Registries for Active Surveillance

DELETA and Automated Device Safety Surveillance

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Frederic S. Resnic, MD MSc
Chairman, Department of Cardiovascular Medicine
Director, Comparative Effectiveness Research Institute
Lahey Clinic Medical Center
Tufts University School of Medicine
Foundations of Automated Prospective Surveillance

Quality Data Sources

Secure Data Exchange

Monitoring System

Safety Expectations

Registries
Claims Datasets
EHR / HIE
Hybrid Datasets

Comparators
Methods
Pre-approval
Evidence

Distributed Models
Secure, Encrypted
Integrated Models

Continuous
Flexible
Transparent
Automated Safety Surveillance Systems
Idealized Safety Monitoring System

Distributed Data Ownership
Idealized Safety Monitoring System

Monitoring System

- Continuously updated
- Array of statistical analytic options
- Monitor multiple analyses simultaneously
- Flexible Alert notification
- Generic structure
- Widely accessible – feedback to source sites

Distributed Data Ownership

Expectation and Risk Adjustment

Reports

Alerts

Safety Analyst
Welcome to DELTA

Data Extraction and Longitudinal Time Analysis System

Engineered to support dynamic safety monitoring in healthcare utilizing various statistical methods.

Supported by grant R01-LM08142 from the National Library of Medicine.

Developed by Coping Systems, Inc.
Delta Version V3.0.1.19a

Links
Fredric S. Resnic, MD, MSc, FACC
Michael Matheny, MD, MS, MPH
Lucila Ohno-Machado, MD, PhD
Coping Systems, Inc.
DELTA2 Documentation Wiki

BRIGHAM AND WOMEN’S HOSPITAL
Specializing in care for a lifetime
Using the MA state-wide PCI device dataset, we explored the *cumulative* post-procedure myocardial infarction rate for new drug eluting stent as compared with propensity matched control DES.

Using 38 clinical variables in propensity match a total of 81.5% of 18,277 new stents were analyzed.

Adapted from: Resnic F et al. JAMA November 2010
Using pooled data from three high volume centers, DELTA performed a propensity matched analysis of 859 Fidelis lead implants versus traditional leads. By 25 months of analysis (dashed line) 3% of Fidelis leads had fractured (red line) whereas only 0.1% (1 of 859) alternative ICD leads had fractured.

We also explored the major vascular complication rates following the introduction of a new vascular closure device. A total of 74.5% of the 10,790 AngioSeal STS devices were successfully matched to concurrent controls. Initial results indicate increased complications early in experience with newly introduced device.

Adapted from: Resnic F et al. JAMA November 2010
Periodic and sensitivity analyses indicate reduced complication rates with increasing experience. Changes in outcome related to changes in anticoagulation practice. In addition, results raise possibility of learning curve effect.

**MA Experience 2005-2007:** St Jude AngioSeal STS vs. Propensity Matched VCD – Major Vasc Complications
Registries for Methodology Development: Device Learning Curve

Preliminary analysis of statewide cardiac registry confirmed operator level learning curve for new VCD.

Source: Sarma A., Normand SL and Resnic FS: Preliminary Analysis
Registries for Methodology Development: Device Learning Curve

.... And provides insights into training/learning differences with specific devices as well as “steady-state” performance and safety.

Source: Sarma A., Normand SL and Resnic FS: Preliminary Analysis
Registries for Methodology Development: Device Learning Curve

In addition, clearly problematic devices can easily be identified....

![Preliminary Propensity Matched Analysis](image)

Device “A”

Device “B”

Source: Sarma A., Normand SL and Resnic FS: Preliminary Analysis
DELTA Automated Surveillance: Prospective Surveillance Network Pilot

Brigham and Women's
Outcomes DB → DELTA 2.0 Agent

Mass General
Outcomes DB → DELTA 2.0 Agent

Lahey Clinic
Outcomes DB → DELTA 2.0 Agent

Beth Israel Deaconess
Outcomes DB → DELTA 2.0 Agent

North Shore Medical Center
Outcomes DB → DELTA 2.0 Agent

DELTA 2.0 Collecting Server

SMTP E-mail Server

E-mail alert

Resnic FS and Robbins S. Preliminary Results
Ongoing DELTA Surveillance Projects

- VA Healthcare System – Catheter safety during complex coronary stenting procedure
- ACC-NCDR Pilots: Vascular Closure Devices and Thrombectomy Devices
- Kaiser-Permamente: Artificial Hip implant safety
Looking Ahead

• **Automated surveillance** is feasible, scalable and applicable to a variety of datasets; and can support timely identification of preliminary safety alerts (require verification)

• **Near Term Goals: (1-3 years)**
  - Open Source Development Collaboration with UCSD National Center for Biomedical Computing (iDASH)
  - Incorporation of Learning Curve adjustment methods

• **Long Term Goals: (3-5 years)**
  - Continuous Automated Surveillance to be included into formal post-approval study
  - Incorporation into national registries for routine safety surveillance of new devices
Thank You!!

