Economic Considerations for Implementing Pharmacogenomics

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VANDERBILT UNIVERSITY MEDICAL CENTER
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What are Economic Considerations?

- Cost of testing
- Cost of returning results
  - Clinical decision support
  - Education
  - Managing data
- Reimbursement
- Savings from improved therapeutic outcomes
- Cost - Effectiveness (CE)
## CE – Specific PGx Scenarios

<table>
<thead>
<tr>
<th>Scenario</th>
<th>ICER ($/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-B 1502 -- Antiepileptics in Asian populations</td>
<td>$7,930 – $136,630</td>
</tr>
<tr>
<td>HLA-B 5701 -- Abacavir</td>
<td>$36,700</td>
</tr>
<tr>
<td>CYP2C19 -- Antiplatelet agents post-PCI</td>
<td>$30,200</td>
</tr>
<tr>
<td>UGT1A1 -- Atazanavir</td>
<td>~$2,000,000</td>
</tr>
</tbody>
</table>

ICER = Incremental Cost-Effectiveness Ratio  
QALY = Quality Adjusted Life Year

CE - Panel Testing

- Economy of scale
- Broadens the opportunities to perform testing
  - Pre-emptive testing
  - “First Indication” testing
- Behavior: No need for physicians to remember to order

- In most cases, panels cost more
- The information may never be used
- Benefits are accrued in the future
Pharmacogenomics: PREDICT Model

Target Clinics

Prognostic Flag for Testing

Preemptively Tested

Reactive/Indication Testing

Genotyped for PREDICT

Genotyping

Genetic Risk

Clinical Application

CYP2C19 Variant

TPMT Variant

VKORC1 + CYP2C9

CYP3A5 Variant

Clopidogrel

Thiopurines

Warfarin

Tacrolimus

Has genetic risk variant

Exposed to new or recent prescription
Cumulative PGx Variant Rates

Van Driest SL, 2013. CPT.
Cumulative Medication Rates

Number of unique medication exposures over time

Probability of being exposed to at least X medications

Years since medical home established

Schildcrout JS, 2012, CPT.
Can Target Patients for Preemptive Genotyping

Schildcrout JS, IHEA 2016
RIGHT Aims

- Compare Genotyping Strategies
  - Base case: No Genotyping
  - Serial Single Gene
  - Universal Preemptive
  - Targeted Preemptive
  - First Indication

- Determine effect of clinician behavior on value of the panel
RIGHT Study: Simulation of Multiplexed Genotyping

Create Patient

Assign characteristics based on base population or simulated patient history

Death (Exit Model)

New Indication

Genotype Tailored Treatment

Standard Treatment

No Event

Delay to Next Cycle

Accumulate outcomes (Adverse Events, QALY)
Stages of Simulation

Predictive Submodel
- Select population for genotyping that optimizes use of variants on panel

Indication Submodel
- Simulate rate of development of drug indications over time

Outcome Assessment Submodel
- Compare outcomes among a genotyped and non-genotyped population
Features of Simulation

- Models the benefits and risks of PGx tailored therapy
  - E.g. the risk of bleeding when prescribing a potent alternative antiplatelet agent

- Manages Competing Risks
  - Secular death assumed based on standard life tables

- Individualizes Cardiac Risk to predict timing of cardiac indications
  - Based on Framingham cohort

- Includes behavioral factors
  - Genetic ordering behavior
  - Use of genetic data to tailor prescription
Drug-Specific Simulations: Simvastatin -SLC01B1
## Results – Single Drug Models

<table>
<thead>
<tr>
<th>PGx Scenario</th>
<th>ICER Compared to No Genotyping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel – CYP2C19</td>
<td>$36,618</td>
</tr>
<tr>
<td>Simvastatin – SLC01B1</td>
<td>$1,405,163</td>
</tr>
<tr>
<td>Warfarin – CYP2C9/VKORC1</td>
<td>$371,649</td>
</tr>
</tbody>
</table>
Comparing Four Genotyping Strategies

