Queensland Pediatric Sepsis Breakthrough Collaborative: Multicenter Observational Study to Evaluate the Implementation of a Pediatric Sepsis Pathway Within the Emergency Department

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Abstract: OBJECTIVES To evaluate the implementation of a pediatric sepsis pathway in the emergency department as part of a statewide quality improvement initiative in Queensland, Australia. DESIGN Multicenter observational prospective cohort study. SETTING Twelve emergency departments in Queensland, Australia. PATIENTS Children less than 18 years evaluated for sepsis in the emergency department. Patients with signs of shock, nonshocked patients with signs of organ dysfunction, and patients without organ dysfunction were assessed. INTERVENTIONS Introduction of a pediatric sepsis pathway. MEASUREMENTS AND MAIN RESULTS Process measures included compliance with and timeliness of the sepsis bundle, and bundle components. Process and outcome measures of children admitted to the ICU with sepsis were compared with a baseline cohort. Five-hundred twenty-three children were treated for sepsis including 291 with suspected sepsis without organ dysfunction, 86 with sepsis-associated organ dysfunction, and 146 with septic shock. Twenty-four (5%) were admitted to ICU, and three (1%) died. The median time from sepsis recognition to bundle commencement for children with septic shock was 56 minutes (interquartile range, 36-99 min) and 47 minutes (interquartile range, 34-76 min) for children with sepsis-associated organ dysfunction without shock; 30% (n = 44) and 40% (n = 34), respectively, received the bundle within the target timeframe. In comparison with the baseline ICU cohort, bundle compliance improved from 27% (n = 45) to 58% (n = 14) within 60 minutes of recognition and from 47% (n = 78/167) to 75% (n = 18) within 180 minutes of recognition (p < 0.05). CONCLUSIONS Our findings on the introduction of protocolized care in a large and diverse state demonstrate ongoing variability in sepsis bundle compliance. Although bundle compliance improved compared with a baseline cohort, continued efforts are required to ensure guideline targets and sustainability are achieved.

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CONCLUSIONS: Our findings on the introduction of protocolized care in a large and diverse state demonstrate ongoing variability in sepsis bundle compliance. Although bundle compliance improved compared with a baseline cohort, continued efforts are required to ensure guideline targets and sustainability are achieved.

KEY WORDS: child; critical care; management; pathway; recognition; septic shock

Sepsis stems from a dysregulated host response to infection causing damage to tissues and organs (1, 2). Sepsis represents a leading cause of death and disability. Over 50% of the global sepsis cases occur in neonates, children, and adolescents (3, 4). The majority of pediatric sepsis deaths occur within 48 hours of admission (5, 6), indicating that the time window for successful intervention is narrow. Evidence highlights that protocolized sepsis management reduces mortality and enhances recovery from organ dysfunction (7–16).
The pediatric Surviving Sepsis Campaign (SSC) advocates the use of a sepsis recognition tool and administration of a treatment bundle consisting of IV antibiotics, lactate, and blood culture sampling, followed by a fluid bolus and consideration for inotropes. Target benchmarks for bundle delivery are less than 60 minutes from recognition for children with septic shock and less than 180 minutes for children with sepsis-associated organ dysfunction without shock (17).

The evidence for pediatric sepsis quality improvement (QI) initiatives stems primarily from large pediatric hospitals in the United States (8, 10, 14, 15, 18). One randomized controlled trial has evaluated early goal-directed therapy for septic shock in children in Brazil; however, this study was conducted over a decade ago and focused on goal-directed central venous oxygen saturation, not protocol implementation (19).

In Australia, one state has reported data following the implementation of a sepsis pathway and demonstrated improved time to treatment, decreased hospital length of stay (LOS), and mortality; however, pediatric numbers were too few for analysis (20). One single-center pediatric emergency department (ED) in Australia demonstrated improvements in time to treatment and hospital LOS with the introduction of a sepsis QI intervention (21). There are limited data available on pediatric sepsis bundle implementation across diverse and smaller or mixed departments which may be more representative of care delivery across the world.

In Queensland, Australia, a statewide QI project, the Queensland Sepsis Breakthrough Collaborative (QSBC), was launched and informed by the National Action Plan for sepsis (22, 23) in order to improve the recognition and management of sepsis.

In this study, we evaluated the implementation of a pediatric sepsis pathway (PSP) in EDs by describing the sepsis bundle compliance against recommendations from the 2020 SSC guidelines. We compared changes in bundle compliance in children with sepsis requiring ICU admission before and after implementation of the PSP.

MATERIALS AND METHODS

Study Design

Our study is a multicenter, prospective observational cohort study including children less than 18 years old diagnosed with suspected sepsis on the PSP in the ED, between August 2018 and December 2019 in 12 hospitals. A retrospective baseline sample (before the QI intervention) of children admitted to ICUs in participating hospitals with sepsis between January 2015 and June 2018 served as a comparison. Ethical approval was gained from Human Research Ethics Committees of Children’s Health Queensland (HREC/18/QRCH/167) and The University of Queensland (20190000093).

A waiver of consent and Public Health Act approval for the use of deidentified data were granted.

