Collective Experience:
A Database-Fuelled, Interdisciplinary Team-Led Learning System

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Technology in Healthcare

- Technology won’t fix broken systems.
- Quality improvement in healthcare requires a multi-disciplinary and collaborative approach.
- Idea of collaboration runs counter to entrepreneurial spirit, thus, preponderance of innovations addressing low-hanging fruits
Technology in Healthcare

• Health is a complex “product” to sell
• Only achieved by numerous successful processes: timely diagnoses, effective treatments, adequate monitoring, consumers doing their part
Technology in Healthcare

• “More” processes – diagnostic tests, screening, procedures, monitoring - do not guarantee better, or even, good health
  – Screening shown to be helpful in only a handful of cancers and diseases
  – Good biomarkers are useless in the absence of effective treatment
  – More data do not necessarily translate to improved outcomes, e.g. continuous outpatient monitoring
Technology in Healthcare

• Coordination is as important as each individual process, and failed coordination leads to poor outcome despite successful care “pieces”

• ~500,000 medical technology, in ~10,000 generic groups, under 12 categories of products

http://www.eucomed.org/medical-technology
Technology in Healthcare

• Reverse engineering in health technology: Build solutions first then look for clinical scenarios where they can be applied.

• Multitudes of “sexy” solutions do not or only partially address the problems they were designed for.

• Very inefficient system of innovation drives healthcare costs
Integrating Data, Models, and Reasoning in Critical Care

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Goals

• Present an overview of clinical research in progress
• Provide a unifying theme as regards the motivation behind the projects
• Introduce a vision of an empiric data-driven day-to-day practice
Evidence-Based Medicine

• Multi-center PRCTs and systematic reviews are gold standard
• PRCTs provide aggregated outcomes – difficult to apply to individual patients
• Benefits may not translate into the real world – efficacy vs. effectiveness
• Errors and biases abound: 41% of the most cited original clinical research later refuted (Ioannidis, JAMA 2005)
Evidence-Based Medicine

• 2007 analysis of >1000 Cochrane systematic reviews
  – 49%: current evidence does not support either benefit or harm
  – 96%: additional research is recommended
• Most of what clinicians do has never been formally put to the test
• Large-scale evidence impossible to obtain for the millions of questions posed in day-to-day practice
Knowledge → Clinical Acumen → Clinical Practice → Local Practice Norms

Experience

Patient Values and Preferences

Guidelines → Expert Opinion

**PROBLEMS**

Variability among clinicians

- Patient may be too ill to communicate
- Discussion not informed by representative empiric data

Relevance to individual cases

- Large cost of evidence creation
- Long lead time for prospective studies
Is there a role for empiric data as captured in clinical information systems in the creation of evidence?
Collective Experience Approach

vs.

Traditional Individual Approach
Select patients similar in important features as regards a specific question, e.g. Will my patient benefit from blood transfusion?
MIMIC: ICU Database from Beth Israel Deaconess Medical Center
1. Commentary

Computer says 2.5 litres – how best to incorporate intelligent software into clinical decision making in the intensive care unit?

Lane K, Boyd O


[Abstract] [Full text] [PDF] [PubMed] [Related articles]

2. Research

An artificial intelligence tool to predict fluid requirement in the intensive care unit: a proof-of-concept study

Celi LA, Hinske LC, Alterovitz G, Szolovits P

Critical Care 2008, 12:R151 (1 December 2008)

[Abstract] [Full text] [PDF] [PubMed] [Related articles] [Cited on BioMed Central]

Research

An artificial intelligence tool to predict fluid requirement in the intensive care unit: a proof-of-concept study

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Workflow

Enter values for parent (or ancestor) nodes.

Predicted range of fluid required, e.g. 275-300 ml/hr

Information provided to clinician as soon as CPOE is accessed. Alternatively, a print-out is provided to the clinician before rounds.
Commentary

Computer says 2.5 litres - how best to incorporate intelligent software into clinical decision making in the intensive care unit?

