CALYPSO
clinical & analytic learning platform for surgical outcomes
assimilating visible and invisible signals
assimilating visible and invisible signals

making personalized predictions
assimilating visible and invisible signals

making personalized predictions

of post-operative surgical complications
assimilating visible and invisible signals

making personalized predictions

of post-operative surgical complications

by knowing ahead of time, can we pre-empt complications?
PRECISION MEDICINE
PRECISION MEDICINE

class discovery // risk stratification // tailored interventions
surgical complications
surgical complications
surgical complications
surgical complications

approximately 15 out of every 100 surgical procedures performed results in a complication
surgical complications

- infectious: $1,398
- cardiovascular: $7,789
- respiratory: $52,466
- thromboembolic: $18,310

In 2014, Duke spent more than $9M on post-operative complications.
## CABG

<table>
<thead>
<tr>
<th></th>
<th>Lowest Risk</th>
<th>Highest Risk</th>
<th>Difference in Payments</th>
<th>Proportion of Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index Hospitalization</td>
<td>$30K</td>
<td>$34K</td>
<td>$3.5K</td>
<td>65%</td>
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<tr>
<td>Readmissions</td>
<td>$2K</td>
<td>$2.4K</td>
<td>$0.4K</td>
<td>7%</td>
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<tr>
<td>Physician Services</td>
<td>$4.8K</td>
<td>$5.6K</td>
<td>$0.8K</td>
<td>14%</td>
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<tr>
<td>Post-Discharge Care</td>
<td>$3.7K</td>
<td>$4.4K</td>
<td>$0.7K</td>
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<tr>
<td>Total Episode</td>
<td>$41K</td>
<td>$46K</td>
<td>$5.0K</td>
<td>100%</td>
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</table>

## AAA

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Index Hospitalization</td>
<td>$22K</td>
<td>$25K</td>
<td>$3.0K</td>
<td>70%</td>
</tr>
<tr>
<td>Readmissions</td>
<td>$1.2K</td>
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<td>7%</td>
</tr>
<tr>
<td>Physician Services</td>
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<td>$3.9K</td>
<td>$0.5K</td>
<td>9%</td>
</tr>
<tr>
<td>Post-Discharge Care</td>
<td>$1.5K</td>
<td>$2.3K</td>
<td>$0.8K</td>
<td>14%</td>
</tr>
<tr>
<td>Total Episode</td>
<td>$28K</td>
<td>$33K</td>
<td>$5.3K</td>
<td>100%</td>
</tr>
</tbody>
</table>

Most extra cost can be recovered at the index hospitalization.

surgical complications

$0
$40,000
$80,000
$120,000
$160,000

all surgical patients

surgical complications

complications can multiply the cost of procedures by a factor of 5

PRECISION MEDICINE

class discovery // risk stratification // tailored interventions
The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP®) was developed by surgeons a decade ago to help hospitals measurably improve patient outcomes and save lives. Today, ACS NSQIP remains the first and only nationally validated, risk-adjusted, outcomes-based program to measure and improve the quality of surgical care across surgical specialties in the private sector.

The program dates back to the mid-1980s, when the Department of Veterans Affairs (VA) developed NSQIP to help its 133 hospitals measure quality of care based on preoperative risk factors and postoperative outcomes. VA hospitals found great success with the program. Hospitals were able to decrease postoperative mortality rates by 47 percent and morbidity rates by 43 percent between 1991 and 2006. Additionally, VA hospitals saw median length of stay fall from nine to four days, and patient satisfaction improved.

In 2001, ACS launched a pilot program funded by the Agency for Healthcare Research and Quality (AHRQ) to show that NSQIP was also effective in private-sector hospitals. Based on the successful pilot, in 2004 ACS began enrolling new private sector hospitals into NSQIP.
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ACS NSQIP  
DUKE NSQIP
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> 2 million patients
> 700 hospitals of all types

DUKE NSQIP

Duke EHR: Maestro Care
Direct access to the electronic health record
ACS NSQIP

> 2 million patients
> 700 hospitals of all types

10 years of data

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Preoperative variables
Procedure factors
Post-operative outcomes

DUKE NSQIP

DUKE NSQIP

~13000 patients

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Original Investigation

Association of Hospital Participation in a Quality Reporting Program With Inpatient Complications and Mortality

David A. Etzioni, MD, MSHS; Nabil Wasif, MD, MPH; Amylou C. Dueck, PhD; Robert R. Cima, MD; Samuel F. Hohmann, PhD; James M. Naessens, ScD; Amit K. Mathur, MD, MS; Elizabeth B. Habermann, PhD, MPH

Original Investigation

Association of Hospital Participation in a Surgical Outcomes Monitoring Program With Inpatient Complications and Mortality