QSBC and the PSP

The state healthcare system, Queensland Health, launched a QI program to implement adult and PSP in ED (Supplements 1 and 2, http://links.lww.com/CCX/A846). The PSP included a screening tool for early recognition and escalation to senior medical officer (SMO) review, a treatment bundle, and antibiotic guidelines. Sixteen of the 20 public EDs in Queensland implemented the PSP, of which 12 captured and reported QI data and are included in this prospective analysis. Sites were grouped for analysis into: 1) a single quaternary pediatric ED, 2) specialized pediatric ED sites (accredited by the Australian College of Emergency Medicine for advanced training in Pediatric Emergency Medicine (24), and 3) mixed EDs without a dedicated pediatric department (Supplement 3, http://links.lww.com/CCX/A846).

Cohort Definitions

The prospective study population included children who presented to the ED at 12 hospitals contributing QI data, between the start of the QSBC (Supplement 2, http://links.lww.com/CCX/A846) and December 31, 2019. Children were included if they were diagnosed with suspected sepsis by a SMO, commenced on the PSP, and received IV antibiotics. These criteria were chosen to capture a pragmatic “intention to treat” group (25). Clinicians had to further categorize children according to signs of shock or other organ dysfunction based on modified 2005 International Pediatric Sepsis Definition Consensus Conference criteria (26). The study population was thereby classified into three mutually exclusive sepsis groups: 1) children “treated for suspected sepsis without organ dysfunction,” 2) children treated for suspected sepsis with signs of “sepsis-associated organ dysfunction without shock,” and 3) children with signs of “septic shock” (Supplement 3,
Data were entered by site-specific trained ED nurses into an electronic case report form using the Research electronic data capture (REDCap) database (27). Records were regularly audited for data quality assurance.

We assessed the impact of the PSP on outcome and process measures in the sickest patients with sepsis, namely those requiring admission to ICU with a diagnosis of sepsis, by comparing a pre-QSBC retrospective baseline cohort with the prospective cohort. This methodology was informed by a similar audit at Children’s Hospital of Philadelphia (10). Several studies have evaluated treatment of sepsis in the ED by reviewing a cohort of children admitted to ICU with sepsis (14, 28). The baseline cohort consisted of children admitted to ICU with a discharge coded diagnosis of sepsis, septic shock, or toxic shock (according to International Classification of Diseases, 10th Edition), having received IV antibiotics, with presentation to participating EDs between January 2015 and June 2018 and no more than 24 hours before admission to ICU. In Australia, ED diagnosis and initiation of treatment prompt escalation of care to an intensivist. There is no prespecified criteria for ICU admission. Process measures for the baseline cohort were retrospectively extracted through manual record review.

The Queensland Health Statistical Services Branch linked the QSBC REDCap sepsis database with the Queensland Hospital Admitted Patient Data Collection, Registry of Births, Deaths and Marriages, and the Australian and New Zealand Pediatric Intensive Care Registry (ANZPIC) using the unique patient record number.

Process and Outcome Measures

Outcome measures collected were as follows: ICU admission, ICU and hospital LOS, interfacility transfer and mortality within 6 months of triage. Process measures collected were as follows: compliance with and timeliness of sepsis bundle delivery and bundle components, including:

1) time from ED triage to SMO review,
2) blood culture sampling and time to blood culture sampling,
3) administration and time to IV antibiotic therapy commencement,
4) administration and time to IV fluid bolus commencement,
5) lactate sampling and time to lactate sampling, and
6) administration and time to sepsis bundle commencement.

The “sepsis bundle” was defined as the administration of four individual bundle elements (blood cultures obtained, IV antibiotics, fluid bolus, and lactate measured). Bundle compliance was defined as commencement of all four elements of the bundle; commencement time was calculated using the time when the last bundle element commenced. Based on the 2020 SSC guidelines, bundle delivery benchmarks were set at 60 minutes “for children with septic shock, and at 180 minutes for children with sepsis-associated organ dysfunction without shock” (17). Two time frames to treatment were calculated as sepsis may be present at triage or may develop later: 1) time from triage (10) and 2) time from SMO review, reflecting recognition time of sepsis (15).

Statistical Analysis

Results are presented as descriptive statistics using median (interquartile range, IQR) and counts with proportions. Process measures within each of the sepsis groups were compared to identify differences in treatment and timing of treatment. Measures were then compared between those admitted and not admitted to ICU to determine the effect of illness severity on bundle compliance. Process and outcome measures were compared between the baseline and prospective ICU cohorts to identify changes associated with the implementation of the pathway. Finally, site differences in process measures were compared for each of the sepsis groups.

Group comparisons were analyzed by the Kruskal-Wallis or Mann-Whitney U test for continuous variables and chi-square test or Fisher exact test for categorical variables. Handling of missing data is described in Supplement 3 (http://links.lww.com/CCX/A846). As this was a QI initiative, the study was not powered for statistical comparisons. Therefore, although a p value of less than 0.05 is used to indicate statistical significance, all results are interpreted with caution, and no corrections for multiple comparisons were undertaken. All analyses were conducted using R (Version 4.0.2) (29).

