Pharmacogenomic Testing: The Economics of Individualized Medicine

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Disclosures

• Beth Devine – I have nothing to disclose
• Kristin (Weitzel) Wiisanen – I have nothing to disclose
CPE Information

• Target Audience: Pharmacists
• ACPE#: 0202-0000-19-012-L04-P
• Activity Type: Knowledge-based
Learning Objectives

At the completion of this knowledge-based activity, participants will be able to:

• Describe the basics of pharmacogenomics and pharmacogenomic testing

• Recognize the impact of genetic testing on therapy plan development

• Discuss the economic impact of genetic testing and future trends for drug development
Assessment Questions

1. In the future, it is likely that genetic information will be:

A. Decreasingly available to individual patients
B. Increasingly used to guide population health decisions
C. Increasingly restricted by patients’ primary care providers
D. Decreasingly used to guide a patient’s individual medical care
2. The Clinical Pharmacogenetics Consortium (CPIC) guidelines:

A. Provide guidance on using pharmacogenetic test results in practice

B. Recommend whether a test should be ordered

C. Recommend when to order a test

D. Are available for the majority of medications
3. The cost of testing, value of a pharmacogenomics test, and insurance reimbursement for testing have implications for:

A. Which drugs have pharmacogenomic information in the Food and Drug Administration (FDA) labeling

B. Which drugs are regulated by the European Medicines Agency

C. Public policy regarding pharmacogenomic testing

D. Whether a drug is approved by FDA
Part 1:

Genomics/Pharmacogenomics and Public Health:

Does This Even Make Sense?
2015 State of the Union: Precision Medicine Initiative
What is the human genome?

- Human genome is the approximately 3 billion nucleotides (comprised of 4 letters) that make up our genetic code

- Humans are about 99.8-99.9% identical

- The 0.1-0.2% is what makes us unique

National Human Genome Research Institute (www.genome.gov)
Human Genome Project

• Human Genome Project was a large international effort to define the human genetic code
  • Completed in 2001; after 13 years and $2.7 Billion
  • Delivered one “complete” human genome

• Human genome sequencing – 2011
  • Costs $5000 to $20,000; and takes a couple weeks

• Human genome sequencing – 2013
  • Costs < $1000 and can be completed in < 1 day

National Human Genome Research Institute (www.genome.gov)
Human Genome Sequencing and Precision Medicine

• Expected that genetic data will increasingly be available on patients
  • 10 million have done direct to consumer (DTC) genotyping
  • Expected to be 100 million by 2021

• In the future, a person’s genome sequence will likely be part of their medical record
  • By 2025 whole genome sequencing expected in 60 million

• At core of concept is one-time nature of genotyping and as needed availability of genetic information

National Human Genome Research Institute (www.genome.gov)
Precision Medicine

• Use of information about an individual, including their family history, diseases, environmental factors, genetic and other unique information to personalize or individualize care

  • Disease risk prediction and diagnosis

  • Cancer (tumor) genetics

  • Drug therapy (pharmacogenetics)

National Human Genome Research Institute (www.genome.gov)
Pharmacogenomics and Public Health

• What about, “the right treatments at the right time, every time to the right person?”
  • Pharmacogenomics and the individual

• Increasing adoption of “Precision” public health
  • “Populations” are the units of intervention that use innovative technology and scientific discovery to improve outcomes

• The “next generation” of public health
  • Using pharmacogenomics and precision medicine to improve public health policy and practice

What is precision public health?

“... if precision medicine is about the individual, precision public health is about populations. It is essentially about delivering ‘the right intervention at the right time, every time to the right population.’”

Muin J. Khoury,
Director Office of Public Health Genomics, CDC
Impact of Pharmacogenomic Testing on Populations
Impact of Pharmacogenomic Testing on Populations
Part 2

Assessing the Evidence and the Current Landscape
Progress of Genetic/Genomic Testing

Time

Single Nucleotide Polymorphism (SNP) = Single Gene Test

Multi-Gene Panel = Tests multiple genes for a single indication

Next Generation Sequencing (NGS) = Measures multiple genes using high speed DNA sequencing technology

Whole Exome Sequencing = Evaluates entire exome (coding regions of the genome)

Whole Genome Sequencing = Evaluates entire genome

Must be supported by evidence of:
1) Analytic validity
2) Clinical validity
Progress and Types of Genetic/Genomic Testing