**Three Drug Model**

$100$ Single Drug Test
and $250$ Panel Test

<table>
<thead>
<tr>
<th>Strategy</th>
<th>ICER to Base*</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>NA</td>
</tr>
<tr>
<td>Reactive Single</td>
<td>118,366</td>
</tr>
<tr>
<td>Reactive Panel</td>
<td>195,256</td>
</tr>
<tr>
<td>Targeted Preemptive Panel</td>
<td>255,173</td>
</tr>
<tr>
<td>Universal Preemptive Panel</td>
<td>318,972</td>
</tr>
</tbody>
</table>
Comparing Four Genotyping Strategies

Cost-effectiveness Plane

- Universal Preemptive Panel
- Reactive Panel
- Targeted Preemptive Panel
- Reactive Single
- None

Average Cost vs. Average Quality-Adjusted Life Years
## IGNITE Antiplatelet CYP2C19 Simulation

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Average Cost</th>
<th>Genotyping Cost</th>
<th>Average Drug Cost</th>
<th>Avg. Event Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel Only</td>
<td>$6,164</td>
<td>NA</td>
<td>$786</td>
<td>$5,378</td>
</tr>
<tr>
<td>CYP2C19 Guided - Prasugrel</td>
<td>$6,137</td>
<td>$100</td>
<td>$1,232</td>
<td>$4,804</td>
</tr>
<tr>
<td>CYP2C19 Guided - Ticagrelor</td>
<td>$6,046</td>
<td>$100</td>
<td>$1,086</td>
<td>$4,860</td>
</tr>
</tbody>
</table>
Sensitivity Analyses: Behavior

3 – Drug Model: Reactive Panel Strategy

<table>
<thead>
<tr>
<th>Clinician Behavior</th>
<th>ICER Compared to No Genotyping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive: Orders and uses 100%</td>
<td>$195,256</td>
</tr>
<tr>
<td>Reactive: Orders 50% and Uses 100%</td>
<td>$235,408</td>
</tr>
<tr>
<td>Universal Preemptive: Order 100% but use 25%</td>
<td>$1,466,076</td>
</tr>
</tbody>
</table>
RATIONAL INTEGRATION OF GENOMIC HEALTHCARE TESTING

RIGHT is a research group based at Vanderbilt University Medical Center estimating the clinical benefits of multiplexed genetic testing across health systems.

FEATURES A
Lorem ipsum dolor sit amet, consectetur adipiscing elit. Sed a Lorem quis neque

FEATURES B
Lorem ipsum dolor sit amet, consectetur adipiscing elit. Sed a Lorem quis neque

FEATURES C
Lorem ipsum dolor sit amet, consectetur adipiscing elit. Sed a Lorem quis neque
Publically Hosted Simulation Tools
https://rightsim.org/RIGHT/

Clopidogrel Simulation

A discrete event simulation model for evaluation of clinical benefit and costs-effectiveness of utilizing pharmacogenomic testing in Simvastatin treatment.

Parameters

- Sample Size: 1000
- Time Horizon (Year): 1 to 10

Simulation Results

<table>
<thead>
<tr>
<th>Event</th>
<th>None</th>
<th>Genotyping</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1000</td>
<td>1000</td>
</tr>
<tr>
<td>Secular Death</td>
<td>127</td>
<td>127</td>
</tr>
<tr>
<td>Single Test</td>
<td>0</td>
<td>1000</td>
</tr>
<tr>
<td>DAPT Start</td>
<td>1000</td>
<td>1000</td>
</tr>
<tr>
<td>Drug Exposure</td>
<td>2000</td>
<td>2000</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>1000</td>
<td>779</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>0</td>
<td>221</td>
</tr>
</tbody>
</table>

Genotyping Strategy (by default no testing)
- CYP2C19 genotyping
The RIGHT Team

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