RESULTS

Cohort Overview

During the 17-month prospective study period, 3,473 patients were screened for sepsis using the PSP. Sepsis was suspected upon SMO review in 523 patients with a
median age of 1.3 years (IQR, 0.2–4.6 yr); of these, 146 were considered as septic shock (28%), 86 as sepsis-associated organ dysfunction without shock (16%), and 291 as suspected sepsis without organ dysfunction (56%) (Table 1). The quaternary ED accounted for 219 sepsis episodes (42%), in comparison with 176 (34%) in sites with dedicated pediatric EDs and 128 (25%) in the mixed EDs (Supplement 4, http://links.lww.com/CCX/A846).

**Process Measures**

There were significant differences across the three sepsis groups in relation to the timing and compliance with the bundle components (Table 2). The median time from triage to SMO review was under an hour for all groups and shorter for children with shock (26 minutes; IQR, 7–58 min) and with organ dysfunction (13 minutes; IQR, 5–38 min).

Delivery of the bundle within 60 minutes from SMO review was achieved in 30% (44) of the septic shock cohort, whereas bundle delivery within 180 minutes was achieved by 40% (34) of those with suspected sepsis with organ dysfunction and 34% (98) without organ dysfunction (Table 3).

For children with septic shock, the highest compliance for administering a bundle element within 60 minutes from SMO review was observed for obtaining a blood culture (73%), followed by lactate (66%), antibiotics (47%), and fluid bolus delivery (43%). For children with sepsis-associated organ dysfunction, the highest compliance within 180 minutes from SMO review was observed for antibiotic administration (90%), followed by obtaining a blood culture (86%), and lactate (71%) and fluid bolus delivery (47%).

Children admitted to PICU received individual bundle elements and the complete bundle significantly faster than children not requiring ICU admission (Supplement 5a and 5b, http://links.lww.com/CCX/A846). Seventy-five percent of children (n = 18) admitted to ICU had the bundle delivered in 180 minutes (and 58%; n = 14 within 60 min), from SMO review compared with 37% of the children (n = 187) not admitted to ICU (and 21%; n = 104 within 60 min).

In children treated for suspected sepsis without organ dysfunction, we observed significantly higher bundle compliance within 60 minutes from SMO review in the quaternary and dedicated pediatric ED compared with the mixed ED (Supplement 6, http://links.lww.com/CCX/A846). No differences were observed in the suspected sepsis with associated organ dysfunction or septic shock groups (Fig. 1) (Supplements 7–11, http://links.lww.com/CCX/A846).

**Outcome Measures**

In total, 24 children (5%) were admitted to PICU in the prospective period, primarily due to septic shock (n = 17) (Table 3). The median hospital LOS of the entire cohort was 4 days (IQR, 3–6 d). In total, 6% (n = 32/523) required interhospital transfer. Three children (1%) died.

**Comparison With Baseline Cohort of Children Admitted to ICU**

To assess the impact of the QSBC on the most unwell children with sepsis, we compared process and outcome measures in children with sepsis and septic shock admitted to ICU with a retrospective baseline cohort (details in Supplement 12, http://links.lww.com/CCX/A846). Overall, compliance with each bundle element improved significantly following the introduction of the PSP (Table 4). Compliance with bundle commencement within 60 minutes from triage increased from 26% (n = 44/167) in the baseline ICU cohort to 54% (n = 13/24) in the prospective ICU cohort (p = 0.01) (Table 5). The hospital LOS and ICU LOS remained similar, and mortality was comparable in the baseline and prospective ICU cohorts (7% vs 8%) (Table 5). There was a significant reduction in the need for interhospital transfer in the prospective cohort (41% vs 12%, p = 0.01).

**DISCUSSION**

Evidence supports the implementation of protocolized care bundles for the recognition and treatment of sepsis in children (17), but reports on multi-institutional sepsis QI programs remain scarce. For those reported, similar findings have been reported pertaining to wanting participation rates and difficulties collecting data to be analyzed and reported (18). To the best of our knowledge, this study represents the only state-wide report on the experience of a large multisite pediatric sepsis QI program outside New York (NY) state (15). This observational study was nested within the state-wide implementation of a PSP across a broad range of dedicated and mixed EDs in Queensland, Australia, covering a pediatric population of approximately 1
TABLE 1.
Demographic Details and Outcome Measures Between Children With Suspected Sepsis, Sepsis-Associated Organ Dysfunction, and Septic Shock

