 38% to 47% (24% improvement) and time to first lactate decreased from 175 to 94 minutes (46% improvement). Using a statistical process control I chart, the preshift mean for time to first lactate measurement was noted to be 179 minutes and the postshift mean was noted to be 81 minutes demonstrating a 55% improvement.

CONCLUSIONS: This multidisciplinary approach led to improvement in time to first lactate measurement, an important step toward attaining our target of lactate measurement within 60 minutes of septic shock identification. Improving compliance is necessary for understanding implications of the 2020 pSSC guidelines on sepsis morbidity and mortality.

KEY WORDS: Improving Pediatric Sepsis Outcomes collaborative; lactic acid; pediatric intensive care unit; quality improvement; sepsis; surviving sepsis campaign

Pediatric severe sepsis and septic shock account for approximately 8% of PICU admissions with a 25% mortality rate globally (1). In the United States alone, the total estimated nationwide cost of pediatric severe sepsis was $7.31 billion in 2016 (2). As a result, multiple international quality improvement (QI) efforts are underway to improve pediatric sepsis care. In the United

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KEY POINTS

Question: The aim of this quality improvement (QI) project was to improve compliance with the Pediatric Surviving Sepsis Campaign (pSSC) guideline of obtaining a lactate measurement within 60 minutes of severe sepsis/shock using an Improving Pediatric Sepsis Outcomes (IPSO) dataset for cohort identification.

Findings: This structured QI initiative resulted in a 24% improvement in compliance with lactate measurement and a 55% improvement in time to first lactate measurement.

Meaning: Our approach demonstrates that using an IPSO dataset is feasible in implementing a pSSC best practice guideline and lays the foundation for future clinical research by establishing compliance to study the impact on morbidity.

States, the Children's Hospital Association has successfully implemented a multiorganization QI learning collaborative entitled Improving Pediatric Sepsis Outcomes (IPSO) (3). In alignment with these national efforts, the pediatric Surviving Sepsis Campaign (pSSC) recently issued the first set of pediatric-focused best practice guidelines (4). These guidelines can serve as a foundation for QI efforts to reduce sepsis-related morbidity and mortality.

In addition to established standards of care, such as obtaining cultures and initiating antibiotics, the pSSC guidelines recommend obtaining an initial lactate measurement within the first 60 minutes of septic shock resuscitation (4). A higher lactate measurement or failure to normalize lactate has been associated with mortality and organ dysfunction (5–10), whereas earlier normalization of lactate has been correlated with decreased mortality and improved outcomes (11–15). Several studies also support early lactate measurement as a useful prognostic tool (16–21). Despite these best practice recommendations and institutional participation in the Children's Hospital Association IPSO collaborative, it was unclear if our PICU had been compliant with the pSSC recommendation of obtaining a lactate measurement within 60 minutes of severe sepsis/shock identification.

The primary aim of this QI project was to establish baseline data and improve compliance with a key pSSC guideline of obtaining a lactate measurement within 60 minutes of severe sepsis/shock originating in our PICU as an important first step toward implementation of other pSSC guideline recommendations. The secondary purpose of this QI project was to test the feasibility of using the IPSO dataset from our single institution to implement the pSSC best practice guideline through locally adapted QI methodology, and widely share our results in alignment with the IPSO practice of collaborative learning (3).

MATERIALS AND METHODS

Design, Settings, and Patients

Sepsis cases were identified and reviewed by our local IPSO team, using the IPSO definition of severe sepsis to identify cases of severe sepsis/shock (22). At our institution sepsis cases were identified by an automated medical record pull with subsequent validation by select clinicians trained to identify and apply IPSO definitions. Sepsis onset was approximated by the validated IPSO definition of "time zero," defined using operationalized, intention-to-treat metrics including the time of an institutional sepsis screen (an electronic medical record [EMR]-based screen of vital signs), bedside provider huddle following a nurse-validated sepsis screen, sepsis order set, or sepsis-specific treatments such as antibiotics and/or fluid boluses (22).

For our study, we limited inclusion to pediatric cases of severe sepsis/shock that originated in our institution's 26-bed academic PICU from December 2018 to December 2021. Thus, patients were excluded if severe sepsis/shock was identified before PICU admission (e.g., in the emergency department or the general care ward). The preintervention cohort included cases identified from December 2018 to December 2020, and the postintervention cohort included those cases identified from January 2021 to December 2021.

