Using Predictive Analytics to Improve Sepsis Outcomes

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The Sepsis Problem
Ubiquitous, deadly, and costly

- 20,000 deaths per day worldwide
- 800,000+/year contract sepsis in the U.S.; 250K-300K sepsis deaths/year
- $20+ billion annual cost to U.S healthcare providers
- Mortality rate for septic shock exceeds 50%... and, untreated, grows 7.6% per hour
Early identification is critical and difficult

“Evidence unwaveringly suggests that early administration of appropriate antibiotics reduces mortality...” (Surviving Sepsis Campaign)

"Lack of early recognition is a major obstacle to sepsis bundle initiation." (Surviving Sepsis Campaign, 2012 Guidelines)
Basic Analytics Approaches
Benchmarking Candidate EHR Rules

• EHR triggers may be proposed to aid early sepsis identification.

• For example, the traditional 4 SIRS criteria require vitals & labs:
  • Heart rate
  • Respiratory rate
  • Temperature
  • White blood cell count, Bands percentage

• Benchmark prior to deployment to estimate clinical impact
  • Using retrospective EHR data
  • Logging results from a live trial implementation
Case Study: SIRS criteria at a 500-bed hospital

- 500-bed U.S. hospital
- Proposed EHR alert requires at least 2 out of 4 SIRS criteria
- Benchmark to estimate alert volume and clinical workload
- Results of running proposed alert on 4 months of real-time data
  - 13142 patients receive the proposed alert
  - Over 100 alerts per day on average
  - Significant burden: alerts require clinical evaluation for infection & sepsis
  - Most alerts are false positives
- Many hospitals end up ignoring or turning off SIRS alerts due to high workload
  - Though it can yield results with continuous training & feedback:
    UC Davis at HIMSS 2014
Case Study: All 4 SIRS criteria, at a 300-bed hospital

- 300-bed U.S. hospital

- Proposed EHR alert requires all 4 out of 4 SIRS criteria
  - A reaction to the overwhelming volume of alerts from 2 out of 4 criteria

- Benchmark to estimate potential impact on earlier IV antibiotics
  - Look for alert 2+ hours before first standard-of-care antibiotic order
  - For patients who eventually receive a diagnosis of sepsis

- Results of running proposed alert on 6 months of real-time data
  - Only 1 patient in the entire 6 months meets the benchmark criteria
  - The alert is unlikely to help significantly improve early antibiotics
Advanced Analytics Approaches
Obtaining Signal from All Available Data
Knowledge-Based Systems

- Experts
- Guidelines
- Research

Knowledge Base

Rules Engine

Individual Patient Data

CDS Alerts/Messages
Data Mining / Machine Learning

Big Patient Data

Trained Model

Individual Patient Data

CDS Alerts/Messages

Offline

Online
Hybrid

Big Patient Data

Knowledge Base

Trained Model

CDS Alerts/Messages

Individual Patient Data

Experts

Guidelines

Research

Offline

Online
Clinical Vigilance™ for Sepsis
Real-time Decision Support

- Clinical decision support software

- Connects to existing hospital information systems and analyzes all patient data 24/7

- Supports early sepsis detection/prediction

- Provides clinical alerts to smartphone/tablet

- Technology:
  - Machine Learning
  - Natural Language Processing
  - Auto-filtering of physiological signals
Clinical Results

• Alerts precede clinician’s standard of care order of antibiotics by > 12 hours for > 45% of alertable sepsis patients, substantially improving upon results already achieved by conventional sepsis initiatives.

• High alerting accuracy (specificity > 99%). Average 1-3 alerts per clinical shift for a 500 bed hospital. Important for avoiding alarm fatigue.
How Does Amara “define” sepsis?

For triggering alerts:
- The **Clinical Vigilance™ for Sepsis** predictive model reasons over >100 clinical variables

For machine learning & evaluation:
- **Timeliness**: To be considered “early” alerts must precede IV antibiotic orders of physicians unassisted by alerts.
- **Accuracy**: An alert is conservatively considered:
  - *True positive* only if the patient goes on to receive a coded diagnosis of sepsis.
  - *False positive* if the patient is never on IV antibiotics.
Research Challenges and Results
Methodological Challenges in Sepsis Research

Previous sepsis studies have faced methodological limitations:
- Interventional trials (e.g. ProCESS) enroll high-acuity patients.
- Chart review studies skew towards high acuity to limit costs.
- Epidemiological studies face accuracy limits of coded data; particularly problematic for low-acuity patients.

