Kernel density estimates to diagnose sepsis in critical care patients

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Sepsis is systemic inflammation due to infection.

**Systemic Inflammatory Response Syndrome (SIRS)**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Normal Range</th>
<th>Abnormal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td>$&lt; 36 , ^{\circ}C$</td>
<td>$&gt; 38 , ^{\circ}C$</td>
</tr>
<tr>
<td>Heart rate</td>
<td>$&gt; 90$ beats/min</td>
<td>$&lt; 90$ beats/min</td>
</tr>
<tr>
<td>Respiratory rate or PaCO$_2$</td>
<td></td>
<td>$&gt; 20$ breaths/min</td>
</tr>
<tr>
<td>White blood cell count</td>
<td></td>
<td>$&lt; 4 \times 10^9$/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$&gt; 10%$ immature granulocytes</td>
</tr>
</tbody>
</table>

BACTEREMIA

INFECTION

SEPSIS

SIRS ≥2 criteria

TRAUMA

BURNS

PANCREATITIS
We aim to diagnose ‘severe’ sepsis (patients with organ system failure).

Neurologic
Respiratory
Cardiovascular
Hepatic
Renal
Hematologic
Severe sepsis is common, often kills, and expensive in New Zealand ICUs.

11.8% incidence
1.5% increase (projected)

26.5% mortality
0.67% increase

0.77 per 1000
NZ population

NZD$100M annually
Sepsis is the 10th leading cause of death in the USA.

6% of all deaths in the USA are sepsis-related (1999 to 2005).
Standard sepsis diagnostics are slow, inaccurate, and measured once daily.

Treat confirmed sepsis within 6h.

Blood culture (24-48h)
51% of sepsis are culture-identified

PCT biomarker (0.5-2.5h)
42-97% of sepsis diagnosed
43-100% of no sepsis diagnosed
Our sepsis biomarker:

Clinical motivation

Biomarker development

Diagnostic performance

PCT comparison
Insulin sensitivity may be a useful sepsis biomarker.

Glucose control decreased sepsis incidence.

Insulin sensitivity can be measured hourly.

Insulin sensitivity decreases with illness.
Our biomarker includes hourly insulin sensitivity and bedside measurements.

36 patients with sepsis
(6000 hours of data)

insulin sensitivity
+ SIRS
 temperature, blood pressure, heart rate, respiratory rate hourly changes
Kernel density estimates provide joint probability density profiles for data hours and classification.

**Raw data**

**Kernel density**

- Diastolic blood pressure (mmHg)
- Log diastolic blood pressure
Our biomarker identifies the majority of sepsis AND no sepsis hours.

75%-94% of no sepsis diagnosed

70%-94% of sepsis diagnosed

99% - 100% - outcomes correct

9% - 38% + outcomes correct
Our biomarker classification model area under the ROC curve (AUC) shows high accuracy.

Max AUC: **0.98**
Cutoff 0.319

Min AUC: **0.78**
Cutoff 0.269
Our biomarker is more accurate than blood culture and PCT.

<table>
<thead>
<tr>
<th>Correct Diagnosis</th>
<th>Culture</th>
<th>PCT</th>
<th>Biomarker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>51%</td>
<td>42% - 97%</td>
<td>70% - 94%</td>
</tr>
<tr>
<td>No sepsis</td>
<td>43% - 100%</td>
<td>75% - 94%</td>
<td></td>
</tr>
</tbody>
</table>
Our hourly biomarker may be faster than PCT.

PCT identified sepsis and treatment began 3h after infection.
Our sepsis biomarker diagnoses severe sepsis more quickly and accurately than existing diagnostic methods.

Treat confirmed sepsis within 6h.

We confirmed 70%-94% of sepsis AND 74% -94% of no sepsis in 1h.

May reduce sepsis mortality, costs, and antibiotic resistance.

May improve quality of care.
Ongoing work

Clinical trial
(Aug 2009 – ongoing)
PCT vs Biomarker

Describe sepsis evolution in time.

Validation trial.

Guide antibiotic therapy.

Reduce mortality.
"The doctor isn't in right now. When you hear the beep, please leave your name, number and a short diagnosis."