We chose to focus on the lactate element of the initial pSSC resuscitation bundle after presentation of current state data to our division, which was obtained using 16 months of data and included 64 cases. Importantly, we found that providers often ordered lactate levels on severe sepsis/shock patients; however, the timing of those measurements was variable. We elicited divisional consensus that timely lactate measurement as part of the pSSC resuscitation bundle was a good initial target due to the following reasons: 1)

institutional prioritization and emphasis on first hour sepsis management, 2) a robust dataset that did not rely on sampling from more invasive forms of access such as central lines, 3) objective current state data indicating that whereas lactate measurement was already part of our division's standard practice, the timing was not necessarily standard, 4) general consensus that clinicians in our division incorporate lactate measurements into their interpretation of illness severity and general clinical decision making, 5) presence of an in-unit blood gas laboratory that could produce results within minutes of sending blood, thereby making this project a practically feasible endeavor, and 6) understanding that focusing on a discrete guideline with a clear end point that is upstream in the pSSC recommended initial resuscitation could influence future initiatives targeting more complex downstream interventions.

After gaining divisional consensus, we developed key drivers and countermeasures in conjunction with our key stakeholders (**Fig. 1**). We then developed a multipronged approach with monthly Plan-Do-Study-Act (PDSA) cycles to assess effectiveness of interventions.

In our institution's PICU, resident physicians and nurse practitioners are frontline ordering providers, with oversight from fellow and attending physicians. These frontline providers are also the first to receive an existing sepsis huddle alert, an EMR, vital sign-triggered automated alert previously developed and implemented by our local IPSO group in September 2019. Our three primary interventions included: 1) creation of a multidisciplinary local sepsis improvement team, 2) comprehensive frontline ordering provider education, and 3) comprehensive bedside nursing education. This QI project was deemed not regulated research by our local Institutional Review Board (IRB HUM00191101).

Interventions

Multidisciplinary Local Sepsis Improvement Team. We created a local, multidisciplinary sepsis improvement

