Accelerating Evidence Generation for Genomic Technologies in a Learning Health Care System

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Background

- Limited evidence available on the effect of using genomic tests on health outcomes
  - Very few RCTs
  - No funding for RCTs for genomic tests
  - RCTs take too long
  - High cost of archiving specimens from therapeutic clinical trials

Phillips K, et al. GIM 2017
Purpose of the Model

<table>
<thead>
<tr>
<th>Analytical Validity</th>
<th>Is the test accurate and reliable?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Validity</td>
<td>Is the test result medically meaningful?</td>
</tr>
<tr>
<td>Clinical Utility</td>
<td>Does the test improve healthcare &amp; health?</td>
</tr>
<tr>
<td>Risk classification</td>
<td>% patient reclassified based on test</td>
</tr>
<tr>
<td>Therapeutic choice</td>
<td>% patents in whom treatment altered</td>
</tr>
<tr>
<td>Patient outcome</td>
<td>Effect on outcomes e.g., adverse effects, QoL</td>
</tr>
<tr>
<td>Economic Validity</td>
<td>Cost benefit &amp; cost effectiveness</td>
</tr>
</tbody>
</table>

CDC’s ACCE model; [http://www.cdc.gov/genomics/gtesting/ACCE/](http://www.cdc.gov/genomics/gtesting/ACCE/)
<table>
<thead>
<tr>
<th>Green</th>
<th>Yellow</th>
<th>Red</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA label requires use of test to inform choice or dose of a drug</td>
<td>FDA label mentions biomarker*</td>
<td>FDA label cautions against use</td>
</tr>
<tr>
<td>CMS covers testing</td>
<td>CMS coverage with evidence development</td>
<td>CMS decision against coverage</td>
</tr>
<tr>
<td>Clinical practice guideline based on systematic review supports testing</td>
<td>Clinical practice guideline, not based on systematic review, supports use of test</td>
<td>Clinical practice guideline recommends against use of test</td>
</tr>
<tr>
<td></td>
<td>Clinical practice guideline finds insufficient evidence but does not discourage use of test</td>
<td>Clinical practice guideline finds insufficient evidence and discourages use of test</td>
</tr>
<tr>
<td></td>
<td>Systematic review, without clinical practice guideline, supports use of test</td>
<td>Systematic review recommends against use</td>
</tr>
<tr>
<td></td>
<td>Systematic review finds insufficient evidence but does not discourage use of test</td>
<td>Systematic review finds insufficient evidence and discourages use</td>
</tr>
<tr>
<td></td>
<td>Clinical practice guideline recommends dosage adjustment, but does not address testing</td>
<td>Evidence available only from published studies without systematic reviews, clinical practice guidelines, FDA label or CMS labels coverage decision</td>
</tr>
</tbody>
</table>

*Can be reassigned to Green or Red if one or more conditions in these categories apply*
Learning Health Care System

Key Areas of Synergy
- Evolution of evidence base for precision medicine and implementation science
- Recognition of underuse and overuse of interventions
- Management of abundance of data

Optimal use of genomics and behavioral data to drive clinical and patient decision making
- Ongoing development of genomics evidence base
- Personalized and population impact

Optimal integration of effective diagnosis, prevention, and treatment
- Understanding of multilevel context
- Theories and strategies to drive health care improvement

Key Areas of Synergy
- Support for implementation of effective practices
- Contextually sensitive improvement of practices

Use of ongoing data to drive health system improvement
- Focus on iterative and ongoing learning
- All stakeholders participate

Improved health, health care, and health systems

Three Building Blocks of the Model

- Stakeholder Engagement & Endorsement
- Temporary Coverage
- Data Networks

Rapid Evidence Generation

Better outcomes

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Stakeholder Engagement & Endorsement

Temporary Coverage
- Manufacturers
- Payers (& employers who decide on insurance benefits)

Leveraging Data Networks
- Manufacturers
- Payers
- Health systems
- EHR vendors
- Providers
- Patients
- Researchers
- Government agencies

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Temporary Coverage

Risk-sharing agreements / Value-based contracts between manufacturers & payers

- Use of genomic tests captured by claims & EHR data systems
- Not the same as CMS’ coverage with evidence development programs
  - Patients must participate in a registry or trial
  - Slow recruitment & data collection
- Costs for evidence generation shared by manufacturers and payers
- Example: Biologics and Biosimilars Collective Intelligence Consortium is a non-profit, collaborative scientific public service initiative

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Leveraging Existing Data Networks

- Avoid limitations of multi-site research
  - Pulling together data elements needed from each site on a project by project basis is time-consuming & expensive
  - Each system has its own data specs
  - Data sharing might be a concern

- Data networks (& analytical toolbox) exist
  - Data networks take time & money to develop
  - Sentinel: ~223 million individuals
  - PCORnet: ~10 million individuals
Harmonized multiple databases

Time & money to develop

Adapted from: http://www.hcsrn.org/asset/b9efb268-eb86-400e-8c74-2d42ac57fa4F/VDW.Infographic031511.jpg
PCORnet Common Data Model v3.1
Each organization can participate in multiple networks
Each network controls its governance and coordination
Other networks can participate
Networks share infrastructure, data curation, analytics, lessons, security, software development
1. User creates and submits query (a computer program)
2. Individual CDRNs/PPRNs retrieve query
3. CDRNs/PPRNs review and run query against their local data
4. CDRNs/PPRNs review results
5. CDRNs/PPRNs return results via secure network
6. Results are aggregated
Challenges

Different EHR and CDS infrastructure across systems

Text reports

Unstructured results

Not storing raw omic data

No omic ancillary systems (OAS)

Disconnect between OAS and EHR

Not querying OAS for CDS
Generating Evidence

Outcomes:

- Patterns of care
- Clinical outcomes
- Costs of care
Building the plane while flying it!
Let’s go together!
Safer, farther, faster
Thank you!

Chris Lu

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