Risk assessment, screening, diagnosis, monitoring of progression

Target or manage medication therapy = pharmacogenomics

Germline biomarkers

Somatic biomarkers (derived from tumor tissue)

Preemptive

Reactive

Must be supported by evidence of clinical utility
Genetic Variation: Drug metabolizing enzymes
An Evidence-Based Approach to Pharmacogenomics

• Evaluation of Genomic Applications in Practice and Prevention (EGAPP)
  • Established by Centers for Disease Control (CDC) Office of Public Health Genomics
  • Develop systematic processes for evidence-based assessment of genetic tests and genomic technology

• Clinical Pharmacogenetics Implementation Consortium (CPIC)
  • Provide guidance on using pharmacogenetic test results in practice instead of advising whether or not a test should be ordered

• Dutch Pharmacogenetics Working Group
• Food and Drug Administration drug product labeling

Evidence-based criteria for evaluating tests

- Analytic validity
- Clinical validity
- Clinical utility
- Ethical, legal, and social implications

Clinical Utility

• Likelihood that a test result will alter clinical outcomes or treatment strategies
  • Usefulness, changes in health outcomes
• Third-party payers increasingly rely on evidence of clinical utility for reimbursement for pharmacogenomic tests
• Utility of test varies based on associated drug therapy and indications (e.g., CYP2C19 testing for clopidogrel)
Clinical Utility

• Level of evidence required for a test to achieve clinical utility
  • Gold standard = randomized, controlled trial
  • Limitations in conducting randomized controlled trials in pharmacogenomics
    • Sampling issues
    • Technology limitations (e.g., different testing platforms)
    • Low prevalence of targeted clinical outcome or variant allele
  • Pharmacogenomics studies
    • Focus on incremental advantages in safety and efficacy in targeted patients
    • “Identifying the outliers”
Evidence of Clinical Validity for PGx Biomarkers in FDA Labels
Evidence of Clinical Utility for PGx Biomarkers in FDA Labels
Treatment Recommendations in FDA Drug Labels
Trends in Strength of Evidence in 137 FDA Labels (Germline Biomarkers)
Major European Initiative: Ubiquitous PGx (U-PGx) Consortium
Translating Evidence Into Practice: IGNITE Network Example
Multisite Investigation of Outcomes With Implementation of CYP2C19 Genotype-Guided Antiplatelet Therapy After Percutaneous Coronary Intervention (PCI)
Kaplan-Meier Survival Estimates of MACE in Relation to CYP2C19 Genotype and Antiplatelet Therapy
A Case for Preemptive Genotyping: The Vanderbilt PREDICT Project
A Case for Preemptive Genotyping: Claims Database
Trends in Proportion of Index Medication Orders for which PGx Test Drawn
Part 3:

Estimating the Value of PGx Tests
Brief Primer on Value Assessment in Health Economics

• Cost effectiveness analysis (CEA)
  • Outcome expressed in natural units

• Cost utility analysis (CUA) – type of CEA
  • Outcome expressed in quality adjusted life years (QALYs)

• Model inputs
  • Costs
  • Outcomes (clinical utility of PGx)
    • Efficacy, safety, health-related quality of life
    • Benefit/risk trade off
  • Probabilities

• Calculate incremental cost-effectiveness ratio (ICER)

\[ ICER = \left( \frac{Cost_2 - Cost_1}{Outcome_2 - Outcome_1} \right) \]
Estimating Value for PGx using CEA

- Costs ($C_{pgx}$) – sample collection, analysis; patient/provider education
- Probability ($P_{var}$) – patient will have clinically relevant variant
- Probability ($P_{drug}$) – patient will be exposed to drug affected by variant
- *Incremental clinical benefit ($B_{pgx}$) – improving effectiveness, avoiding harm, per patient tested and receiving drug
  - Probability ($P_O$) patient experiences the outcome
  - Measured in quality-adjusted life years (QALYs)
- *Incremental healthcare costs ($C_{sav}$) – saved or spent by improving effectiveness or avoiding harm, per patient tested and receiving drug

*Complex to estimate

Value Landscape of PGx Screening
Cost-effectiveness of Guideline-dosed warfarin, PGx-Warfarin and Direct Oral Anticoagulants (DOACs)
Risk-Benefit Analysis of Clopidogrel, Prasugrel (PGx) in Acute Coronary Syndrome (ACS)/PCI
Risk-Benefit Analysis of Clopidogrel Prasugrel (PGx) in ACS/PCI
# Quality Adjusted Life Year (QALY) Gains