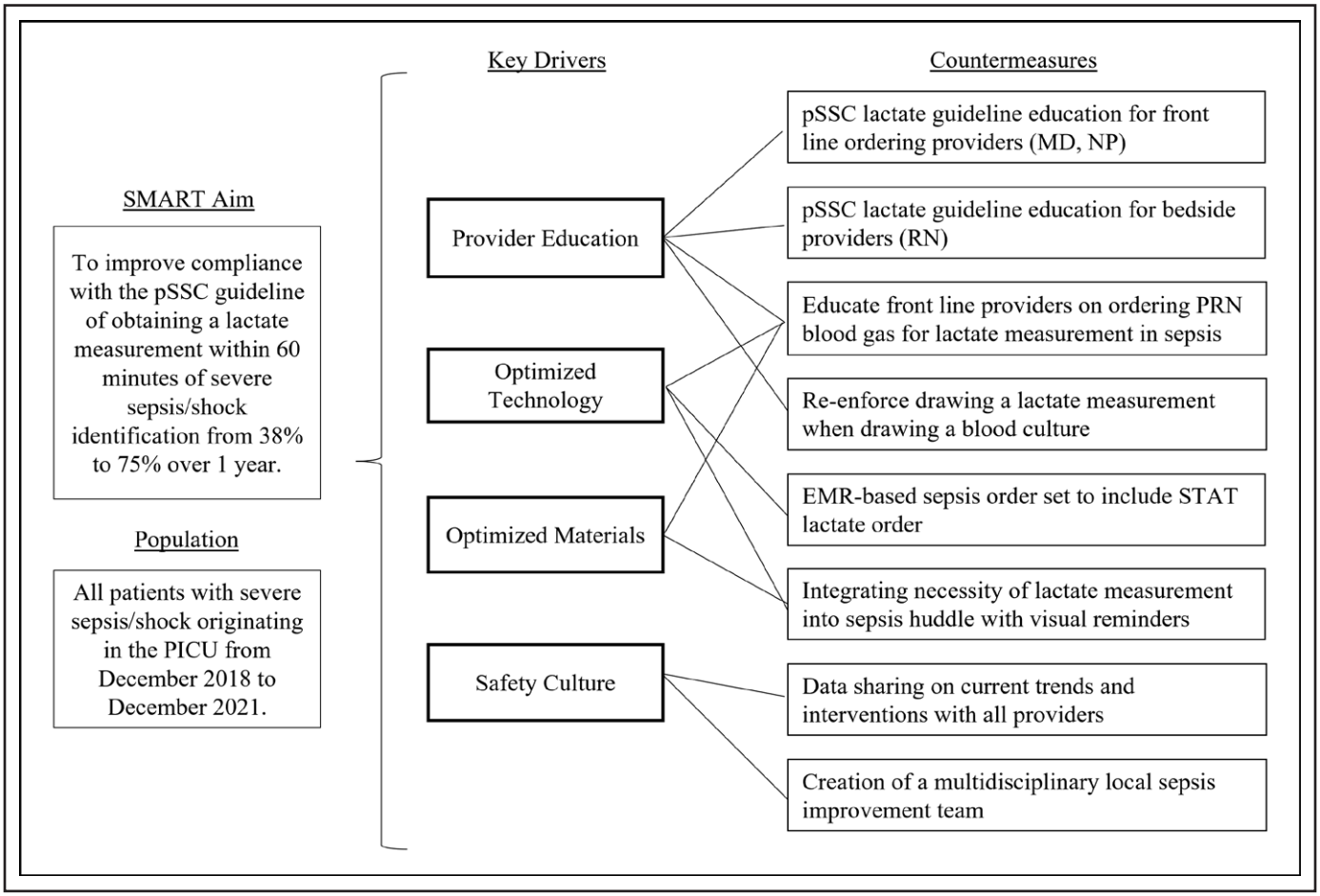

Figure 1. Key driver diagram and interventions for specific, measurable, applicable, realistic, timely (SMART) aim. EMR = electronic medical record, MD = medical doctor, NP = nurse practitioner, PRN = as needed, pSSC = pediatric Surviving Sepsis Campaign, RN = registered nurse, STAT = urgent priority.

team with quarterly meetings. This team included PICU nurses, nurse practitioners, fellow physicians, pharmacists, and attending physicians and served to quickly generate ideas, troubleshoot problems with key stakeholders, and provide real-time feedback for dissemination. Although this group began with a focus on obtaining initial lactates, its scope has expanded to oversee other pSSC-based QI projects in our PICU.

Frontline Ordering Provider Education. The educational materials for our PICU nurse practitioners and residents included: 1) monthly education during the regularly scheduled orientation for resident physicians during their first week in the PICU, 2) educational signage about pSSC in frontline provider work areas, 3) badge card reminders of both sepsis definitions and key pSSC first-hour interventions to be used during bedside huddles, and 4) information about pSSC guidelines in dedicated sepsis educational talks. The monthly education was a standard set of slides that were reviewed by the on-service fellow physician and included the following topics: 1) overview of the pSSC guidelines and key first-hour tasks for septic shock, 2) education on a sepsis order set which includes an order for lactate measurement, 3) education on ability to add an as needed blood gas order which includes a lactate measurement so that bedside nurses can draw a blood gas without an order-placement lag time, and 4) sepsis huddle documentation completion.

Bedside Nursing Education Program. We created a targeted nursing education program developed and led by nurses involved in our multidisciplinary local sepsis improvement team. Materials developed included: 1) use of existing weekly email communication from PICU nursing leadership to disseminate pSSC information and 2) a peer-to-peer education program highlighting key concepts from pSSC, the importance of key first-hour tasks including lactate measurement, data sharing of our local PICU current state and impact on local practice, and a standard work process to draw a lactate measurement at the same time as a blood culture.

Regular Feedback to Key Stakeholders. Throughout our multiple PDSA cycles, we updated key stakeholders and elicited regular feedback regarding countermeasure implementation and interval progress for key metrics. Faculty, fellows, and nurse practitioners were updated through presentations at division meetings and research progress meetings approximately two to three times per year. Bedside nurses were updated through email updates and the established nursing education program by nurse champions involved with our multidisciplinary team.

Measurements

Our primary outcome measure was compliance with lactate measurement within 60 minutes of severe sepsis/shock onset. A lactate measured via any method, including whole blood and blood gas measurements (arterial, venous, or capillary), was considered acceptable. Our process measure was time to first lactate measurement after severe sepsis/shock onset to understand more subtle trends, as compliance could only be achieved once time to first lactate measurement reached a 60-minute threshold. Cases without a lactate measurement and those cases with a lactate measurement drawn greater than 24 hours after time zero were excluded from calculations for our process measure analysis given group consensus that these measurements were unlikely to have been drawn in association with the onset of sepsis as identified by time zero.

Secondary outcomes as defined and gathered by our local IPSO team included number of IV antibiotic days, number of vasoactive days, number of ICU days, and number of ventilator days (22). IV antibiotic days were defined as the number of days a patient was on IV antibiotics for any part of a day in the 30 days after time zero, with each antibiotic counting as 1 day if on multiple antibiotics. Vasoactive days were defined as the number of days a patient was on vasoactive infusions for any part of a day beginning at time zero until discharge, death, or 30 days, whichever came first. PICU length of stay was defined as the number of days a patient was in the PICU for any part of a day beginning at time zero until discharge, death, or 30 days, whichever came first. Ventilator days were defined as the number of days a patient was on ventilation (including noninvasive positive pressure ventilation such as continuous positive airway pressure or bilevel positive airway pressure) for any part of a day beginning at time zero until discharge, death, or 30 days, whichever came first.