For more information contact: frederic.resnic@lahey.org
## DELTA: Array of Statistical Methods

<table>
<thead>
<tr>
<th></th>
<th>Uniform</th>
<th>Stratified</th>
<th>Risk Adjusted</th>
</tr>
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<tbody>
<tr>
<td><strong>Frequentist</strong></td>
<td>Statistical Process Control (SPC)</td>
<td>Stratified SPC</td>
<td>Logistic Models</td>
</tr>
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<td></td>
<td>CUSUM</td>
<td>SPRT Propensity Match</td>
</tr>
<tr>
<td><strong>Bayesian</strong></td>
<td>Bayesian Updating System (BUS)</td>
<td>Stratified Bayesian</td>
<td>Hierarchical (Bayesian)</td>
</tr>
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<td>Logistic Regression (HLR)</td>
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**Expectation**

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Propensity matching selected as primary analysis as a strategy to reduce treatment selection bias based on ability to communicate to public and policy makers.

Table 2. Distribution of Clinical Covariates in Patients Receiving Taxus Express2 or Alternative Drug-Eluting Stents

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Total Study Population</th>
<th>Propensity Matched</th>
<th>Unmatched Patients¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Taxus Express2 (n = 18,277)</td>
<td>Alternative (n = 28,327)</td>
<td>Standard Difference</td>
</tr>
<tr>
<td></td>
<td>Taxus Express2 (n = 14,893)</td>
<td>Alternative (n = 14,893)</td>
<td>Standard Difference</td>
</tr>
<tr>
<td></td>
<td>Taxus Express2 (n = 3384)</td>
<td>Alternative (n = 3384)</td>
<td>Standard Difference</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>64.6 (12.2)</td>
<td>64.8 (12.6)</td>
<td>1.60</td>
</tr>
<tr>
<td>Women</td>
<td>31.0</td>
<td>30.1</td>
<td>2.00</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>30.6</td>
<td>30.2</td>
<td>0.90</td>
</tr>
<tr>
<td>History of MI</td>
<td>27.8</td>
<td>29.3</td>
<td>3.30</td>
</tr>
<tr>
<td>Current smoker</td>
<td>21.6</td>
<td>20.4</td>
<td>2.90</td>
</tr>
<tr>
<td>History of renal insufficiency</td>
<td>5.26</td>
<td>6.25</td>
<td>4.30</td>
</tr>
<tr>
<td>History of PAD</td>
<td>13.5</td>
<td>13.7</td>
<td>0.60</td>
</tr>
<tr>
<td>Ejection fraction &lt;30%</td>
<td>41.9</td>
<td>43.8</td>
<td>3.80</td>
</tr>
<tr>
<td>Emergent procedure</td>
<td>16.2</td>
<td>15.1</td>
<td>3.00</td>
</tr>
<tr>
<td>Acute MI on presentation</td>
<td>36.3</td>
<td>35.3</td>
<td>2.10</td>
</tr>
<tr>
<td>Left main vessel disease &gt;=50%</td>
<td>5.91</td>
<td>6.27</td>
<td>1.50</td>
</tr>
<tr>
<td>Vein graft lesion</td>
<td>5.08</td>
<td>6.20</td>
<td>4.90</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa antagonist</td>
<td>29.3</td>
<td>34.5</td>
<td>11.10</td>
</tr>
<tr>
<td>Final stent diameter, mean (SD), mm</td>
<td>3.15 (0.52)</td>
<td>3.22 (0.49)</td>
<td>0.07</td>
</tr>
<tr>
<td>Maximum lesion length, mean (SD), mm²</td>
<td>17.8 (9.9)</td>
<td>17.1 (9.7)</td>
<td>7.10</td>
</tr>
</tbody>
</table>

Adapted from: Resnic F et al. JAMA November 2010