Katie Lane and Owen Boyd

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See related research by Celi et al., http://ccforum.com/content/12/6/R151


Abstract

What will be the role of the intensivist when computer-assisted decision support reaches maturity? Celi’s group reports that Bayesian theory can predict a patient’s fluid requirement on day 2 in 78% of cases, based on data collected on day 1 and the known associations between those data, based on observations in previous patients in their unit. There are both advantages and limitations to the Bayesian approach, and this test study identifies areas for improvement in future models. Although such models have the potential to improve diagnostic and therapeutic accuracy, they must be introduced judiciously and locally to maximize their effect on patient outcome. Efficacy is thus far undetermined, and these novel approaches to patient management raise new challenges, not least medicolegal ones.

Bayesian network generated from observed data alone

This pilot study differs from most previous attempts at computerized decision making in two respects. First, it addresses a therapeutic rather than diagnostic question. Second, the very predictive system itself has been generated from data unique to that patient, rather than an algorithm or guideline integrating opinion and best available medical evidence. The Bayesian system is a type of decision support system, as are logistic regression models and neural networks. The Bayesian approach has several practical advantages applicable to critical care, such as its ability to deal with uncertainties, for instance missed readings.
Mortality Prediction

- Universally lack clinically acceptable accuracy at an individual patient level (poorly calibrated)
- Poor performance on specific subsets of ICU patients, e.g. patients with AKI
- Variable accuracy among ICU populations in different regions of the world
- Model fade
Advances in Critical Care Engineering

Edited by:
Ming-Chien Chyu, PhD, PE

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Hypothesis

• “Home-brewed” mortality prediction model for 3 subsets of patients will perform better than standard severity score, e.g. SAPS
• Capturing evolution of physiologic variables over time will perform better than traditional physiologic snapshot during the first 24 hours in the ICU
Machine Learning Algorithms

- Logistic Regression
- Bayesian Network
- Artificial Neural Network
1400 ICU patients with Acute Kidney Injury

933 patients (Training Set)

467 patients (Validation Set)

Split 1 of 5 (Fold 1)
Split 2 of 5
Split 3 of 5
(Fold 4)
Test Set 5
Test Set 1
Test Set 2
(Fold 2)
Test Set 3
(Fold 3)
Split 4 of 5
Split 5 of 5 (Fold 5)

Report AUC and accuracy from Validation Set

Report average AUC and accuracy from Training Set

Best Performing Model on Test Set

Extract beta coefficients

467 patients (Validation Set)
Discussion

• Local customized modeling performed better than traditional scoring systems when predicting mortality of specific patient subsets.

• Large database studies present unique challenges compared to traditional studies
  – Missing data
  – Curse of dimensionality
  – Data noise
Completed and Ongoing Projects

• Markov modeling to determine optimal time for trial of aggressive care among patients with high probability of poor outcome
  – Peggy Lai, Mark Shrime, Joon Lee, Daniel Scott, Stuart McLennan, Leo Anthony Celi

• Mining nurses notes using natural language processing: Can we detect ambivalence towards care provision perceived as futile?
  – Anna Rumshisky, Julie Callahan, Stuart McLennan, Leo Anthony Celi
Completed and Ongoing Projects

• Trends in the acuity, treatment and outcomes of elderly patients in the ICU from 2001-2008
  – Leo Anthony Celi, Catherine Chronaki, Lior Fuchs, Victor Novack, Shinhyuk Park, Daniel Talmor, Stuart McLennan, Roger Mark

• Will a patient presenting with GI bleed require an urgent intervention?
  – George Cheng, Katherine Germansky, Avraham Cooper, Peter Clardy, Anjala Tess, Ciaran Kelly, Leo Anthony Celi
Completed and Ongoing Projects

• Predicting laboratory results using multi-parameter time series data
  – Federico Cismondi, Leo Anthony Celi

• Transfusion and the non-bleeding ICU patient with a hemoglobin between 7.0 and 10.0 g/dl
  – Andre Dejam, Brian Malley, Saira Samani, Shinyuk Park, Zahra Samani, Leo Anthony Celi
Completed and Ongoing Projects

• Long-term outcome of minor troponin elevations in the ICU
  – Adrian Velasquez, Marzyeh Ghassemi, Kumaran Kolandaivelu, Juan Osorio, Leo Anthony Celi

• The use of diuretics to facilitate fluid mobilization during recovery from septic shock
  – Frank Volpicelli, Ruben Perreira, Daniele Ramazzotti, Sabina Hunziker, Dinna Cruz, Una-May O’Reilly, Leo Anthony Celi
Completed and Ongoing Projects