Analysis

The primary outcome of compliance with obtaining a lactate measurement in 60 minutes was calculated for

the preintervention and postintervention groups as a simple percentage of those meeting compliance criteria. A Wilcoxon rank-sum test (Graph Pad PRISM 8, Dotmatics, San Diego, California) was used to compare preintervention and postintervention secondary outcomes, with a p value of less than 0.05 considered to be statistically significant.

Statistical process control (SPC) charts were used to analyze primary and process measure outcomes (23–25). SPC charts are used to identify common cause variation, or random variation, and special cause variation, or variation that may be attributable to either an implemented intervention or other changes in circumstances. SPC charts are sensitive to small changes over time, a feature typically omitted in traditional statistical methodology.

Percentage of initial lactates obtained within 60 minutes (primary outcome) was tracked using a P chart, with the centerline set as the preintervention cohort mean. Time to first lactate (process measure) was tracked using an I chart, with the centerline set as the mean of all datapoints, using 20–30 points to calculate the baseline. Standardly accepted rules were used to identify special cause variation, including observing eight points above or below the centerline (shift), which is a probability-based rule roughly corresponding to p less than 0.01 (26). Upper and lower control limits were set at three SDs above and below the centerline.

RESULTS

We reviewed 166 unique severe sepsis/shock cases for 156 unique patients. The preintervention cohort (December 2018 to December 2020) included 115 unique sepsis events, and the postintervention cohort (January 2021 to December 2021) included 51 unique sepsis events. Patient characteristics compared in the preintervention and postintervention cohorts are noted in **Table 1**.

Primary Outcome Measure

In the preintervention cohort, 44 of 115 cases (38%) were compliant with obtaining a lactate measurement within 60 minutes compared with 24 of 51 postintervention cohort cases (47%), demonstrating a 24% improvement. In the postintervention cohort, five datapoints are noted above the mean, whereas eight datapoints are required to note a true shift (23, 24). The SPC chart depicting these data is shown in **Figure 2**.

Process Measure

In the preintervention cohort, five cases had no lactate drawn and four cases had a lactate drawn greater than 24 hours after time zero compared with four cases and two cases, respectively, in the postintervention cohort. With these cases excluded, the average time to first lactate in the preintervention cohort was 175 minutes (2.9 hr) compared with 94 minutes (1.6 hr) in the postintervention cohort, demonstrating a 46% improvement.

Using the SPC chart (**Fig. 3**), the preshift centerline was noted to be 179 minutes. A shift in the data was noted mid-January 2021 with 12 consecutive points noted below the original centerline. The postshift centerline was noted to be 81 minutes, demonstrating a 55% improvement. Interventions as part of sequential PDSA cycles are also noted in Figure 3.

Secondary Outcome Measures

A comparison of preintervention versus postintervention cohort secondary outcome measures including total IV antibiotic days, vasoactive days, ICU days, and ventilator days are shown in **Table 2**. None of the secondary outcomes had statistically significant differences between the preintervention and postintervention cohorts. The preintervention cohort had an all-cause mortality of 12 of 115 (10%) compared with the postintervention cohort which had 13 of 51 (26%; $p = 0.01$).

DISCUSSION

Using a multipronged QI approach that included multidisciplinary key stakeholders, we were successful in improving time to first lactate. This work leveraged the IPSO database and demonstrated our team's ability to use QI methodology to implement a pSSC best practice guideline. Overall, our QI efforts led to a 55% improvement in time to first lactate measurement and a 24% improvement in overall compliance with the pSSC best practice of obtaining a lactate measurement within 60 minutes of time zero.

Although we found no significant shift in the dichotomous primary outcome measure of compliance with a lactate measurement based on SPC process control charts, a significant shift was noted in the continuous process, or leading, measure of time to first lactate measurement, a promising sign of improvement.

TABLE 1.
Characteristics of the Preintervention and Postintervention Cohorts

	Preintervention Cohort (*n* = 115)	Postintervention Cohort (*n* = 51)
Median age on hospital arrival (IQR)	3 (0.5–13)	10 (2–15)
Gender, *n* (%)		
Male	59 (51)	24 (47)
Ethnicity/race, *n* (%)		
White or Caucasian	76 (66)	33 (65)
Black or African American	19 (17)	10 (20)
Hispanic	7 (6)	2 (4)
Asian	3 (3)	0 (0)
Other	6 (5)	3 (6)
Unknown	4 (3)	3 (6)
Functional time zero determination, *n* (%)		
Screen time	19 (17)	21 (41)
Huddle time	3 (3)	0 (0)
Order set time	0 (0)	0 (0)
First antibiotic time	39 (34)	6 (12)
Bolus one time	51 (44)	24 (47)
Arrival time	3 (3)	0 (0)
Median days from admission to functional time zero (IQR)	1 (0–3)	1 (0–5)
Lactate measurement after time zero, *n* (%)		
Obtained at all	110 (96)	47 (92)
Obtained within 60 min	44 (38)	24 (47)
Median value of initial lactate measurement after time zero (IQR)	1.4 mmol/L (1–2.775 mmol/L)	1.8 mmol/L (1.25–4.35 mmol/L)
Lactate sample type, *n* (%)		
Arterial blood gas	48 (42)	17 (33)
Venous blood gas	56 (49)	23 (45)
Capillary blood gas	5 (4)	1 (2)
Whole blood	1 (1)	0 (0)
Interventions after a lactate measurement, *n* (%)		
Bolus	41 (36)	11 (23)
Antibiotic	33 (29)	25 (53)
Vasoactive	36 (31)	11 (23)
Any intervention	75 (65)	34 (72)