| Characteristics                                      | Overall, N = 523 | Suspected Sepsis Without Organ Dysfunction, N = 291 | Sepsis-Associated Organ Dysfunction Without Shock, N = 86 | Septic Shock, N = 146 |
|------------------------------------------------------|------------------|------------------------------------------------------|----------------------------------------------------------|-----------------------|
| Demographics                                         |                  |                                                      |                                                          |                       |
| Age (yr)                                              | 1.3 (0.2–4.6)    | 1.2 (0.2–3.8)                                        | 1.7 (0.1–6.5)                                            | 1.1 (0.2–4.8)         |
| Gender, n (%)                                         |                  |                                                      |                                                          |                       |
| Male                                                 | 305 (58)         | 172 (59)                                             | 48 (56)                                                  | 85 (58)               |
| Female                                               | 218 (42)         | 119 (41)                                             | 38 (44)                                                  | 61 (42)               |
| Weight (kg)†                                          | 11 (5–18)        | 11 (5–18)                                            | 11 (5–20)                                                | 11 (5–19)             |
| Triage category, n (%)                                |                  |                                                      |                                                          |                       |
| 1                                                    | 41 (8%)          | 6 (2%)                                               | 16 (19%)                                                | 19 (13)               |
| 2                                                    | 297 (57)         | 163 (56)                                             | 53 (62)                                                  | 81 (56)               |
| 3                                                    | 154 (30)         | 98 (34)                                              | 17 (20)                                                  | 39 (27)               |
| 4                                                    | 26 (5)           | 21 (7)                                               | 0 (0)                                                    | 5 (4)                 |
| 5                                                    | 1 (0.2)          | 1 (0.3)                                              | 0 (0)                                                    | 0 (0)                 |
| Focus of infection, n (%)                            |                  |                                                      |                                                          |                       |
| Sepsis where meningitis possible or bacterial meningitis | 171 (33)        | 85 (29)                                              | 40 (47)                                                  | 46 (32)               |
| Sepsis (source unknown, but bacterial meningitis excluded) | 101 (19)       | 52 (18)                                              | 14 (16)                                                  | 35 (24)               |
| Pneumonia                                            | 84 (16)          | 43 (15)                                              | 15 (17)                                                  | 26 (18)               |
| Intra-abdominal                                      | 21 (4)           | 14 (5)                                               | 2 (2)                                                    | 5 (3)                 |
| Urinary                                              | 48 (9)           | 25 (9)                                               | 6 (7.0)                                                  | 17 (12)               |
| Cellulitis/skeletal/soft tissue                      | 17 (3)           | 10 (3)                                               | 1 (1)                                                    | 6 (4)                 |
| Central venous access device                         | 1 (0.2)          | 1 (0.3)                                              | 0 (0)                                                    | 0 (0)                 |
| Febrile neutropenia                                  | 12 (2)           | 5 (2)                                                | 5 (6)                                                    | 2 (1)                 |
| Other                                                | 38 (7)           | 22 (8)                                               | 5 (6)                                                    | 11 (8)                |
| Organ dysfunction, n (%)                             |                  |                                                      |                                                          |                       |
| No organ dysfunction                                 | 291 (56)         | 291 (100)                                            | 0 (0)                                                    | 0 (0)                 |
| 1 or more organ dysfunctions                         | 232 (44)         | 0 (0)                                                | 86 (100)                                                 | 146 (100)             |
| CNS dysfunction                                      | 98 (19)          | 0 (0)                                                | 59 (69)                                                  | 39 (27)               |
| Cardiovascular system dysfunction                    | 146 (28)         | 0 (0)                                                | 0 (0)                                                    | 146 (100)             |
| Renal dysfunction                                    | 7 (1)            | 0 (0)                                                | 3 (4)                                                    | 4 (3)                 |
| Hematologic dysfunction                              | 17 (3)           | 0 (0)                                                | 9 (10)                                                   | 8 (6)                 |
| Respiratory dysfunction                              | 28 (5)           | 0 (0)                                                | 11 (13)                                                  | 17 (12)               |
| Hepatic dysfunction                                  | 19 (4)           | 0 (0)                                                | 12 (14)                                                  | 7 (5)                 |

*Statistics presented: median (interquartile range).*

Overall, 40% of nonshocked children with signs of sepsis-associated organ dysfunction received the complete bundle within 3 hours of sepsis recognition and 30% of children with signs of septic shock received the bundle within 1 hour. Importantly, this statewide ED cohort of children classified as sepsis
TABLE 2.
Compliance With and Time to Process Measures in Children With Suspected Sepsis, Sepsis-Associated Organ Dysfunction, and Septic Shock