• Red blood cell distribution width and ICU outcomes
  – Sabina Hunziker, Leo Anthony Celi, Joon Lee, Michael Howell

• Impact of 24/7 intensivist coverage
  – Jennifer Stevens, Joon Lee, Leo Anthony Celi, Daniel Talmor, Victor Novack, Peter Clardy, Michael Howell

• Variation in the management of hypotension
  – Miles Boone, Joon Lee, Daniel Scott, Julie Callahan, Daniel Talmor, Michael Howell, Leo Anthony Celi
Completed and Ongoing Projects

• Is morbid obesity really protective in the ICU?
  – Samuel Hugueny, Trishan Panch, Leo Anthony Celi

• Prediction of clinical outcomes among elderly patients undergoing open heart surgery
  – Bala Subramaniam*, Sean Galvin*, Joon Lee, Kamal Khabbaz, Valerie Banner-Goodspeed, Leo Anthony Celi

• Quantifying the risks of unnecessary antibiotic coverage
  – Graham Snyder, Mai Pho, Jenna Wiens, Monica Golik, Leo Anthony Celi
Completed and Ongoing Projects

• Will a patient presenting with GI bleed require an urgent intervention?
  – George Cheng, Katherine Germansky, Avraham Cooper, Peter Clardy, Anjala Tess, Ciaran Kelly, Leo Anthony Celi

• Clinical outcomes of ICU boarders
  – Jennifer Stevens, Leo Anthony Celi
Completed and Ongoing Projects

• Modeling dynamic treatments and physiologic response to predict cardiac function
  – Leo Anthony Celi

• ICU resource utilization of patients with psychiatric disorder
  – Leo Anthony Celi

• Propofol vs. midazolam for sedation: Does it affect clinical outcomes
  – John Marshall, Leo Anthony Celi
Selective Serotonin Reuptake Inhibitors and ICU Outcomes

Background

• 2010: anti-depressants 2\textsuperscript{nd} most frequently prescribed medication in US with 253.6 million prescriptions

• SSRIs most commonly prescribed anti-depressants in most countries, including US

• Serotonin affects many bodily functions, e.g. vasoconstriction, platelet aggregation, cardio-respiratory function, appetite
Background

• Scant literature on effect of SSRIs on clinical outcomes

• Recent paper suggests SSRI use associated with higher risk of stroke among women in a 6-year follow-up study (HR 1.39; 95% CI, 1.13–1.72) (Pan et al., 2011)

• Does SSRI use affect ICU outcomes?
Methods and Results

• Patient cohort:
  – 1388 in SSRI group
  – 8446 in control group

• Primary outcome: hospital mortality

• Secondary outcomes
  – 1-year mortality
  – Requirement for vasopressor agents
  – Requirement for mechanical ventilation
  – Requirement for blood transfusion
## Methods and Results

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th></th>
<th>SSRI Group</th>
<th></th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD or Median (IQ Range)</td>
<td></td>
<td>Mean ± SD or Median (IQ Range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>63.8 ± 0.5</td>
<td></td>
<td>63.0 ± 0.5</td>
<td></td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Sex (Men, %)</strong></td>
<td>60%</td>
<td></td>
<td>43%</td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>SAPS</strong></td>
<td>13.6 ± 5.4</td>
<td></td>
<td>13.1 ± 5.3</td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>SOFA</strong></td>
<td>5.7 ± 4.0</td>
<td></td>
<td>5.2 ± 3.8</td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Elixhauser Score</strong></td>
<td>1.5 ± 2.1</td>
<td></td>
<td>1.5 ± 2.5</td>
<td></td>
<td>0.22</td>
</tr>
<tr>
<td><strong>ICU Length-of-stay</strong></td>
<td>2.07 (1.00, 2.56)</td>
<td></td>
<td>2.14 (1.00, 2.66)</td>
<td></td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Hospital Length-of-stay</strong></td>
<td>7 (1, 6)</td>
<td></td>
<td>6 (1, 6)</td>
<td></td>
<td>0.65</td>
</tr>
</tbody>
</table>
## Logistic Regression for Hospital Mortality