IQR = interquartile range.

[a]21 mmol/L was the highest lab value reportable on blood gases at our institution and was used as a surrogate for values "above reportable range."

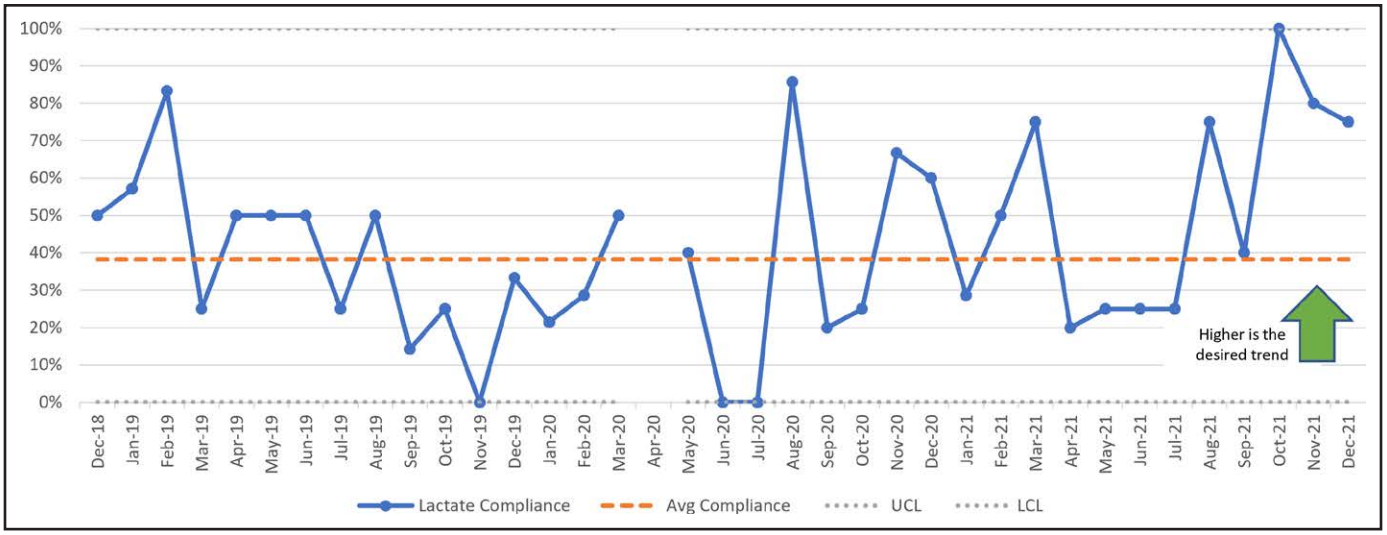

Figure 2. P chart for primary outcome measure (lactate measurement obtained within 60 min of severe sepsis/shock identification). *Datapoints* represent monthly percentage of patients who had a lactate measurement within 60 min. *Dashed centerline* represents the preintervention cohort mean. *Dotted lines* represent the upper control limit (UCL) and lower control limit (LCL) set at three SDs above and below the mean.