Jyothi R. Thumma, MPH; Justin B. Dimick, MD, MPH; Nicholas H. Osborne, MD, MS; Lauren H. Nicholas, PhD; Andrew M. Ryan, PhD; Nicholas H. Osborne, MD, MS; Lauren H. Nicholas, PhD; Andrew M. Ryan, PhD; Jyothi R. Thumma, MPH; Justin B. Dimick, MD, MPH
In this study, we analyzed approximately 345,000 hospitalizations, of which approximately half were performed in hospitals that participated in the NSQIP. NSQIP hospitals had improvements in outcomes during the study period. This was assessed with a difference-in-differences model, which demonstrated a year-over-year improvement in risk differences for complications (0.14%; 95% CI, 0.02%-0.26%) and mortality (0.29%; 95% CI, 0.19%-0.39%). Unadjusted rates of complications were 4.8% for NSQIP hospitals compared to 5.0% for non-NSQIP hospitals. Rates of serious complications were lower for NSQIP hospitals, with an adjusted odds ratio of 1.00 (95% CI, 0.97-1.03). Serious complications had a risk difference of 0.14% (95% CI, 0.02%-0.26%) and mortality was lower for NSQIP hospitals (0.16%; 95% CI, 0.02%-0.34%). The proportions of hospitalizations occurring at NSQIP vs non-NSQIP hospitals were 2.02 vs 1.79, respectively. The NSQIP hospitals had better outcomes, with adjusted mortality rates lower at NSQIP hospitals relative to non-NSQIP hospitals (2.02 vs 1.79). The study was limited by factors inherent to administrative coding. Furthermore, the analysis was restricted to elective operations and complications, and included Medicare Case Mix Index. Additionally, the study found preliminary evidence that, while rates of complications and serious complications were similar between NSQIP and non-NSQIP hospitals, rates of postoperative outcomes improved in NSQIP hospitals. Medicare Case Mix Index. The study also found preliminary evidence that, while rates of complications and serious complications were similar between NSQIP and non-NSQIP hospitals, rates of postoperative outcomes improved in NSQIP hospitals.
"Weighing a pig does not make the pig fatter."

data processing
prediction
clinical action
Quality of the NSQIP data is also superior to other national surgical datasets. A site's trained and certified Surgical Clinical Reviewer (SCR) captures these data using a variety of methods including medical chart abstraction. To ensure the data collected are of the highest quality, Inter-Rater Reliability (IRR) Auditing of selected participating sites are conducted periodically. The IRR Audit process involves the review of multiple charts, some of which are selected randomly and others selected based on criteria designed to identify potential reporting errors, including operating room logs. Sites that have a greater than 5% disagreement rate are removed from reporting in the public dataset, and will undergo additional auditing following training and education recommendations from the ACS.

Public NSQIP data is freely available to all NSQIP-participating institutions and to date contains more than 2 million records from more than 600 hospitals from 2005-2013. Dr. Christopher Mantyh, one of the co-PIs on this project, is the NSQIP surgical champion at our institution and oversees all NSQIP data analysis and reporting processes at our institution.

Preliminary work

Using NSQIP data, we have created preliminary prediction models utilizing Elastic net penalized logistic regression (Meier, J. R. Stat. Soc. Ser. B Stat. Methodol. 2008). Traditional logistic regression suffers from issues with multicollinearity and overfitting; the penalized method alleviates this problem by introducing a penalty for complexity of the model. Elastic net incorporates this penalty term by linearly combining L1 and L2 penalties of the coefficients to shrink insignificant variables to zero (Zou, J. R. Stat. Soc. Ser. B Stat. Methodol. 2005). The optimal coefficient vector is estimated by solving the optimization problem as displayed in Equation 1, minimizing the equation over possible values for the \( \beta \) and \( \lambda \).

\[
L = X^2 \lambda + \sum \beta_i^2 + \sum \beta_i
\]

Utilizing this methodology, we predict surgical endpoints including wound complications (superficial surgical, deep surgical, organ/space surgical site infections; wound disruption/dehiscence), cardiac complications (myocardial infarction, cardiopulmonary arrest requiring cardiopulmonary resuscitation), pulmonary complications (pneumonia, failure to wean off ventilator greater than 48 hours after surgery), renal complications (acute renal insufficiency, postoperative renal failure), postoperative septic syndromes (sepsis, septic shock), urinary tract infection, reoperation for any reason within 30 days, postsurgical length of stay in the hospital, unplanned readmission within 30 days, and mortality within 30 days. These study outcomes

Modeling Goals

1. Model big data with sparse predictors and outcomes
2. Accurately predict outcomes
3. Provide interpretable relationship between outcomes & variables