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI Lower Bound</th>
<th>95% CI Upper Bound</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI vs. Control</td>
<td>1.74</td>
<td>1.40</td>
<td>2.17</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age</td>
<td>1.02</td>
<td>1.01</td>
<td>1.03</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Gender</td>
<td>0.78</td>
<td>0.66</td>
<td>0.93</td>
<td>0.006</td>
</tr>
<tr>
<td>SAPS</td>
<td>1.09</td>
<td>1.07</td>
<td>1.11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SOFA</td>
<td>1.14</td>
<td>1.11</td>
<td>1.18</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Elixhauser Score</td>
<td>1.32</td>
<td>1.28</td>
<td>1.37</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

AUC = 0.82  
Hosmer-Lemeshow p value = 0.77
Kaplan-Meier Survival Curves

- **Unadjusted Control Group**
- **Adjusted Control Group**
- **Unadjusted SSRI/SNRI Medication**
- **Adjusted SSRI/SNRI Medication**

*Graph showing survival rates over time for different groups.*
## Odds Ratio of SSRI vs. Control in Various Patient Subsets

<table>
<thead>
<tr>
<th>Patient Subset</th>
<th>Odds Ratio</th>
<th>95% CI Lower Bound</th>
<th>95% CI Upper Bound</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Disease</td>
<td>1.90</td>
<td>1.46</td>
<td>2.46</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1.42</td>
<td>0.71</td>
<td>2.81</td>
<td>0.321</td>
</tr>
<tr>
<td>Acute Renal Failure</td>
<td>1.61</td>
<td>1.07</td>
<td>2.42</td>
<td>0.022</td>
</tr>
<tr>
<td>Acute respiratory failure and COPD</td>
<td>1.72</td>
<td>1.22</td>
<td>2.42</td>
<td>0.002</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1.89</td>
<td>1.16</td>
<td>3.10</td>
<td>0.011</td>
</tr>
<tr>
<td>Patients on mechanical ventilation</td>
<td>1.77</td>
<td>1.36</td>
<td>2.30</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Patients who received vasopressor therapy</td>
<td>1.76</td>
<td>1.27</td>
<td>2.44</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
## Difference in Initial Laboratory Values between SSRI and Control Groups

<table>
<thead>
<tr>
<th>Laboratory Value</th>
<th>Control Group (Mean ± SD)</th>
<th>SSRI Group (Mean ± SD)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>12.6 ± 2.2</td>
<td>12.2 ± 2.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Red cell width distribution</td>
<td>14.3 ± 1.8</td>
<td>14.6 ± 1.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Platelet count</td>
<td>250 ± 109</td>
<td>264 ± 118</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Chloride</td>
<td>103 ± 5.6</td>
<td>102 ± 6.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Anion gap</td>
<td>15.2 ± 4.0</td>
<td>15.5 ± 4.2</td>
<td>0.015</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>100 ± 103</td>
<td>111 ± 114</td>
<td>0.001</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.6 ± 0.7</td>
<td>3.5 ± 0.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CK-MB</td>
<td>29 ± 77</td>
<td>21 ± 71</td>
<td>0.02</td>
</tr>
<tr>
<td>PTT</td>
<td>35 ± 22</td>
<td>32 ± 18</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Carbon dioxide partial pressure</td>
<td>42 ± 11</td>
<td>43 ± 13</td>
<td>0.002</td>
</tr>
</tbody>
</table>
Difference in the First 24-Hour Vital Signs between SSRI and Control Groups

<table>
<thead>
<tr>
<th>Laboratory Value</th>
<th>Control Group (Mean ± SD)</th>
<th>SSRI Group (Mean ± SD)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum blood pressure (MAP)</td>
<td>92.7 ± 17.8</td>
<td>95.3 ± 18.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Minimum blood pressure (MAP)</td>
<td>62.5 ± 13.7</td>
<td>61.3 ± 13.7</td>
<td>0.005</td>
</tr>
<tr>
<td>Blood pressure variability</td>
<td>8.5 ± 5.0</td>
<td>9.3 ± 4.8</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
Discussion

• Higher hospital and 1-year mortality among patients on SSRI after adjustment for age, sex, severity of illness and co-morbidities
• Seen in most patient subsets but at varying degrees
• Findings need to be validated in other databases
• Is it the drug or is it the disease?
Discussion

• Study highlights the need for clinical data mining as a standard in this age of electronic medical records

• Side effects of treatments and accuracy of tests in various medical contexts, including critical illness, and interactions between treatments and tests not routinely adequately investigated in clinical trials
Dynamic Data during Hypotension Improves Mortality Prediction among Patients with Septic Shock