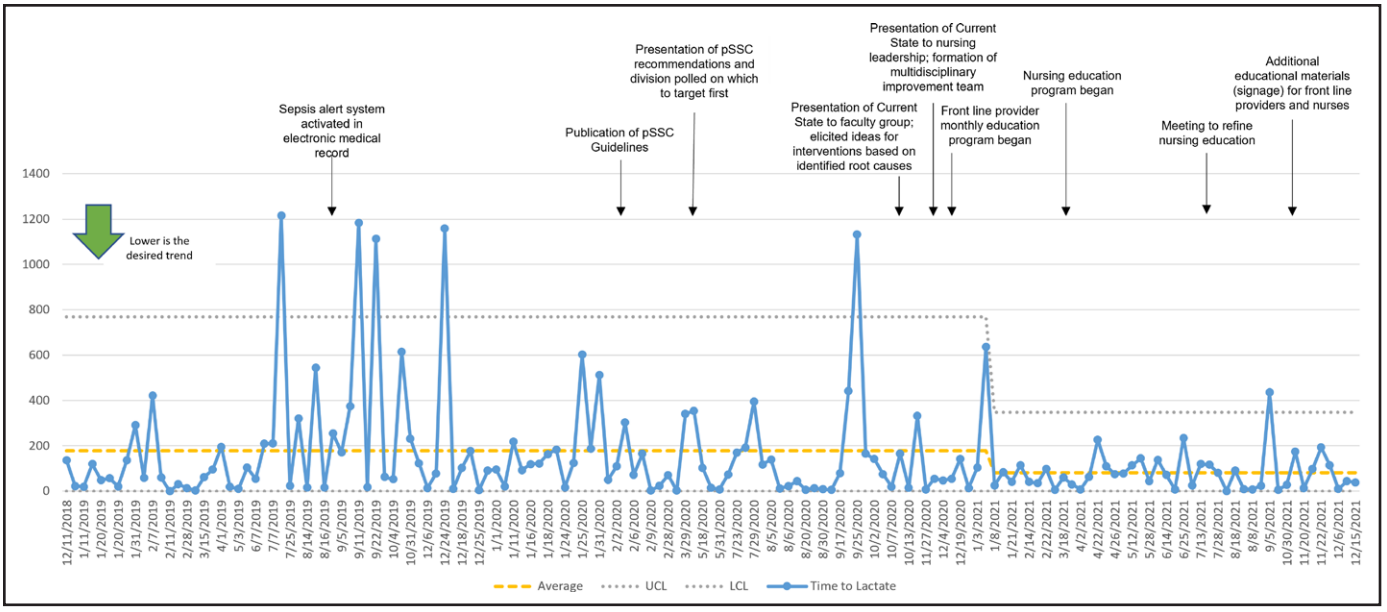

Figure 3. I chart for process measure (time to initial lactate measurement). *Datapoints* represent unique sepsis encounters. *Dashed centerline* represents preintervention and postintervention means with a shift indicating special cause variation noted in January 2021. Preintervention mean is 179 min and postintervention mean is 81 min, representing a 55% reduction. *Dotted lines* represent the upper control limit (UCL) and lower control limit (LCL) set at three SDs above and below the mean. pSSC = pediatric Surviving Sepsis Campaign.

Although the former finding indicates that random variation may be explanative, the latter finding more clearly indicates that the calculated improvement is likely due to special cause variation. We attribute the special cause variation in our process measure to our longitudinal interventions given the shift in January 2021 following the initiation of our first interventions in mid-December 2020. We also attribute the sustained gains for subsequent months to our interventions, noting tighter control limits and less variation from January 2021 to December 2021.

For lactate measurement to influence provider management most effectively and thereby affect patient care, a measurement must be obtained in a reliable and time-sensitive manner. Although we did have improvement in our primary outcome of overall compliance, we did not

TABLE 2.
Secondary Outcome Measures in the Preintervention and Postintervention Cohorts

	Median (IQR)		
	Preintervention Cohort (*n* = 115)	Postintervention Cohort (*n* = 51)	*p*
Total IV antibiotic days[a]	16.0 (8.3–27.0)	14.0 (7.8–23.3)	0.19
Vasoactive days[b]	3.0 (1.0–5.0)	2.0 (1.0–4.5)	0.44
PICU length of stay[c]	12.0 (5.0–17.8)	9.0 (4.0–17.0)	0.33
Ventilator days[d]	8.0 (2.0–16.0)	5.0 (3.0–12.5)	0.40

IQR = interquartile range.

[a]Number of days a patient is on IV antibiotics for any part of a day in the 30 d after time zero. If a patient is on multiple antibiotics, each antibiotic counts as 1 d.

[b]Number of days patient was on vasoactives for any part of a day beginning at time zero until discharge, death, or 30 d, whichever comes first. Vasoactives included epinephrine, dopamine, norepinephrine, milrinone, and dobutamine.

[c]Number of days patient was in the ICU for any part of a day beginning at time zero until discharge, death, or 30 d, whichever comes first.

[d]Number of days patient was on ventilation (including noninvasive positive pressure ventilation such as CPAP or BIPAP) for any part of a day beginning at time zero until discharge, death, or 30 d, whichever comes first.

achieve the desired degree of change. However, we do anticipate that this outcome will improve as our time to first lactate process measure continues to improve to 60 minutes or less through serial PDSA cycles. Although we cannot endorse titration to early goal-directed therapy (27), consistent, early lactate measurement is certainly one important tool to aid in clinician understanding of a patient's current clinical state and judgment surrounding severe sepsis/shock resuscitation.

