Bayesian analytics to identify relationships between cancer treatment regimens, patient co-morbidities and specific toxicity risk: ToxScreen.care demonstration project

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\begin{itemize}
\item \textsuperscript{1} Primary Endpoint Solutions
\item \textsuperscript{2} Harvard Medical School
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\item \textsuperscript{4} National Institute of Nursing Research
\item \textsuperscript{5} Dana-Farber Cancer Institute and Brigham and Women’s Hospital
\end{itemize}
Nothing to Disclose
Background

- Patients are not at equivalent risk for cancer-regimen related toxicities (CRRT).
- Multivariable regression models across heterogenous populations and have collectively shown that model-based approaches can improve risk stratification.
- Multivariable regression models typically
  - focus on the prediction of singular endpoints
  - rely on the assumption of linearity
The Opportunity:

With the novel collection of Big Data in medicine, we can use personalized medicine algorithms to analyze the impact of synergistic variables which contribute to an individual’s CRRT risk and unify outputs into a clinically actionable tool.
Methods

• Data retrieved from the NIH Biomedical Translational Research Information System using screening criteria of cancer diagnosis treated with chemotherapy (n=14,400).

• All patients on NIH protocols enrolled from 1999 vs. conventional regimens.

• Of 14,400 patients who were screened, 9209 met our criteria of including timestamped longitudinal data including:
  – Cancer diagnosis
  – Chemotherapy Regimen
  – Comorbidities
  – Toxicities
Methods: Definitions

- **Type 1 Diabetes Mellitus, HTN, HLD**
  - 1 Jan

- **Comorbidity**
  - 30 Jun

- **Neutropenia**
  - 1 Apr

- **Chemo Start**
  - 31 Jan

- **Toxicity**
  - 1999

- **Neuropathic pain**
  - 28 Oct

- **Toxicity**
  - 1999
Methods: Predicting risk

1. 22% (N=2000) of patients were diagnosed with breast cancer.

2. Of the 2000 patients diagnosed with breast cancer, 40% presented with a comorbidity of Type II Diabetes Mellitus.

3. The ratio of patients that developed a toxicity of neutropenia differed for each regimen.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Neutropenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etoposide</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin</td>
<td></td>
</tr>
<tr>
<td>Paclitaxel</td>
<td></td>
</tr>
<tr>
<td>5-FU</td>
<td></td>
</tr>
</tbody>
</table>
Risk metrics meaningful to patients

**Absolute Risk:** Chance of Toxicity With Med - Chance of Toxicity Without Med

**Relative Risk:** Chance of Toxicity With Med / Chance of Toxicity Without Med

- **LOW AR, HIGH RR**
  - LOW Patient Impact
  - 0.1% vs. 0.9%

- **HIGH AR, LOW RR**
  - HIGH Patient Impact
  - 20% vs. 30%
Visit http://ToxScreen.care to try the demonstration project

Welcome to ToxScreen

Toxscreen.care is a demonstration project that was created to assess the feasibility and potential utility of a novel, multi-variable web-based platform by which health providers could compare toxicity risks in patients about to undergo cancer therapy (CRRT).

Toxscreen's algorithms are based on data provided from the National Institutes of Health and consisted of 14,000 cancer patients of which 10,000 were randomly selected.

We focused on the following variables: tumor diagnosis, treatment regimen and comorbidities. And we created a program, embodied by this web-interface, to predict a patient's CRRT based on these variables.

Although the current iteration is limited by the scope of information provided by the NIH's unique cohort, it was critical in enabling proof-of-concept.

Additional, prospective clinical, genomic, demographic and epigenomic data which we hope to incorporate should increase the predictive value of the tool to help clinicians assess a patient's CRRT risk in an accessible, user-friendly, web-based interface.

To begin, enter the following,

Patient Cancer Diagnosis:  
Add a diagnosis
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To begin, enter the following,

Patient Cancer Diagnosis:  lym  lymphoma
Visit [http://ToxScreen.care](http://ToxScreen.care) to try the demonstration project.
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### Patient Cancer Diagnosis:
- lymphoma

### Toxicity to Screen For:
- hypokalemia

### Toxicity Suggestions:
- hypokalemia
- fever in other diseases
- constipation
- dehydration

### Patient Comorbidities:
- anemia

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>etoposide</th>
<th>doxorubicin</th>
<th>Risk: Absolute</th>
<th>Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (307/307)</td>
<td>2.9%</td>
<td>5.5%</td>
<td>6.9%</td>
<td>28/110</td>
</tr>
<tr>
<td>anemia (75/307)</td>
<td>25.4%</td>
<td>15.5%</td>
<td>25.4%</td>
<td>19/212</td>
</tr>
</tbody>
</table>
Conclusions

We produced an online demonstration (URL ToxScreen.care) of a clinical tool for data-driven personalized prediction of CRRT risk using Bayesian Analytics using a model capable of analyzing large amount of multifaceted/complex medical data.

This platform can be easily translated to other patient databases and expanded to other medical fields:
- Post-op surgical complications
- Antibiotic toxicities
- Anesthesia adverse effects
Next Steps

We will continue to develop an interface for clinicians to translate personalized medicine into their practice.

Latent factor multiplex analysis for predicting chemotherapy toxicity.