Analysis of Clinically Actionable Preemptive Pharmacogenomic (PGx) Information to Impact In-Hospital Prescribing

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BACKGROUND

- Traditional “one size fits all” vs Precision medicine
- Pharmacogenomics (PGx) goal: ↓ adverse drug response, ↑ drug efficacy
- Various institutions have begun implementing PGx

3 issues on implementation

a. Test approach: Reactive vs preemptive

b. Standard for clinical actionable information: CPIC, FDA, DPWG
   - CPIC: Clinical Pharmacogenetics Implementation Consortium
   - FDA: table of PGx biomarkers in drug labels
   - DPWG: Dutch Pharmacogenetics Working Group

c. Genotype population: Everyone vs high-risk groups

2. Johnson et al. Pharmacogenomics 2013
HIGH STAKES SETTING

- At University of Chicago, 1200 Patients Project\(^1\)
  - Preemptively genotype patients seen by MD at outpatient clinic
  - Literature for clinically actionable pharmacogenes
  - Risk signals in U of Chicago Genomic Prescribing System (GPS)

Stakes are high in the hospital

- \(~35\) million hospital admissions per year in US \(^2\)
- Average 45% of discharge medications newly started in hospital \(^3\)
- Acutely ill patients – at risk of adverse drug reactions (ADR)
- ADR – 5.3% hospitalizations; higher rates in elderly \(^4\)

References:

2. Health Forum LLC; American Hospital Association 2014
3. Thompson-Moore, AJHP 2012
HYPOTHESIS & AIM

- HYPOTHESIS: Clinically actionable preemptive PGx information made available in high volume and high stakes in-hospital setting, can significantly influence drug prescribing

- AIM: Pilot study to determine the potential opportunities for PGx information to influence drug prescribing
METHODS

• Retrospective analysis of outpatient genotyped cohort

Outpatient genotyped cohort (N=867) → Hospitalizations at University of Chicago Medical Center 2012 to 2015 → Germline PGx information
  ▪ CPIC-A list (35 drugs)
  ▪ FDA list (104 drugs)
  ▪ U Chicago GPS list (46 drugs)

Medication changes: Compare admission and discharge med list
### RESULTS: PATIENT DEMOGRAPHICS

<table>
<thead>
<tr>
<th>CHARACTERISTICS – NO. (%)</th>
<th>OUTPATIENT GENOTYPED (N=867)</th>
<th>HOSPITALIZED (N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD, years)</td>
<td>61.3 ± 15.5</td>
<td>78.2 ± 12.3*</td>
</tr>
<tr>
<td>Male</td>
<td>394 (45.4)</td>
<td>13 (65.0)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>536 (58.8)</td>
<td>12 (60.0)</td>
</tr>
<tr>
<td>African-American</td>
<td>290 (31.8)</td>
<td>7 (35.0)</td>
</tr>
<tr>
<td>Asian</td>
<td>29 (3.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>More than one race/other</td>
<td>27 (3.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>26 (2.9)</td>
<td>1 (5.0)</td>
</tr>
<tr>
<td>American Indian/Alaska native/ Pacific islander</td>
<td>4 (0.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>No. of medications (mean ± SD)</td>
<td>5.0 ± 3.2</td>
<td>8.8 ± 3.9 *</td>
</tr>
</tbody>
</table>

*P<0.0001
### HOSPITALIZATION DETAILS

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>HOSPITALIZED, N=20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of hospitalizations</td>
<td>38</td>
</tr>
<tr>
<td>Hospitalization rate per patient</td>
<td>1.9 (range 1 – 6)</td>
</tr>
<tr>
<td>Length of stay in hospital (days)</td>
<td>4.3 (range 0 – 22.6)</td>
</tr>
<tr>
<td>No. of baseline comorbidities (mean ± SD)</td>
<td>7.4 ± 4.8</td>
</tr>
</tbody>
</table>

#### Admitting service (N=38 admissions)

<table>
<thead>
<tr>
<th>Service</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal med</td>
<td>44.7</td>
</tr>
<tr>
<td>Surgery</td>
<td>23.7</td>
</tr>
<tr>
<td>Neurology</td>
<td>13.2</td>
</tr>
<tr>
<td>Hem/Onc</td>
<td>10.5</td>
</tr>
<tr>
<td>Cardiology</td>
<td>7.9</td>
</tr>
</tbody>
</table>
53% of the Hospitalizations involved PGx drug

Total 159 medications changed (74 distinct drugs)

- Per hospital visit: average 3.8 medications changed
  - 30% medications changed involved PGx drug

Medications with PGx information (74 distinct drugs)

- CPIC-A: N=7, 9.5%
- FDA: N=12, 16.2%
- GPS: N=14, 18.9%
NEW MEDICATIONS WITH PGx INFORMATION

- Out of 74 distinct drugs changed, 66% were new medications.
- 7 (14%) new medications had PGx info from at least 2 sources.

- Carvedilol, omeprazole
- Simvastatin
- Clopidogrel, warfarin
- Codeine, tramadol
- 7 new PGx drugs affected 45% hospitalized patients
CONCLUSIONS

1. Majority of hospitalized patients undergo medication changes

2. Having PGx information from broad preemptive genotyping made available could significantly impact in-hospital prescribing

3. Preemptive genotype population: elderly, multiple medications

Future: Prospective study of broad preemptive PGx implementation among hospitalized patients

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