Advanced clinical analytics enables new kinds of sepsis studies:
- Comprehensive data on a large scale with no chart review costs
  - Across the entire sepsis acuity spectrum
- Including detailed real-time clinical data
- Including events identified using natural language processing
Assessing the True Sepsis Burden
[from data presented at ISICEM 2014]

• Total of **216,550 patients** over 36 months from 2 hospitals
• **34,465 patients** got IV antibiotics (suspected infection; sepsis)
• This minority of patients (16%) has a majority (63%) of in-hospital deaths
Automatically Compute Complex Severity Scores

PIRO sepsis staging: Predisposition, Infection, Response, Organ failure


- **P Score**
  - Age
    - < 65: 0
    - 65-80: 1
    - > 80: 2
  - COPD: 1
  - Liver Disease: 2
  - Nursing Home Resident: 2
  - Malignancy: 2
  - Without metastases: 1
  - With metastases: 2
  - Total Possible P Points: 9

- **I Score**
  - Points
    - Pneumonia: 4
    - Skin/soft tissue infection: 0
    - Any other infection: 2
    - Total Possible I Points: 4

- **R Score**
  - Points
    - Respiratory rate > 20: 3
    - Bands > 5%: 1
    - Heart rate > 120: 2
    - Total Possible R Points: 6

- **O Score**
  - Points
    - BUN > 20: 2
    - Resp failure/hypoxemia: 3
    - Lactate > 4.0: 3
    - Systolic Blood Pressure < 70: 4
    - 70-90: 2
    - > 90: 0
    - Platelet Count < 150,000: 2
    - Total Possible O Points: 14

**P + I + R + O = PIRO**

Mortality vs PIRO score, manually abstracted [Howell et al.]:

Mortality vs PIRO score, computed automatically [our data]:

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AMARA HEALTH ANALYTICS

capsule™

CHRISTIANA CARE HEALTH SYSTEM
CV:Sepsis Alert [preliminary data]

- *Clinical Vigilance™ for Sepsis* (CV:Sepsis) screened all patients
- Alerts logged in the background (non-interventional)
- Alert triggered on 3986 of 30479 patients who received IV antibiotics (13%)
- IV Antibiotic patients with CV:Sepsis alert notification had increased mortality and hospital length of stay.

[Bar chart showing comparison between patients with and without alerts]

- **Mortality %**
  - Alert (n=3986)
  - No alert (n=30479)

- **Median Length of Stay (days)**
  - Alert (n=3986)
  - No alert (n=30479)
Antibiotic Timing and Mortality

- Surviving Sepsis, NY Sepsis Regulations, etc. prioritize early antibiotics.
- Mortality & LOS for varying delay from CV:Sepsis alert to IV antibiotics

For 2217 patients with moderate initial severity (PIRO score 5-14)

Earlier antibiotics after CV:Sepsis alert are associated with better outcomes.
Lactate Timing and Mortality
[from data presented at ISICEM 2014]

• **3-hour sepsis bundle** includes: “Measure lactate level”
• Compare mortality for:
  • **Early Lactate** (measured 0-3 hours after CV:Sepsis alert)
  • **Delayed Lactate** (more than 3 hours after CV:Sepsis alert)

- The timing of the assessment, *independent of lactate level*, was prognostic of outcome.
Serial Lactate
[from data presented at ISICEM 2014]

- Surviving Sepsis Bundles & NY Sepsis Regulations Guidance include: “Remeasure lactate if initial lactate was elevated.”
- For patients with initial lactate > 4, compare mortality based on serial lactate measurement.

- Unmeasured serial lactate, and serial lactate ≥ 4, are associated with large mortality burden.
Competitive Analysis

Response
Percentage of CV:Sepsis Performance

- CV:Sepsis
- SIRS
- Vanderbilt
- Michigan
- BJH
- Epic
- Cerner
- Truven
- CSC

0% 20% 40% 60% 80% 100%
Hospital Value: Better Outcome & Lower Costs

- Significantly lower mortality and higher quality of life for survivors

- Example estimated impact at a 500-bed community hospital:
  - 750 fewer sepsis bed-days per year and lower mortality
  - Correspondingly shorter ICU stays
  - Projected direct savings of >$2.5M per year

- >10X annual ROI on purchase of Clinical Vigilance™ for Sepsis
Internal System Architecture

- Sepsis Model
- Data Mining & Machine Learning
- Reasoning Engine
- Clinical NLP
- Multisource Integration
- Medical Ontologies
- Time Series Processing

- ADT
- Labs
- EHR
- CPOE
- Admin
- Devices

Disease Modeling
Patient Timeline
Feature Extraction
Data Acquisition

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CHRISTIANA CARE HEALTH SYSTEM
Patient Timeline Data for Research & Reporting
Clinical Results: *Sepsis 2012* data

R.C. Arnold, S.M. Hollenberg, R.P. Dellinger. *Sepsis 2012*

Data from a 300-bed community hospital

<table>
<thead>
<tr>
<th>Time</th>
<th>Median LOS (days)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>no alert</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>abx order 24-0 hrs prior to alert</td>
<td>4</td>
<td>3.3</td>
</tr>
<tr>
<td>abx order 0-12 hrs after alert</td>
<td>6</td>
<td>8.9</td>
</tr>
<tr>
<td>abx order &gt;12 hrs after alert</td>
<td>8</td>
<td>9.6</td>
</tr>
</tbody>
</table>

Patients experienced better outcomes when treatment was initiated sooner, compared to the time of the *Clinical Vigilance™ for Sepsis* alert.