Early-Detection Pediatric Sepsis Algorithm

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Boston Children’s Hospital
Until every child is well

HARVARD MEDICAL SCHOOL
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Conflict of Interest

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Agenda

• Background
• Creating a pediatric sepsis detection algorithm
• Algorithm performance
• Implementation into clinical workflows
• Future directions
Learning Objectives

• Recognize the process used to develop and evaluate the pediatric sepsis algorithm at Boston Children’s Hospital

• Describe the range of operating characteristics of the pediatric sepsis algorithm based on different changes to the algorithm

• Identify the strategy for inserting the algorithm into clinical workflows

• Discuss the plans to iterate on the algorithm moving forward
Background

• Pediatric vs. adult sepsis

• Quality improvement efforts in pediatric sepsis

Source: www.childrenshospitals.org
2017 Children’s Hospital Photo Exhibit
Rory Staunton, a 12 year-old cut his arm during basketball practice in school.

March 28

Rory woke up vomiting and complaining of pain in his leg. He later developed a fever of 104.

March 29 - morning

Rory went to the emergency room and was discharged two hours later, after being diagnosed with "acute febrile gastritis" (the flu).

March 29 – 7:14 pm

Rory Staunton died in intensive care of septic shock brought on by the infection.

April 1

https://rorystauntonfoundationforsepsis.org/
Pediatric Sepsis

- 4,000 children die annually of sepsis in the U.S.
  - more than cancer (~1,800) or gun violence (~1,700)
- #1 cause of mortality in children worldwide
- Adults vs. Kids
  - Adult sepsis criteria – SCCM/ES-ICM Sepsis 3 (JAMA 2016)
    - Defines sepsis with organ dysfunction
    - Organ dysfunction not a sensitive sign in pediatrics
    - Children develop shock later in course
### The Challenge of Recognition

**Adults**
- Sepsis identification tools based on one set of criteria
- Organ dysfunction included in sepsis definition
- Hypotension an earlier sign

**Children**
- Vital sign & lab criteria differ based on age groups
- Tools must incorporate many different age-based cutoffs
- Organ dysfunction a later sign
- Hypotension occurs late
<table>
<thead>
<tr>
<th>Care Element</th>
<th>Pre-intervention Adherence, n (%)</th>
<th>Post-intervention Adherence, n (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recognition within 5 min</td>
<td>180 (79)</td>
<td>113 (97)</td>
<td>.011</td>
</tr>
<tr>
<td>Vascular access within 5 min</td>
<td>84 (67)</td>
<td>104 (90)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>60 mL/kg IV fluid within 60 min</td>
<td>47 (37)</td>
<td>85 (73)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antibiotics within 60 min</td>
<td>88 (70)</td>
<td>99 (86)</td>
<td>.02</td>
</tr>
<tr>
<td>Vasoactive agents started at 60 min</td>
<td>44 (35)</td>
<td>79 (68)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Overall bundle adherence</td>
<td>24 (19)</td>
<td>90 (78)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Appropriate fluid mechanism used (pressure bag, rapid-infuser, manual push)</td>
<td>62 (49)</td>
<td>110 (95)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Algorithmic Alert</td>
<td>Physician Judgement (PJ)</td>
<td>Combination</td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severe Sepsis +</td>
<td>Severe Sepsis +</td>
<td>Severe Sepsis -</td>
</tr>
<tr>
<td>Alert +</td>
<td>81</td>
<td>64</td>
<td>95</td>
</tr>
<tr>
<td>Alert -</td>
<td>7</td>
<td>24</td>
<td>19,341</td>
</tr>
<tr>
<td>Sum</td>
<td>88</td>
<td>88</td>
<td>19,436</td>
</tr>
<tr>
<td>PPV</td>
<td>2.5</td>
<td>40.3</td>
<td>Either +</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>92</td>
<td>73</td>
<td>Either +</td>
</tr>
</tbody>
</table>

- Proportion of all patients with a positive screen for potential sepsis
  - algorithmic alerts - 16.9% (3,301)
  - physician judgment (PJ) - 0.8% (159)
  - combined either positive - 17.1% (3,334)