Penalized Logistic Regression

1. Penalizes model for complexity
2. Shrinks insignificant variables to zero
3. Learn shrinkage parameter through a tuning grid
<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>EVENT RATE %</th>
<th>AUC</th>
<th>BRIER SCORE</th>
<th>NULL BRIER SCORE</th>
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</thead>
<tbody>
<tr>
<td>MORTALITY</td>
<td>1.3</td>
<td>0.931</td>
<td>0.013</td>
<td>0.017</td>
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<tr>
<td>ANY MORBIDITY</td>
<td>9</td>
<td>0.802</td>
<td>0.096</td>
<td>0.118</td>
</tr>
<tr>
<td>PNEUMONIA</td>
<td>1.2</td>
<td>0.868</td>
<td>0.015</td>
<td>0.016</td>
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<tr>
<td>CARDIAC</td>
<td>0.8</td>
<td>0.857</td>
<td>0.006</td>
<td>0.007</td>
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<tr>
<td>SSI</td>
<td>3.6</td>
<td>0.8</td>
<td>0.044</td>
<td>0.048</td>
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<tr>
<td>UTI</td>
<td>1.5</td>
<td>0.789</td>
<td>0.016</td>
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<tr>
<td>DVT</td>
<td>0.9</td>
<td>0.881</td>
<td>0.004</td>
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<tr>
<td>RENAL FAILURE</td>
<td>0.6</td>
<td>0.883</td>
<td>0.008</td>
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</table>
prediction: learning relationship between predictors & outcomes

<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>most predictive variables</th>
<th>% risk increase</th>
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<tbody>
<tr>
<td><strong>30-day Mortality</strong></td>
<td>ASA Class 5</td>
<td>55%</td>
</tr>
<tr>
<td></td>
<td>Totally dependent functional status</td>
<td>19%</td>
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<tr>
<td></td>
<td>Preoperative septic shock</td>
<td>18%</td>
</tr>
<tr>
<td></td>
<td>DNR status</td>
<td>17%</td>
</tr>
<tr>
<td></td>
<td>Preoperative ventilator dependence</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td>Liver disease (varices or ascites)</td>
<td>9%</td>
</tr>
<tr>
<td><strong>30-day Any Morbidity</strong></td>
<td>Dx-Esophageal cancer</td>
<td>27%</td>
</tr>
<tr>
<td></td>
<td>Totally dependent functional status</td>
<td>25%</td>
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<tr>
<td></td>
<td>Preoperative septic shock</td>
<td>24%</td>
</tr>
<tr>
<td></td>
<td>Dx-Nutritional deficiency</td>
<td>21%</td>
</tr>
<tr>
<td></td>
<td>Dx-Injury</td>
<td>21%</td>
</tr>
<tr>
<td></td>
<td>ASA Class 4</td>
<td>19%</td>
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</table>
http://ouwen.github.io/calypso/#/

http://ouwen.github.io/calypso-dist/#/
ERAS/NSQIP EDC/DB

TRANSFER LEARNING

PREDICTIVE MODEL

Health System EHR

Health System EDW

NATIONAL DATA

PREDICTIVE MODEL

LOCAL DATA

<table>
<thead>
<tr>
<th>Outcomes (2 of 8)</th>
<th>AUC - NoTransferLearning</th>
<th>AUC - TransferLearning</th>
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<tr>
<td>Pneumonia</td>
<td>0.832</td>
<td>0.848</td>
</tr>
<tr>
<td>Cardiac</td>
<td>0.909</td>
<td>0.920</td>
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CONTINUOUS LEARNING

<table>
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<th>Outcomes (2 of 8)</th>
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other use cases
other use cases
other use cases

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Name</th>
<th>Age</th>
<th>Gender</th>
<th>Procedure</th>
<th>Complication</th>
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<tbody>
<tr>
<td>2101</td>
<td>Bee Smith</td>
<td>45 y/o F</td>
<td></td>
<td>POD 0 Pancreatoduodenectomy</td>
<td>DVT</td>
</tr>
<tr>
<td>2103</td>
<td>Bill Doe</td>
<td>75 y/o M</td>
<td></td>
<td>POD 0 Lap Cholecystectomy</td>
<td>UTI</td>
</tr>
<tr>
<td>2112</td>
<td>Nancy Oh</td>
<td>47 y/o F</td>
<td></td>
<td>POD 0 Lap R Hemicolecetomy</td>
<td>CV</td>
</tr>
<tr>
<td>2118</td>
<td>Fred Jones</td>
<td>62 y/o M</td>
<td></td>
<td>POD 0 Low Anterior Resection</td>
<td></td>
</tr>
<tr>
<td>ID</td>
<td>Name</td>
<td>Age</td>
<td>Gender</td>
<td>Procedure</td>
<td>Condition</td>
</tr>
<tr>
<td>-----</td>
<td>-----------------</td>
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<td>--------</td>
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Statistical Sciences
Katherine Heller
Joe Futoma
Liz Lorenzi
Stephanie Brown

Surgery
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Christopher Mantyh
Julie Thacker
Alan Kirk

Nephrology
Blake Cameron
Uptal Patel

Office of Research Informatics
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Matt Gardner
Darin London
Darrin Mann
Donald Murry
Steve Woody
Iain Sanderson

DCRI
Ben Neely

DIHI
Mark Sendak
Will Elliası
Suresh Balu

DTRI
Victoria Christian
Shelley Rusincovitch
Ashley Dunham