In addition to improving local practice, this QI project adds to the literature as a key published report of local compliance with an important first-hour best practice pSSC recommendation. Our analysis shares a practical methodology for cohort identification and improvement tracking in future initiatives by merging an existing local QI database (IPSO) with the newest best practice guidelines from pSSC. Finally, our approach combines the strengths of a multidisciplinary local QI team model with stakeholder-endorsed strategies to effectively improve lactate measurement practices. At our institution, the model provided by the PICU has been recognized, adapted to areas outside of the PICU at the institutional level, and enabled us to proceed to incorporate other pSSC guideline components as a next step.

The key to success in this project centered around a multidisciplinary approach involving key stakeholders at each step of the implementation process. We first gained an in-depth understanding of our local current state, leaning on our key stakeholders to understand how best to integrate the workflows of bedside providers. We used this local, objective data to generate shared consensus on the importance of the work, securing early involvement of those frontline groups responsible for immediate recognition and response to pediatric sepsis in our PICU. Through our multidisciplinary group, we intermittently shared countermeasure implementation progress and interval metrics with key stakeholders and received real-time feedback to analyze our problem, understand key drivers, and develop additional countermeasures as part of PDSA cycles. Finally, by tracking a process measure, time to first lactate measurement, we were also able to better understand nuanced changes that may impact our primary outcome measure goal.

Our approach to this QI project has several strengths including our opportunity to leverage our institutional IPSO infrastructure, which provides robust, ongoing data collection, a rich dataset, and operationalized, validated definitions (22). Although alternate cohort methods, such as tracking of *International Classification of Diseases*, 10th Revision codes, rely on consistency in provider documentation, the IPSO cohort is identified not only through specific coded diagnoses, but also through ordered interventions and sepsis-specific huddles, thereby providing a more robust cohort of patients. Through this analysis, we found that it is feasible to use our institution's IPSO dataset to identify a more inclusive cohort of patients for QI initiatives related to the pSSC guidelines.

Limitations to this study include limited generalizability as institutional IPSO participation is required for this method of data gathering. Although the IPSO time

zero definition has been validated for QI purposes, it is predicated on provider recognition and intention-to-treat sepsis, rather than the traditional vital sign and end-organ dysfunction-based definitions (22, 28). Additionally, provider rationale for obtaining blood gas sampling and interventions cannot be accurately ascertained through retrospective chart review. We also noted a difference in baseline age in the preintervention and postintervention cohorts and acknowledge that younger age may have influenced ease and ability to draw a lactate level. Our cohorts spanned the COVID-19 pandemic, which may have contributed to variations in patient populations and severity of illness at presentation. Finally, secondary outcome analysis, including all-cause mortality, is currently limited given insufficient power; however, as data gathering continues and compliance improves, we can further analyze these important secondary outcomes.

We share this methodology and results as a framework for sepsis-related QI initiatives both in our institution and elsewhere. Although pSSC has provided evidence-based guidelines, additional work is still needed to optimize implementation at the bedside. Once effectively implemented, QI efforts targeting compliance with our current understanding of best practices can then synergize with future clinical research regarding the impact that effective implementation can have on sepsis morbidity and mortality.

CONCLUSIONS

Our multidisciplinary approach led to improvement in time to first lactate measurement, a key step to improving overall compliance with obtaining a lactate measurement within 60 minutes of severe sepsis/shock identification. Improving compliance is a necessity to understand the implications of the 2020 pSSC guidelines on sepsis morbidity and mortality. This QI project also demonstrated the ability to synergize hospital efforts through the use of an IPSO database to track compliance improvement with a key pSSC guideline. Future directions include continuing PDSA cycles to further improve compliance, and adaptation of the methodology described to improve compliance with other pSSC recommendations.

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REFERENCES

1. Weiss SL, Fitzgerald JC, Pappachan J, et al; Sepsis Prevalence, Outcomes, and Therapies (SPROUT) Study Investigators and Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network: Global epidemiology of pediatric severe sepsis: The sepsis prevalence, outcomes, and therapies study. *Am J Respir Crit Care Med* 2015; 191:1147–1157
2. Carlton EF, Barbaro RP, Iwashyna T, et al: Cost of pediatric severe sepsis hospitalizations. *JAMA Pediatr* 2019; 173:986–987
3. Larsen GY, Brilli R, Macias CG, et al; IMPROVING PEDIATRIC SEPSIS OUTCOMES COLLABORATIVE INVESTIGATORS: Development of a quality improvement learning collaborative to improve pediatric sepsis outcomes. *Pediatrics* 2021; 147:e20201434
4. Weiss SL, Peters MJ, Alhazzani W, et al: Surviving Sepsis Campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. *Pediatr Crit Care Med* 2020; 21:e52–e106
5. Smith I, Kumar P, Molloy S, et al: Base excess and lactate as prognostic indicators for patients admitted to intensive care. *Intensive Care Med* 2001; 27:74–83
6. Kim YA, Ha E, Jhang WK, et al: Early blood lactate area as a prognostic marker in pediatric septic shock. *Intensive Care Med* 2013; 39:1818–1823
7. Scott HF, Brou L, Deakyne SJ, et al: Lactate clearance and normalization and prolonged organ dysfunction in pediatric sepsis. *J Pediatr* 2016; 170:149–155.e1–e4