2 Step Alert Process

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>Process measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>- sepsis mortality</td>
<td>- initial clinical assessment</td>
</tr>
<tr>
<td>- rapid transfers and bounce backs</td>
<td>- timely first and third bolus</td>
</tr>
<tr>
<td></td>
<td>- timely antibiotics</td>
</tr>
<tr>
<td></td>
<td>- timely transfer to ICU</td>
</tr>
<tr>
<td>Balancing measure</td>
<td>Supplemental measures</td>
</tr>
<tr>
<td>- false positive rate</td>
<td>- hospital LOS</td>
</tr>
<tr>
<td></td>
<td>- ICU LOS</td>
</tr>
<tr>
<td></td>
<td>- days on vasopressors</td>
</tr>
<tr>
<td></td>
<td>- lab bundle obtained (cbc, lactate, blood cx)</td>
</tr>
</tbody>
</table>
Creating a Pediatric Sepsis Detection Algorithm

• Algorithm creation

• Defining sepsis “gold standard”

Source: www.childrenshospitals.org
2017 Childrens’ Hospital Photo Exhibit
Project Goal

• Develop an automated sepsis screening tool to alert clinicians of children at risk of severe sepsis
  – Earlier detection → more rapid intervention
  – Prevent missed cases
Partnering with the Vendor

- Vendor had pre-existing adult sepsis screening tool
  - Not designed for use in children
- Vendor team
  - Performance improvement strategists
  - Statisticians
- BCH team
  - Critical care and emergency medicine physicians
Challenges

• Difficult to distinguish sepsis from vital signs/labs alone
  – Most detection tools have low specificity
  – High risk of alarm fatigue

• Sepsis and severe sepsis are not easily defined
  – Gold standard needed to evaluate tool performance
  – Diagnosis codes inaccurate
Methods

• Alerts based on accepted vital sign and lab values* for:
  – Systemic inflammatory response syndrome (SIRS)
  – Sepsis
  – Severe sepsis/Septic shock
• Run tool in silent mode for 5 months
• Compare silent “alerts” to pre-defined gold standard cohort to assess/maximize tool performance

Alert Levels:

• **SIRS alert**: 2, 3 or 4 SIRS criteria without organ dysfunction

• **Sepsis alert**: SIRS with 1 organ dysfunctions (non-cardiac)
  – Suspected infection planned for future eval

• **Severe sepsis**: SIRS and cardiac dysfunction or 2 other organ dysfunctions
SIRS Criteria

- Body Temperature
- WBC
- Heart Rate
- Respiration Rate

Temp. or WBC?

≥ 2 SIRS?

YES

NO

NO

Continue Monitoring

Organ Dysfunctions

Cardiovascular (CVD)

Hematologic

Hepatic

Neurologic

Renal

Respiratory

Any Od?

YES

NO

≥ 2 OD or CVD?

YES

NO

SIRS-2, SIRS-3, or SIRS-4 Alert

Sepsis Alert

Severe Sepsis Alert
Defining Organ Dysfunction

- Cardiovascular
  - Hypotension or vasoactive drug or
  - ≥2 of: acidosis, elevated lactate, oliguria, prolonged capillary refill, core → peripheral temp gap
- Respiratory: Hypoxia, hypercarbia, ventilator support
- Neurologic: Altered mental status
- Hematologic: Low platelets, elevated INR
- Renal: Elevated creatinine
- Hepatic: Elevated bilirubin or ALT

Organ Dysfunction Sub Algorithms

- High Capillary Refill
- High ALT
- Low Platelets
- Low Systolic BP
- High INR
- Low PaO2
- Low PaCO2
- High Temp

Risk For Infection Sub Algorithm

- High Band Manual
- Infection
- Immune Deficiency
- Inborn Error of Metabolism
- Central Access
- Foley Inserted

SIRS Sub Algorithms
Defining gold standard sepsis cohort

- No single test defines sepsis
- ICD codes are inaccurate
- Defined gold standard by clinician “intention to treat” severe sepsis
  - Also adopted by IPSO sepsis collaborative
Defining severe sepsis

• Patient with suspected infection (SI)
  – SEPSIS-3* Criteria: Blood culture within 72 hours before/24 hours after IV antibiotic

AND

• One of the following between 4 hours before and 6 hours after SI
  – ≥35 cc/kg or 2 L or 2 boluses of isotonic IVF within 2 hours
  – or IV vasopressor
  – or transfer to ICU