| Characteristics                                      | Overall, $N = 523$ | Suspected Sepsis Without Organ Dysfunction, $N = 291$ | Sepsis-Associated Organ Dysfunction Without Shock, $N = 86$ | Septic Shock, $N = 146$ | $p^b$ |
|------------------------------------------------------|--------------------|--------------------------------------------------------|---------------------------------------------------------------|------------------------|------|
| Time from triage to SMO review (min)$^a$             | 31 (10–73)         | 40 (17–97)                                             | 13 (5–38)                                                      | 26 (7–58)              | < 0.001 |
| Blood culture                                        |                    |                                                        |                                                               |                        |      |
| Blood cultures collected, n (%)                      | 510 (98)           | 283 (97)                                               | 84 (98)                                                       | 143 (98)               | 0.928 |
| Time from triage to blood culture (min)$^a$          | 71 (40–126)        | 81 (49–142)                                            | 50 (28–83)                                                    | 64 (34–98)             | < 0.001 |
| Blood cultures collected within 60 min from triage, n (%) | 213 (41)         | 95 (33)                                                | 50 (58)                                                       | 68 (47)                | < 0.001 |
| Blood cultures collected within 180 min from triage, n (%) | 440 (84)         | 232 (80)                                               | 76 (88)                                                       | 132 (90)               | 0.008 |
| Time from SMO review to blood culture (min)$^a$      | 30 (15–55)         | 31 (18–60)                                             | 22 (10–40)                                                    | 30 (15–52)             | 0.038 |
| Blood cultures collected within 60 min from SMO review, n (%) | 348 (67)         | 180 (62)                                               | 62 (72)                                                       | 106 (73)               | 0.039 |
| Blood cultures collected within 180 min from SMO review, n (%) | 433 (83)         | 229 (79)                                               | 74 (86)                                                       | 130 (89)               | 0.018 |
| Antibiotics                                          |                    |                                                        |                                                               |                        |      |
| Time from triage to antibiotics (min)$^a$            | 121 (67–202)       | 144 (85–218)                                           | 80 (45–151)                                                   | 102 (53–172)           | < 0.001 |
| Antibiotics commenced within 60 min from triage, n (%) | 115 (22)         | 40 (14)                                                | 35 (41)                                                       | 40 (27)                | < 0.001 |
| Antibiotics commenced within 180 min from triage, n (%) | 361 (69)         | 178 (62)                                               | 71 (83)                                                       | 112 (77)               | < 0.001 |
| Time from SMO review to antibiotics (min)$^a$        | 68 (35–116)        | 81 (40–122)                                            | 45 (26–82)                                                    | 62 (35–116)            | < 0.001 |
| Antibiotics commenced within 60 min from SMO review, n (%) | 227 (43)         | 107 (37)                                               | 51 (59)                                                       | 69 (47)                | < 0.001 |
| Antibiotics commenced within 180 min from SMO review, n (%) | 439 (84)         | 237 (81)                                               | 77 (90)                                                       | 125 (86)               | 0.161 |
| Fluid bolus                                          |                    |                                                        |                                                               |                        |      |
| Fluid bolus commenced, n (%)                         | 265 (51)           | 131 (45)                                               | 45 (52)                                                       | 89 (61)                | 0.007 |
| Time from triage to fluid bolus (min)$^a$           | 86 (47–154)        | 117 (70–180)                                           | 56 (32–92)                                                    | 64 (34–123)            | < 0.001 |
| Fluid bolus commenced within 60 min from triage, n (%) | 94 (18)          | 27 (9)                                                 | 24 (28)                                                       | 43 (29)                | < 0.001 |
| Fluid bolus commenced within 180 min from triage, n (%) | 211 (40)          | 98 (34)                                                | 39 (45)                                                       | 74 (51)                | 0.002 |
| Time from SMO review to fluid bolus (min)$^a$       | 44 (25–77)         | 58 (35–90)                                             | 35 (25–56)                                                    | 34 (17–59)             | < 0.001 |
| Fluid bolus commenced within 60 min from SMO review, n (%) | 165 (32)         | 66 (23)                                                | 36 (42)                                                       | 63 (43)                | < 0.001 |
| Fluid bolus commenced within 180 min from SMO review, n (%) | 234 (45)         | 112 (38)                                               | 40 (47)                                                       | 82 (56)                | 0.002 |

(Continued)
TABLE 2. (Continued).

Compliance With and Time to Process Measures in Children With Suspected Sepsis, Sepsis-Associated Organ Dysfunction, and Septic Shock

| Characteristics | Overall, N = 523 | Suspected Sepsis Without Organ Dysfunction, N = 291 | Sepsis-Associated Organ Dysfunction Without Shock, N = 86 | Septic Shock, N = 146 | p<sup>b</sup> |
|-----------------|-----------------|-----------------------------------------------|-------------------------------------------------|--------------------------|-----------------|
| Lactate         |                 |                                               |                                                |                          |                 |
| Lactate collected, n (%) | 444 (85)       | 238 (82)                                      | 71 (83)                                         | 135 (92)                 | 0.011           |
| Time from triage to lactate (min)<sup>a</sup> | 65 (33–115)    | 80 (42–138)                                   | 41 (21–74)                                      | 52 (24–95)               | <0.001          |
| Lactate collected within 60 min from triage, n (%) | 209 (40)       | 93 (32)                                       | 45 (52)                                         | 71 (49)                  | <0.001          |
| Lactate collected within 180 min from triage, n (%) | 393 (75)       | 207 (71)                                      | 64 (74)                                         | 122 (84)                 | 0.018           |
| Time from SMO review to lactate (min)<sup>a</sup> | 26 (10–50)     | 29 (13–60)                                    | 18 (9–32)                                       | 26 (8–44)                | 0.014           |
| Lactate collected within 60 min from SMO review, n (%) | 301 (58)       | 148 (51)                                      | 56 (65)                                         | 97 (66)                  | 0.002           |
| Lactate collected within 180 min from SMO review, n (%) | 366 (70)       | 186 (64)                                      | 61 (71)                                         | 119 (82)                 | <0.001          |

SMO = senior medical officer.

<sup>a</sup>Statistics presented: median (interquartile range).
<sup>b</sup>Statistical tests performed: Kruskal-Wallis test, χ<sup>2</sup> test of independence, Fisher exact test.

and septic shock by clinical staff had a low acuity with less than 5% requiring ICU admission and a mortality of 1%. When analyzing children admitted to PICU with sepsis and septic shock, the QI program significantly improved compliance with the delivery of the sepsis bundle and of other process measures as compared to a pre-QSBC baseline cohort.