Hypotensive Episode

Treatments:
- Fluids
- Vasopressors

Physiologic Response to Treatments

Initial Presentation

Event -> Treatment -> Response

Outcome Prediction
Methods

<table>
<thead>
<tr>
<th>Time</th>
<th>Onset-24h</th>
<th>Onset-2h</th>
<th>Onset-offset</th>
<th>Offset+2h</th>
<th>Offset+24h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heamodynamics</td>
<td></td>
<td></td>
<td>ABP Mean – Sys – Dia – Pulse</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SpO2 – Breathing Rate - Temperature</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lab Values</td>
<td></td>
<td>K, Na, Cl, Art.pH, HbG, platelets, creatine, Ca, Na, WBC, Glucose, Mg, P</td>
<td></td>
<td>SAPS-I, K, Na, Cl, Art.pH, HbG, platelets, creatine, Ca, Na, WBC, Glucose, Mg, P</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td>Fluids</td>
<td></td>
<td>Pressors</td>
</tr>
<tr>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Genetic Algorithm

• Search technique to find the best solution to a problem using processes involved in evolution
  – Selection
  – Cross-over
  – Mutation
• Candidate solutions are represented as chromosomes
• Initial generation of chromosomes are randomly generated
Genetic Algorithm

• For each generation, every chromosome is evaluated as regards some fitness function, e.g. how well it solves the problem.
• Best chromosomes of each generation are selected, then recombined +/- mutated to produce the next generation of better chromosomes.
• Children of the fittest parents bump off the weakest parents.
Genetic Algorithm

• Algorithm stops
  – When a chromosome is found to have threshold fitness
  – After a maximum number of generations
  – New generations no longer producing more fit children
  – Allocated budget is reached (time or space)
  – Combination of above
Methods
<table>
<thead>
<tr>
<th>Variable</th>
<th>Effect Size Estimate</th>
<th>P Value</th>
<th>% of GA Runs Variable was Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>∆Magnesium</td>
<td>-0.29</td>
<td>&lt; 0.001</td>
<td>98</td>
</tr>
<tr>
<td>INR after</td>
<td>+0.25</td>
<td>0.003</td>
<td>99</td>
</tr>
<tr>
<td>Van Walraven score</td>
<td>+0.24</td>
<td>0.005</td>
<td>96</td>
</tr>
<tr>
<td>Hypotension Length</td>
<td>+0.22</td>
<td>0.011</td>
<td>97</td>
</tr>
<tr>
<td>∆Glucose</td>
<td>+0.21</td>
<td>0.014</td>
<td>93</td>
</tr>
<tr>
<td>SAPS on admission</td>
<td>+0.20</td>
<td>0.019</td>
<td>91</td>
</tr>
<tr>
<td>SpO2 after</td>
<td>+0.20</td>
<td>0.017</td>
<td>88</td>
</tr>
<tr>
<td>PaCO2 after</td>
<td>-0.19</td>
<td>0.029</td>
<td>81</td>
</tr>
<tr>
<td>Creatinine prior</td>
<td>-0.18</td>
<td>0.004</td>
<td>78</td>
</tr>
<tr>
<td>∆CVP</td>
<td>-0.15</td>
<td>0.078</td>
<td>58</td>
</tr>
<tr>
<td>Pressors</td>
<td>+0.12</td>
<td>0.14</td>
<td>39</td>
</tr>
<tr>
<td>MAP prior</td>
<td>-0.13</td>
<td>0.13</td>
<td>42</td>
</tr>
<tr>
<td>∆MAP</td>
<td>-0.13</td>
<td>0.16</td>
<td>34</td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>Hosmer-Lemeshow Statistic</th>
<th>Net Reclassification Improvement</th>
<th>Integrated Discrimination Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPS-I</td>
<td>0.58</td>
<td>25.5</td>
<td>-0.06</td>
<td>-0.05</td>
</tr>
<tr>
<td>APACHE3</td>
<td>0.59</td>
<td>15.3</td>
<td>-0.02</td>
<td>-0.04</td>
</tr>
<tr>
<td>Van Walraven</td>
<td>0.64</td>
<td>18.5</td>
<td>-0.06</td>
<td>-0.00</td>
</tr>
<tr>
<td>APACHE4</td>
<td>0.68</td>
<td>11.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dynamic Model</td>
<td>0.85</td>
<td>3.4</td>
<td>1.04</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
</tr>
</tbody>
</table>
Discussion