*Singer, JAMA, 2016
Intention to Treat

SI (Cultures)

72h

24h

ABX

Intervention

4h 6h
Defining severe sepsis

• To ensure no missed cases, also reviewed all charts of:
  – Patients with diagnosis code for severe sepsis or septic shock
  – Patients who died and had diagnosis code for infectious disease
Results: Data set

• All Inpatient and ED encounters over 5 months in 2016
  – 31,286 encounters
  – 22,766 unique persons

• Excluded neonatal ICU
  – Neonatal sepsis is different entity, has different definitions
  – Excluded both alerts and episodes of sepsis that occurred in NICU
    • Exception: patient alerted in another location (e.g. ED) then transferred to NICU
Results: Gold Standard Cohort

• 342 patient encounters (1.5%) met gold standard
  – Intention to treat: 335 encounters
  – Severe sepsis diagnosis code: 7 unique encounters
  – Death with infectious disease diagnosis code: 0 unique encounters
Algorithm Performance

• Performance of the initial algorithm
• Iterations to improve performance
• Final performance characteristics

Source: www.childrenshospitals.org
2017 Childrens’ Hospital Photo Exhibit
Alert location on patient & encounter level

GS alerts = alert within 48 hours of meeting “gold standard” for sepsis
Alert by severity level
Contribution of variables to alerts
Iterations of algorithm analyzed

- Goldstein reference ranges
- Different respiratory rate ranges:
  - No Respiratory Rates
  - 25% and 50% increases in Goldstein RR ref. ranges
  - 25% and 50% increases in Goldstein RR ref. ranges without SIRS-2 alerts
  - Bonafide 75th, 80th, 85th and 90th percentile RR for ref. range cutoffs
- Different lookback periods
  - HR AND Temp within 30 minutes of each other
  - Temp. 4h, blood gases 6h, other labs 24h
- Different SIRS variables
  - No SIRS-2 alerts
  - Restrictive SIRS
- Different iterations of bands:
  - Immature Granulocytes instead of bands
  - No bands

# Alternate Vital Sign Criteria

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Goldstein RR</th>
<th>Bonafide 75% RR</th>
<th>Bonafide 95% RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 days</td>
<td>50</td>
<td>48</td>
<td>62</td>
</tr>
<tr>
<td>7-29 days</td>
<td>40</td>
<td>48</td>
<td>62</td>
</tr>
<tr>
<td>1 month - 1 year</td>
<td>34</td>
<td>40</td>
<td>51</td>
</tr>
<tr>
<td>2-5 years</td>
<td>22</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td>6-12 years</td>
<td>18</td>
<td>26</td>
<td>33</td>
</tr>
<tr>
<td>13-17 years</td>
<td>14</td>
<td>21</td>
<td>27</td>
</tr>
</tbody>
</table>

## Test Characteristics of Alert Iterations

<table>
<thead>
<tr>
<th>Metric</th>
<th>Goldstein</th>
<th>Bonafide 75%</th>
<th>Bonafide 95%</th>
<th>No RR</th>
<th>No SIRS-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>87.7%</td>
<td>83.9%</td>
<td>80.4%</td>
<td>75.4%</td>
<td>79.8%</td>
</tr>
<tr>
<td>Specificity</td>
<td>86.9%</td>
<td>91.4%</td>
<td>93.2%</td>
<td>94.2%</td>
<td>92.8%</td>
</tr>
<tr>
<td>PPV</td>
<td>9.2%</td>
<td>13.0%</td>
<td>15.2%</td>
<td>16.5%</td>
<td>14.4%</td>
</tr>
<tr>
<td>Person Alerts (%)</td>
<td>14.2%</td>
<td>9.7%</td>
<td>7.9%</td>
<td>6.8%</td>
<td>8.3%</td>
</tr>
</tbody>
</table>

Unit specific performance

### Emergency Department

<table>
<thead>
<tr>
<th>Alert Severity</th>
<th># Alerts</th>
<th># Alerted Persons</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIRS</td>
<td>1,157</td>
<td>1,085</td>
<td>9%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>136</td>
<td>115</td>
<td><strong>20%</strong></td>
</tr>
<tr>
<td>Severe Sepsis</td>
<td>104</td>
<td>95</td>
<td><strong>36%</strong></td>
</tr>
<tr>
<td>All</td>
<td>1,397</td>
<td>1,213</td>
<td>12%</td>
</tr>
</tbody>
</table>