The overall compliance with the sepsis bundle was comparable with previously published pediatric QI implementation studies (30–32); however, direct comparison is challenging due to different case mix, hospital settings and varying study designs. Despite improvement, time targets were not met in more than half of patients. Our findings parallel the experience in other programs, most notably that of NY state where compliance in pediatric hospitals remained at 24.9%. There are important differences; our project only involved EDs, whereas the NY state report included inpatient areas and ICUs, with higher patient severity. In our cohort, when restricting analyses to children with sepsis presenting to ED who then required ICU admission, 58% and 75% of patients received the bundle within 60 minutes and 180 minutes, respectively.

In the entire cohort, bundle compliance was highest for blood culture and lactate sampling and delivery of antibiotics. Children adjudicated to have shock or signs of organ dysfunction received SMO review and delivery of sepsis bundles significantly faster than children without signs of organ dysfunction. Similar patterns were observed when assessing time from triage or time from sepsis diagnosis (SMO review), which may result in more optimistic or pessimistic comparisons to other studies (10, 14, 32). Of note, the QI program and the PSP emphasized education around the notion “Could this be sepsis?” in order to prompt early escalation to senior ED medical staff who acted as the sentinel decision point to decide whether to deliver the sepsis bundle. We posit that this approach, further enhanced by multidisciplinary clinician education and awareness programs, may have favored early consideration of sepsis during the QSCB, prompting a large number of children with mild disease to be treated early with sepsis bundles. ED clinicians are required to make rapid, presumptive clinical diagnoses, albeit the majority of febrile children will not develop organ dysfunction (23, 33, 34).
Our cohort included a low number of ICU admissions despite 146 children diagnosed as septic shock. Children may be initially diagnosed and treated for shock and respond well to early treatment that prevents deterioration and ICU admission. Other children may not respond, requiring ICU admission, yet both groups are treated for septic shock highlighting the challenges around application of pediatric sepsis definitions in the ED. Furthermore, discrepant adjudication of criteria for sepsis and septic shock between clinicians and prospective research settings is well known (2, 35). Finally, we cannot rule out that improved recognition, and early treatment for children without organ dysfunction or shock (26) during the QSBC may have decreased illness severity (36), reducing progression from infection to sepsis and shock (32).

Of note, 49% of children in our entire cohort did not receive a fluid bolus in the ED despite a presumptive diagnosis of sepsis, perhaps reflecting the relatively low acuity of our cohort, and aligned with the reality in contemporary high-income pediatric ED settings (23, 36, 37).

TABLE 3.
Bundle Compliance and Reported Outcome Measures in Children With Suspected Sepsis, Sepsis-Associated Organ Dysfunction, and Septic Shock

| Characteristic | Overall, N = 523 | Suspected Sepsis Without Organ Dysfunction, N = 291 | Sepsis-Associated Organ Dysfunction Without Shock, N = 86 | Septic Shock, N = 146 | p<sup>b</sup> |
|---------------|-----------------|---------------------------------------------------|-----------------------------------------------------|-----------------------|--------|
| Bundle: four component | | | | | |
| Received all four bundle elements, n (%) | 245 (47) | 118 (41) | 41 (48) | 86 (59) | 0.001 |
| Time from triage to four bundle commencement (min)<sup>a</sup> | 110 (65–197) | 140 (85–214) | 72 (52–133) | 95 (50–156) | < 0.001 |
| Received the four bundle elements within 60 min from triage, n (%) | 56 (11) | 13 (5) | 17 (20) | 26 (18) | < 0.001 |
| Received the four bundle elements within 180 min from triage, n (%) | 175 (33) | 78 (27) | 33 (38) | 64 (44) | 0.001 |
| Time from SMO review to four bundle commencement (min)<sup>a</sup> | 59 (40–109) | 70 (48–120) | 47 (34–76) | 56 (36–99) | 0.012 |
| Received the four bundle elements within 60 min from SMO review, n (%) | 118 (23) | 47 (16) | 27 (31) | 44 (30) | < 0.001 |
| Received the four bundle elements within 180 min from SMO review, n (%) | 205 (39) | 98 (34) | 34 (40) | 73 (50) | 0.004 |
| Outcomes | | | | | |
| Admitted to ICU, n (%) | 24 (4.6) | 2 (1) | 5 (6) | 17 (12) | < 0.001 |
| ICU length of stay (hr)<sup>a</sup> | 47 (25–93) | 52 (32–71) | 42 (25–49) | 50 (29–96) | 0.577 |
| Hospital length of stay (d)<sup>a</sup> | 4.0 (3.0–6.0) | 3.5 (3.0–5.0) | 4.0 (3.0–6.5) | 4.0 (3.0–6.5) | 0.042 |
| Interhospital transfer, n (%) | 32 (6) | 13 (5) | 5 (6) | 14 (10) | 0.188 |
| Mortality (within 6 mo of hospital triage), n (%) | 3 (1) | 1 (0.3) | 0 (0) | 2 (1) | 0.261 |

SMO = senior medical officer.
<sup>a</sup>Statistics presented: median (interquartile range).
<sup>b</sup>Statistical tests performed: Kruskal-Wallis test, χ² test of independence, Fisher exact test.
However, our findings question the utility of assessing bundle compliance inclusive of fluid bolus delivery as a key metric, considering the equipoise around fluid use in sepsis, and an increasing body of evidence for potential harm with fluid overload (38). The NY state sepsis mandate evaluation observed no mortality benefit from timely fluid bolus administration in adult and pediatric populations (15, 16).