• Significant improvement in mortality prediction using information during a hypotensive event
• Two of the most frequently selected variables are change in Mg and change in glucose
<table>
<thead>
<tr>
<th></th>
<th>Survivors (n= 80) Mean (Range)</th>
<th>Non-Survivors (n=99) Mean (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔMagnesium*</td>
<td>0.20 (0.00-0.52)</td>
<td>0.00 (-0.15-0.40)</td>
</tr>
<tr>
<td>Magnesium level</td>
<td>1.80 (1.60-2.00)</td>
<td>2.00 (1.70-2.25)</td>
</tr>
<tr>
<td>Magnesium administered</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ΔAlbumin</td>
<td>-0.10 (-0.40-0.28)</td>
<td>-0.10 (-0.38-0.05)</td>
</tr>
<tr>
<td>ΔGlucose*</td>
<td>-16.50 (-51.00-28.37)</td>
<td>8.00 (-34.88-43.50)</td>
</tr>
<tr>
<td>Glucose level</td>
<td>137.25 (110.50-170.25)</td>
<td>136.50 (105.00-164.00)</td>
</tr>
<tr>
<td>Insulin administered (%)</td>
<td>24.72%</td>
<td>18.75%</td>
</tr>
</tbody>
</table>

*p < 0.05
Discussion

• Animal models: pleiotropic role of Mg in regulating inflammatory cytokines and mitochondrial function in septic shock

• Mg and glucose metabolism closely linked: low Mg closely associated with insulin resistance

• Future studies investigating glucose homeostasis in septic shock should take into account Mg metabolism
What Matters During a Hypotensive Event? Fluids, Vasopressors, or Both?

Lee J, Kothari R, Ladapo J, Scott DJ, Celi LA
Practice Variation

• Variability in care not explained by patient or contextual factors

• Up to 85% variation in care (Millenson, *Health Aff* 1997)
  – Provider training
  – Provider knowledge base and experience
  – Local culture

• Treatment variation: Does it translate to variation in clinical outcomes?
Practice Variation

• Hypotension in the ICU: assess fluid responsiveness and optimize cardiac preload, \( \pm \) vasopressors
• Currently no standard way of assessing fluid responsiveness
• Variable opinion among clinicians as regards harm from excess fluid and risk of vasopressor use
Methods

• Definition of hypotensive episode
• Interventions: fluid rate, use of vasopressors
• Primary outcome: Hospital mortality
• Secondary outcomes
  – 2-year mortality
  – Duration and degree of hypotensive episode
  – Rise in creatinine within 3 days after the hypotensive event
  – ICU length-of-stay among survivors
Methods

• Control variables or confounders:
  – SAPS
  – Elixhauser score
  – Average MAP 3 hours prior to the hypotensive event
  – Urine output 3 hours prior to the hypotensive event
  – Creatinine prior to the hypotensive event

• Multivariate regression analysis
  – All patients
  – Only patients who got treated
  – Only patients who received fluids
  – Evaluate interaction term between volume of fluids administered and vasopressor use

• Propensity score analysis: vasopressors vs. mortality
Results

Fluid rate during hypotensive event
## Results

Multivariate analysis for HE area (N=2289, AUC=0.62, Hosmer-Lemeshow p=0.34)

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid administration</td>
<td>1.21</td>
<td>0.96 - 1.51</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td>0.69</td>
<td>0.56 – 0.85</td>
</tr>
<tr>
<td>Age</td>
<td>1.01</td>
<td>1.00 – 1.01</td>
</tr>
<tr>
<td>Gender</td>
<td>0.86</td>
<td>0.73 – 1.03</td>
</tr>
<tr>
<td>SAPS</td>
<td>0.99</td>
<td>0.99 – 1.01</td>
</tr>
<tr>
<td>Elixhauser score</td>
<td>1.14</td>
<td>1.01 – 1.27</td>
</tr>
<tr>
<td>Average MAP prior to HE</td>
<td>0.98</td>
<td>0.97 – 0.99</td>
</tr>
<tr>
<td>Urine output prior to HE</td>
<td>1.10</td>
<td>0.92 – 1.30</td>
</tr>
<tr>
<td>Serum creatinine prior</td>
<td>0.99</td>
<td>0.91 – 1.08</td>
</tr>
</tbody>
</table>
## Results