PPV in other inpatient services 5%

### Intensive Care Unit

<table>
<thead>
<tr>
<th>Alert Severity</th>
<th># Alerts</th>
<th># Alerted Persons</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIRS</td>
<td>424</td>
<td>228</td>
<td>12%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>384</td>
<td>177</td>
<td>12%</td>
</tr>
<tr>
<td>Severe Sepsis</td>
<td>767</td>
<td>234</td>
<td>27%</td>
</tr>
<tr>
<td>All</td>
<td>1,575</td>
<td>443</td>
<td><strong>19%</strong></td>
</tr>
</tbody>
</table>

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Implementation into Clinical Workflows

• Current state

• Implementation in the emergency department

Source: www.childrenshospitals.org
2017 Children’s Hospital Photo Exhibit
Current state of sepsis process

• Sepsis screening tool
  – Emergency department: embedded in EHR
  – Rest of hospital: paper form

• Sepsis/septic shock order sets

• Tracking board icons: ED only

• Sepsis huddles

• QI: Education/socialization, PDSA cycles, measurement
Caution: alert fatigue

• Children frequently have abnormal vital signs when febrile, scared or in pain
  – Few of these children actually have severe sepsis
• Most children with severe sepsis are identified by clinicians
  – “Added value” of alert can be low
• Risk of alert fatigue is high
Caution: alert fatigue

• Recent study of an electronic sepsis surveillance system in an adult ER showed high alert fatigue and no improvement in outcomes
  – Sensitivity of alert 80%; PPV 15%
• Alert fatigue
  – Only two-thirds of patients with documented sepsis had a clinician respond to the alert
  – >20% of patients with sepsis had a clinician respond that sepsis was not present

Austrian, JAMIA, 2017
How to reconcile

• Alerts are important but PPV is low
• Clinician judgment still necessary
  – Healthy vs. immunocompromised
  – “Sick” vs. “Not sick”
• Solution in BCH ED: 2 stage process
  – SIRS or Sepsis alert → secondary screen
  – Severe sepsis alert (higher PPV): sepsis huddle
Stage 1: Automated Alert

+ SIRS/SEPSIS ALERT

- Alert goes to attending, trainee and RN assigned on tracking board
- No assignment → Any RN with “relationship”
Stage 2: Active Screening

RN Fills out Sepsis Screen

+SIRS/SEPSIS ALERT
Active Screen

• Link within discern notification to clickable form
• **Question 1:** Does patient have fever or do you suspect infection
  – If no → form closes
  – If yes → answer question 2
• **Question 2:** Does the patient have any of the following:
  – Immuno-compromise or high risk of sepsis (e.g. CVL)
  – Altered mental status
  – Altered pulses/perfusion
• “Positive screen” if yes to both questions
ED sepsis protocol

Routine Care

RN Fills out Active Screen

Positive

Sepsis Huddle

Shock?

Not shock

Q15 Min Vital Signs x 2 hrs

Any other time MD or RN is concerned for sepsis

+SIRS/SEPSIS ALERT

+SЕВЕRЕ SEPSIS ALERT

Negative
Future Directions

• Project impact and results

• Version 2 and beyond

Source: [www.childrenshospitals.org](http://www.childrenshospitals.org)
2017 Children’s Hospital Photo Exhibit
What’s next

• Continued cycles of improvement
• Adding to the model to further improve PPV
  – Risk of infection
    • History of chemo order, indwelling lines
  – Suspected infection
    • Microbial test or antimicrobial given
  – Changes in vital signs
What’s next

• Complete ED implementation and evaluate
  – Prospective study ongoing
  – Outcomes: missed cases, timeliness of interventions, ICU LOS, mortality

• Test and apply in other venues within the hospital
  – Different rules based on location
    • ICUs vs inpatient surgical vs medical or oncology
  – Different notification and suppression rules
Thank you

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• Abbey Logan, Strategist
• Justin Kimbrell, Sr. Strategist
Questions

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