This study was not powered to assess temporal trends and outcome differences across sites during the QSBC. We decided a priori to compare children with sepsis and septic shock requiring ICU admission during the QSBC with a baseline cohort covering the preceding 3.5 years at the QSBC sites, to test the impact of the QSBC on the group of patients where bundle compliance was most likely to make a difference to outcomes (10). Linkage with the mandatory ANZPIC registry (6, 39, 40) enabled identification of all children admitted to ICU. There was a significant improvement in all process measures and bundle compliance compared with the baseline cohort: Time to bundle delivery halved, the proportion receiving the bundle within 1 hour from recognition was almost three-fold higher, and 96% of children who were admitted to ICU during the QSBC had antibiotics delivered within 3 hours from triage (32). Due to the high centralization of PICU services to large...
metropolitan areas (41), interhospital transfers of children with sepsis to ICU were collected as a balancing measure and were found to decrease significantly compared to the baseline period.

Several unique features are worth highlighting. The geographical challenges pertinent to the large state of Queensland impact on the ED service delivery model: the majority of EDs are mixed, and exposure

| TABLE 4. Compliance With and Time to Process Measures Between the ICU Baseline and ICU Prospective Cohort |
| --- |
| Characteristics | Baseline, \( N = 167 \) | Prospective, \( N = 24 \) | \( p^b \) |
| Time from triage to SMO review (min)\( ^a \) | 12 (3–31) | 8 (2–20) | 0.327 |
| Blood culture | | | |
| Blood cultures obtained, \( n \) (%) | 163 (98) | 24 (100) | 0.999 |
| Time from triage to blood culture (min)\( ^a \) | 48 (26–91) | 25 (15–47) | 0.007 |
| Blood cultures obtained within 60 min from triage, \( n \) (%) | 95 (57) | 20 (83) | 0.024 |
| Blood cultures obtained within 180 min from triage, \( n \) (%) | 150 (90) | 24 (100) | 0.136 |
| Time from SMO review to blood culture (min)\( ^a \) | 30 (13–70) | 20 (10–28) | 0.018 |
| Blood cultures obtained within 60 min from SMO review, \( n \) (%) | 94 (56) | 22 (92) | 0.002 |
| Blood cultures obtained within 180 min from SMO review, \( n \) (%) | 121 (72) | 22 (92) | 0.076 |
| Antibiotics | | | |
| Time from triage to antibiotics (min)\( ^a \) | 91 (35–156) | 44 (26–83) | 0.004 |
| Antibiotics commenced within 60 min from triage, \( n \) (%) | 68 (41) | 16 (67) | 0.030 |
| Antibiotics commenced within 180 min from triage, \( n \) (%) | 136 (81) | 23 (96) | 0.086 |
| Time from SMO review to antibiotics (min)\( ^a \) | 63 (22–130) | 28 (18–46) | 0.007 |
| Antibiotics commenced within 60 min from SMO review, \( n \) (%) | 68 (41) | 18 (75) | 0.003 |
| Antibiotics commenced within 180 min from SMO review, \( n \) (%) | 117 (70) | 22 (92) | 0.048 |
| Fluid bolus | | | |
| Fluid bolus commenced, \( n \) (%) | 142 (85) | 22 (92) | 0.538 |
| Time from triage to fluid bolus (min)\( ^a \) | 62 (20–158) | 40 (22–54) | 0.058 |
| Fluid bolus commenced within 60 min from triage, \( n \) (%) | 67 (40) | 17 (71) | 0.009 |
| Fluid bolus commenced within 180 min from triage, \( n \) (%) | 107 (64) | 22 (92) | 0.014 |
| Time from SMO review to fluid bolus (min)\( ^a \) | 40 (10–110) | 28 (16–40) | 0.294 |
| Fluid bolus commenced within 60 min from SMO review, \( n \) (%) | 74 (44) | 19 (79) | 0.003 |
| Fluid bolus commenced within 180 min from SMO review, \( n \) (%) | 92 (55) | 20 (83) | 0.016 |
| Lactate | | | |
| Lactate obtained, \( n \) (%) | 139 (83) | 22 (92) | 0.380 |
| Time from triage to lactate (min)\( ^a \) | 57 (22–141) | 21 (8–43) | 0.002 |
| Lactate obtained within 60 min from triage, \( n \) (%) | 73 (44) | 18 (75) | 0.008 |
| Lactate obtained within 180 min from triage, \( n \) (%) | 111 (66) | 22 (92) | 0.023 |
| Time from SMO review to lactate (min)\( ^a \) | 36 (11–104) | 8 (-3–28) | \(< 0.001 \) |
| Lactate obtained within 60 min from SMO review, \( n \) (%) | 75 (45) | 19 (79) | 0.003 |
| Lactate obtained within 180 min from SMO review, \( n \) (%) | 97 (58) | 20 (83) | 0.032 |

SMO = senior medical officer.
\( ^a \)Statistics presented: median (interquartile range).
\( ^b \)Statistical tests performed: Kruskal-Wallis test, \( \chi^2 \) test of independence, Fisher exact test.
to pediatric sepsis is accordingly small. Thus, our QSBC focused on implementation of a standardized PSP across the state to leverage lessons learnt from dedicated pediatric sites (9–11, 15, 18). We observed variation between the quaternary and dedicated pediatric sites compared with mixed EDs for the suspected sepsis without organ dysfunction group, although sepsis numbers per site were not sufficient to compare individually. Large variation within site groups prevented identification of differences in bundle compliance for the suspected sepsis with organ dysfunction and septic shock group.