Multivariate analysis for hospital mortality (N=2289, AUC=0.83, Hosmer-Lemeshow p=0.23)

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluid administration</strong></td>
<td>0.89</td>
<td>0.61 – 1.13</td>
</tr>
<tr>
<td><strong>Vasopressor use</strong></td>
<td>2.71</td>
<td>1.96 – 3.74</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>1.01</td>
<td>1.00 – 1.02</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>0.94</td>
<td>0.70 – 1.26</td>
</tr>
<tr>
<td><strong>SAPS</strong></td>
<td>1.14</td>
<td>1.11 – 1.18</td>
</tr>
<tr>
<td><strong>Elixhauser score</strong></td>
<td>1.24</td>
<td>1.14 – 1.36</td>
</tr>
<tr>
<td><strong>Average MAP prior to HE</strong></td>
<td>1.02</td>
<td>1.01 – 1.04</td>
</tr>
<tr>
<td><strong>Urine output prior to HE</strong></td>
<td>0.66</td>
<td>0.49 – 0.88</td>
</tr>
<tr>
<td><strong>Serum creatinine prior</strong></td>
<td>1.07</td>
<td>0.96 – 1.19</td>
</tr>
</tbody>
</table>
## Results

Multivariate analysis for 2-year mortality (N=2289, AUC=0.75, Hosmer-Lemeshow p<0.01)

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluid administration</strong></td>
<td>0.92</td>
<td>0.74 – 1.13</td>
</tr>
<tr>
<td><strong>Vasopressor use</strong></td>
<td>1.64</td>
<td>1.36 – 1.97</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>1.02</td>
<td>1.02 – 1.03</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>1.20</td>
<td>1.02 – 1.42</td>
</tr>
<tr>
<td><strong>SAPS</strong></td>
<td>1.08</td>
<td>1.06 – 2.00</td>
</tr>
<tr>
<td><strong>Elixhauser score</strong></td>
<td>1.22</td>
<td>1.05 – 1.42</td>
</tr>
<tr>
<td><strong>Average MAP prior to HE</strong></td>
<td>1.01</td>
<td>1.00 – 1.02</td>
</tr>
<tr>
<td><strong>Urine output prior to HE</strong></td>
<td>0.86</td>
<td>0.73 – 1.02</td>
</tr>
<tr>
<td><strong>Serum creatinine prior</strong></td>
<td>1.08</td>
<td>1.02 – 1.15</td>
</tr>
</tbody>
</table>
Survival Curves of Different Treatment Groups
## Results

Multivariate analysis for Creatinine Rise (N=1955, AUC=0.64, Hosmer-Lemeshow p=0.24)

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid administration</td>
<td>1.12</td>
<td>0.88 – 1.42</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td>1.44</td>
<td>1.15 – 1.81</td>
</tr>
<tr>
<td>Age</td>
<td>1.01</td>
<td>1.00 – 1.01</td>
</tr>
<tr>
<td>Gender</td>
<td>1.08</td>
<td>0.89 – 1.31</td>
</tr>
<tr>
<td>SAPS</td>
<td>1.02</td>
<td>1.00 – 1.04</td>
</tr>
<tr>
<td>Elixhauser score</td>
<td>1.35</td>
<td>1.14 – 1.59</td>
</tr>
<tr>
<td>Average MAP prior to HE</td>
<td>1.00</td>
<td>0.99 – 1.01</td>
</tr>
<tr>
<td>Urine output prior to HE</td>
<td>0.76</td>
<td>0.63 – 0.92</td>
</tr>
<tr>
<td>Serum creatinine prior</td>
<td>1.00</td>
<td>0.92 – 1.10</td>
</tr>
</tbody>
</table>
## Results

Multivariate analysis for ICU length-of-stay (N=2081, AUC=0.72, Hosmer-Lemeshow p=0.62)