8. Schlapbach LJ, MacLaren G, Festa M, et al; Australian & New Zealand Intensive Care Society (ANZICS) Centre for Outcomes & Resource Evaluation (CORE) and Australian & New Zealand Intensive Care Society (ANZICS) Paediatric Study Group: Prediction of pediatric sepsis mortality within 1 h of intensive care admission. *Intensive Care Med* 2017; 43:1085–1096
9. Trzeciak S, Dellinger RP, Chansky ME, et al: Serum lactate as a predictor of mortality in patients with infection. *Intensive Care Med* 2006; 33:970–977
10. Mikkelsen ME, Miltiades AN, Gaieski DF, et al: Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. *Crit Care Med* 2009; 37:1670–1677
11. Jansen TC, van Bommel J, Mulder PG, et al: Prognostic value of blood lactate levels: Does the clinical diagnosis at admission matter? *J Trauma Inj Infect Crit Care* 2009; 66:377–385
12. Jansen TC, van Bommel J, Schoonderbeek J, et al: Early lactate-guided therapy in intensive care unit patients. *Am J Respir Crit Care Med* 2010; 182:752–761
13. Walker CA, Griffith DM, Gray AJ, et al: Early lactate clearance in septic patients with elevated lactate levels admitted from the emergency department to intensive care: Time to aim higher? *J Crit Care* 2013; 28:832–837
14. Vincent J, Quintairos e Silva A, Couto L Jr, et al: The value of blood lactate kinetics in critically ill patients: A systematic review. *Crit Care* 2016; 20:257
15. Masyuk M, Wernly B, Lichtenauer M, et al: Prognostic relevance of serum lactate kinetics in critically ill patients. *Intensive Care Med* 2019; 45:55–61
16. Duke TD, Butt W, South M: Predictors of mortality and multiple organ failure in children with sepsis. *Intensive Care Med* 1997; 23:684–692
17. Shapiro NI, Howell MD, Talmor D, et al: Serum lactate as a predictor of mortality in emergency department patients with infection. *Ann Emerg Med* 2005; 45:524–528
18. Howell MD, Donnino M, Clardy P, et al: Occult hypoperfusion and mortality in patients with suspected infection. *Intensive Care Med* 2007; 33:1892–1899
19. Gorgis N, Asselin JM, Fontana C, et al: Evaluation of the association of early elevated lactate with outcomes in children with severe sepsis or septic shock. *Pediatr Emer Care* 2017; 35:661–665
20. Vink EE, Bakker J: Practical use of lactate levels in the intensive care. *J Intensive Care Med* 2018; 33:159–165
21. Baysan M, Baroni GD, van Boekel AM, et al: The added value of lactate and lactate clearance in prediction of in-hospital mortality in critically ill patients with sepsis. *Crit Care Explo* 2020; 2:e0087
22. Scott HF, Brilli RJ, Paul R, et al; Improving Pediatric Sepsis Outcomes (IPSO) Collaborative Investigators: Evaluating pediatric sepsis definitions designed for electronic health record extraction and multicenter quality improvement. *Crit Care Med* 2020; 48:e916–e926
23. Benneyan JC, Lloyd RC, Plsek PE: Statistical process control as a tool for research and healthcare improvement. *Qual Saf Health Care* 2003; 12:458–464
24. Perla R, Provost L, Murray S: The run chart: A simple analytical tool for learning from variation in healthcare processes. *BMJ Qual Saf* 2011; 20:46–51
25. Provost L, Murray S: *The Healthcare Data Guide*. San Francisco, CA, John Wiley & Sons, 2011
26. Wheeler T, Davis J, Brilli R: The aggregate point rule for identifying shifts on P charts and U charts. *Pediatr Qual Saf* 2018; 3:e103
27. Rowan KM, Angus DC, Bailey M, et al; The PRISM Investigators: Early, goal-directed therapy for septic shock—a patient-level meta-analysis. *N Engl J Med* 2017; 376:2223–2234
28. Goldstein B, Giroir B, Randolph A, et al; International Consensus Conference on Pediatric Sepsis: International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med* 2005; 6:2–8