Performance monitoring and feedback to clinicians is recognized as an important feature of successful implementation programs (42). Decreased exposure and confidence in treating critically unwell pediatric patients in mixed EDs can be partially overcome by targeted training including simulation (43, 44). This prompted the coupling of the pathway implementation with a widespread multidisciplinary education drive that may have contributed to the relative success. However, although the statewide healthcare system encouraged hospital and health services to participate in the QSBC, the implementation of the PSP was neither mandatory nor were services exposed to financial incentives or penalties depending on performance, which may have contributed to variation in compliance across sites. Data collection was manual, which precluded rapid performance feedback in a timeframe to encourage immediate practice change. Automatic digital data collection in the future will facilitate the collection, analysis, and feedback of performance data.

Several limitations of this study need to be considered. First, a large proportion of sites were operating without electronic medical records, resulting in using paper-based PSP data collection that may prompt selection bias. Second, no effect on mortality or LOS or to perform severity adjusted outcome analyses was reported as the prospective cohort had unexpectedly low disease severity as evidenced by the low ICU admission rate and mortality. Third, the baseline ICU population was retrospectively constructed using ICU codes for sepsis, increasing the risk of bias related to coding errors and historic data collection. There is no prespecified ICU

### TABLE 5.
Bundle Compliance and Reported Outcome Measures Between the ICU Baseline and ICU Prospective Cohort

| Characteristics | Baseline, N = 167 | Prospective, N = 24 | p<sup>b</sup> |
|----------------|------------------|---------------------|---------------|
| **Bundle: four component** | | | |
| Received all four bundle elements, n (%) | 124 (74) | 20 (83) | 0.476 |
| Time from triage to four bundle commencement (min)<sup>a</sup> | 113 (42–214) | 52 (38–86) | 0.007 |
| Received the four bundle elements within 60 min from triage, n (%) | 44 (26) | 13 (54) | 0.011 |
| Received the four bundle elements within 180 min from triage, n (%) | 84 (50) | 20 (83) | 0.005 |
| Time from SMO review to four bundle commencement (min)<sup>a</sup> | 81 (25–175) | 39 (28–59) | 0.024 |
| Received the four bundle elements within 60 min from SMO review, n (%) | 45 (27) | 14 (58) | 0.004 |
| Received the four bundle elements within 180 min from SMO review, n (%) | 78 (47) | 18 (75) | 0.018 |
| **Outcomes** | | | |
| Admitted to ICU, n (%) | 167 (100) | 24 (100) | – |
| ICU length of stay (hr)<sup>a</sup> | 44 (28–93) | 47 (25–93) | 0.978 |
| Hospital length of stay (d)<sup>a</sup> | 7 (4–14) | 6 (5–14) | 0.454 |
| Interhospital transfer, n (%) | 68 (41) | 3 (12) | 0.014 |
| Mortality (within 6 mo of hospital triage), n (%) | 12 (7) | 2 (8) | 0.999 |

SMO = senior medical officer.
<sup>a</sup>Statistics presented: median (interquartile range).
<sup>b</sup>Statistical tests performed: Kruskal-Wallis test, χ² test of independence, Fisher exact test.
Dash indicates not applicable.
admission criteria for children in Queensland; however, this limitation exists in both the prospective and baseline populations. Fourth, although standardized training was provided to clinicians and data collectors at each site, the heterogeneity of sites and differences in dedicated resourcing during the QSBC may have resulted in variable implementation. However, we did not observe consistent differences across the sites in terms of process measure compliance. Finally, the prospective data collection was conducted for a relatively short period, reflecting an early phase of PSP implementation. There was no lead-in time prior to sites collecting data due to the constraints of a QI initiative and associated funding, which may reflect less compliance in the initial months of PSP implementation. It should be noted that EDs were familiar with the key components of sepsis management prior to PSP implementation. Further longitudinal audits are necessary to measure the sustainability and long-lasting impact of the QI initiative.

CONCLUSIONS

This statewide study demonstrates the positive impact of implementing a standardized PSP in EDs, with the impact being most clearly observed in the most unwell children admitted to ICU. Although the findings indicate significant improvement in compliance with SSC recommendations compared with a baseline cohort, bundle compliance varied substantially, and the majority of children with sepsis not requiring ICU admission were not treated within recommended timeframes. Future initiatives should focus on investigation of barriers to bundle compliance, facilitate provision of standardized resources on pediatric-specific education, and promote digital solutions to enable ongoing evaluation and sustainability.

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