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid administration</td>
<td>0.72</td>
<td>0.56 – 0.92</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td>1.32</td>
<td>1.03 – 1.69</td>
</tr>
<tr>
<td>Age</td>
<td>0.99</td>
<td>0.99 – 0.99</td>
</tr>
<tr>
<td>Gender</td>
<td>0.96</td>
<td>0.79 – 1.16</td>
</tr>
<tr>
<td>SAPS</td>
<td>1.12</td>
<td>1.10 – 1.15</td>
</tr>
<tr>
<td>Elixhauser score</td>
<td>1.23</td>
<td>1.17 – 1.30</td>
</tr>
<tr>
<td>Average MAP prior to HE</td>
<td>1.04</td>
<td>1.02 – 1.05</td>
</tr>
<tr>
<td>Urine output prior to HE</td>
<td>0.77</td>
<td>0.64 – 0.93</td>
</tr>
<tr>
<td>Serum creatinine prior</td>
<td>1.02</td>
<td>0.93 – 1.12</td>
</tr>
</tbody>
</table>
# Results

Propensity Score Model (N=2289, AUC=0.73, Hosmer-Lemeshow p=0.07)

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.99</td>
<td>0.98 – 0.99</td>
</tr>
<tr>
<td>Gender</td>
<td>1.52</td>
<td>1.22 – 1.90</td>
</tr>
<tr>
<td>SAPS</td>
<td>1.12</td>
<td>1.09 – 1.14</td>
</tr>
<tr>
<td>Elixhauser</td>
<td>1.16</td>
<td>1.03 – 1.29</td>
</tr>
<tr>
<td>Average MAP prior to HE</td>
<td>1.01</td>
<td>0.99 – 1.02</td>
</tr>
<tr>
<td>Urine output prior to HE</td>
<td>0.70</td>
<td>0.57 – 0.87</td>
</tr>
<tr>
<td>Serum creatinine prior</td>
<td>1.01</td>
<td>0.92 – 1.11</td>
</tr>
</tbody>
</table>
Results

Propensity Score Analysis (N=695, AUC=0.577, Hosmer-Lemeshow p=0.66)

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid administration</td>
<td>0.93</td>
<td>0.75 – 1.15</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td>1.50</td>
<td>1.24 – 1.81</td>
</tr>
<tr>
<td>Vasopressor propensity</td>
<td>0.49</td>
<td>0.26 – 0.91</td>
</tr>
</tbody>
</table>
Sensitivity Analyses

• Vasopressor use associated with worse clinical outcomes among
  – Cohort limited to the patients who were treated during the hypotensive episode
  – Cohort limited to patients who were administered fluids during the hypotensive episode
Discussion

- Vasopressor use during a hypotensive event is an independent predictor of mortality
  - Multivariate logistic regression
    - All patients
    - Only patients administered fluids
  - Propensity score analysis
- Mean vasopressor load associated with increased risk of 28-day mortality (Dunser, *Crit Care* 2009)
- Side effects
  - Impaired microcirculation
  - Increased metabolic demands
  - Altered immune response
Discussion

• Needs to be validated in other ICU databases
• Degree of hypotension that needs to be treated likely varies from patient to patient, and perhaps even within the same patient in different contexts
• Clinical data mining challenge: How do we “personalize” the blood pressure goal?
Conclusions

• Clinical databases such as MIMIC present an opportunity to study areas where practice variation exists

• Large-scale evidence impossible to obtain for the millions of questions posed in day-to-day practice - impractical, expensive, “unethical”

• Data mining might allow us to catch-up with a century of non-evidence-based medicine
Collective Experience

Data engineers and clinicians working together
Collaborative learning

Clinical Question

Interrogate MIMIC Database
Build Model
Iterate until model accurately answers the question
Interpret and Evaluate Model
Feedback to Clinician

Clinical Practice
Collective Experience is a data-fueled, inter-disciplinary team-led learning system that aggregates and analyzes day-to-day experimentations, where new knowledge is constantly extracted and propagated for quality improvement, and where practice is driven by outcomes, and less so by individual clinician knowledge base and experience and the local medical culture.”
• Dr. Joon Lee
• Dr. Dan Scott
• Dr. Victor Novack
• Professor Roger Mark

• Federico Cismondi
• Andre Fialho
• Marzyeh Ghassemi
• Samuel Hugueny
• Brian Malley
• Louis Mayaud
• Christopher Moses
• Shinho Park
• Ruben Pereira
• Daniele Ramazzotti
• Anna Ruchimsky
• Jenna Wiens