<table>
<thead>
<tr>
<th>Reference</th>
<th>Average clinical benefit per patient tested and receiving drug (QALYs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schackman BR, et al. The cost-effectiveness of HLA-B*5701 genetic screening to guide initial antiretroviral therapy for HIV. <em>AIDS</em> 2008;22:2025-2033 (PMID 18784465)</td>
<td>0.003</td>
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**Veenstra DL.** *The value of routine pharmacogenomic screening—Are we there yet? A perspective on the costs and benefits of routine screening—shouldn’t everyone have this done?* *Clin Pharmacol Ther.* 2016;99:164-6.
Value: Cost-Utility Analysis of Multi-, Single, No PGx Testing for ACS/PCI Patient
## Cost-Utility Analysis of Multi-, Single, No PGx Testing for ACS/PCI Patient

<table>
<thead>
<tr>
<th></th>
<th>Mean Cost</th>
<th>Incremental Cost</th>
<th>QALY</th>
<th>Incremental QALY</th>
<th>ICER (cost/QALY)</th>
<th>Net Monetary Benefit*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Multi PGx Test</strong></td>
<td>$13,275</td>
<td></td>
<td>0.97</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Single PGx Test</strong></td>
<td>$14,921</td>
<td>-$1,646</td>
<td>0.93</td>
<td>0.04</td>
<td>Dominated by MPGx</td>
<td></td>
</tr>
<tr>
<td><strong>No PGx Test</strong></td>
<td>$24,643</td>
<td>-$11,368</td>
<td>0.80</td>
<td>0.17</td>
<td>Dominated by MPGx</td>
<td></td>
</tr>
</tbody>
</table>

*Net monetary benefit (NMB) based on $100,000 willingness-to-pay (WTP) per QALY

MPGx = Multigene panel
SPGx = Single gene panel
QALY = quality-adjusted life year
ICER = incremental cost-effectiveness ratio

Cost-Utility Analysis of Multi-, Single, No PGx Testing for ACS/PCI Patient
Cost-Utility Analysis of Multi-, Single, No PGx Testing for ACS/PCI Patient
Value: Modeling Costs of Clinical Decision Support (CDS) for PGx

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low</th>
<th>Current</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial cost for single rule</td>
<td>$4000</td>
<td>$6600</td>
<td>$7500</td>
</tr>
<tr>
<td>Maintenance rate (proportion of initial cost)</td>
<td>10%</td>
<td>20%</td>
<td>25%</td>
</tr>
<tr>
<td>Patients with testing per institution</td>
<td>200</td>
<td>500</td>
<td>41250</td>
</tr>
<tr>
<td>Number of rules</td>
<td>3</td>
<td>9</td>
<td>300</td>
</tr>
<tr>
<td>Probability rule fires for patient</td>
<td>0.25%</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Efficiency for additional rules</td>
<td>70%</td>
<td>80%</td>
<td>85%</td>
</tr>
<tr>
<td>Number of institutions</td>
<td>2</td>
<td>10</td>
<td>500</td>
</tr>
<tr>
<td>Efficiency for additional institutions</td>
<td>70%</td>
<td>99%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Modeling Costs of Clinical Decision Support (CDS) for PGx
Part 4:

Policy Implications of Pharmacogenomics
Next Generation Sequencing (NGS)

- **Single Nucleotide Polymorphism (SNP) = Single Gene Test**
- **Multi-Gene Panel** = Tests multiple genes for a single indication
- **Next Generation Sequencing (NGS)** = Measures multiple genes using high speed DNA sequencing technology
- **Whole Exome Sequencing** = Evaluates entire exome (coding regions of the genome)
- **Whole Genome Sequencing** = Evaluates entire genome

*Must be supported by evidence of:*
1) Analytic validity
2) Clinical validity
CMS Covering Next Generation Tumor Sequencing (NGTS)
Practical Resources for Reimbursement
Horizon Scan of Clinical Laboratories offering PGx Testing
RCT of PGx-CDS in Home Health Patients
Steps to Implement Preemptive PGx
Steps to Translate PGx Result into Clinically Useful Action
The Genomics Enabled Learning Healthcare System
Part 5:

Pharmacist Reimbursement – Emerging Practice Models and Trend
Building Momentum for Emerging Practice Models

- Non-academic, community based health systems
- Physician- or pharmacist-led outpatient clinics
- Community pharmacies
- As a component of Medication Therapy Management or other established pharmacy services
Visit 2

- Patient leaves with clinical summary report
- All documentation is added to EHR and forwarded to previously selected clinicians
- Pharmacist or medical genetist discloses genomic results and how they may affect current and future drug therapy based on discussions with relevant clinicians and published literature
- Genetic counselor or nurse practitioner obtains updated medication list and other pertinent data

Duke University: Pharmacist-Led Medication Therapy Management (MTM) Services in Outpatient Cardiology Clinic

MTM Visit 1
- Complete medication history
- Review of pharmacogenetic testing with patient
- Collect blood sample

Between Visits
- Pharmacist reviews results
- Discuss recommendations with cardiologist

MTM Visit 2
- Review pharmacogenetic test results with patient
- Discuss recommended treatment changes based on results

Cleveland Clinic: Provider-Requested Pharmacogenomics Consultation Service

- Electronic Health Record (EHR)-driven Pharmacogenomics Consult Service
- Ambulatory Pharmacogenomics Clinic
  - Provider referral to clinic
  - Patient has 1-hour visit with pharmacist/physician-geneticist
  - Consult note/recommendation into EHR
  - Physician-geneticist bills for visit according to appropriate CPT/billing code

University of Florida (UF) Health Pharmacogenetics Consult Clinic

Clinic Visit 1
- Patient education
- Medication history
- Sample collection

UF Pathology
- Analyzes sample
- Uploads results to EHR

Interpretation
- Interpretation note written by PGx pharmacist placed in patient chart
- Discussion with physician

Clinic Visit 2
- Patient report handout
- Patient education
- Medication changes

Community-Pharmacy Based Models

**Pre-Implementation:** Collaborative Practice Agreement established with community physician to authorize PGx test order from pharmacy

**Patient Identification:** At point of dispensing history

**Pharmacist Visit 1:** Medication history and buccal swab for commercial lab PGx testing

**Between Visits:** Pharmacist receives result; recommendations communicated to physician by fax or telephone; response communicated to pharmacist

**Pharmacist Visit 2:** Pharmacist reviews recommendations and drug therapy changes; Visits billed using pharmacy-specific MTM codes

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Trends/Characteristics of Emerging Practice Models

- May be driven by single pharmacist or group
- Partner with commercial laboratories
  - Perform pharmacogenetic testing
  - Coordinate prior authorization for testing
  - Provide upfront, out-of-pocket price to patient based on sliding scale
- Focused on outpatient, clinic-based setting
- Incorporate reimbursement for pharmacist time/service
- May not focus on single gene-drug pairs
- May expand recommendations beyond CPIC guidelines
- May utilize external software/services for interpreting and applying test results to patient care
Explore Ways to Incorporate PGx into Established Models of Pharmacist Care

• Potential Practice Models
  • Collaborative practice agreements
  • Standing order or protocol-based
  • Medication Therapy Management
  • Value-Based Care (e.g., pharmacist supports practice’s ability to meet quality or other measures that affect provider reimbursement)
  • Self-funded mechanisms (e.g., executive health or self-insured programs)
  • Fee-for-service
Explore Ways to Incorporate PGx into Established Models of Pharmacist Care

• Potential Factors Influencing Pharmacist Compensation
  • Individual State Rules or Regulations
    • Pharmacist scope of practice
    • Collaborative drug therapy agreements
    • Pharmacist provider status
  • Individual Practice Setting
    • Physician office
    • Clinical service integrated into health system infrastructure
    • Community pharmacy
  • Patient population
    • Outpatient vs. inpatient
    • Medicare vs. other payers
    • Disease states and medication use
Opportunities for Pharmacists: Provider Status
Example: Annual Wellness Visit (AWV) and Comprehensive Medication Management (CMM)

• Mountain Area Health Education Center/University of North Carolina at Chapel Hill
• Pharmacist-provided AWV (including all Medicare-required components) and CMM with additional CMM visits at 3 and 6 months
• Return on Investment (ROI) analysis demonstrated positive net gain of $2,644 and an ROI of 38.1%

Conclusions

• Major initiatives are underway
• Although uptake of PGx into clinical practice has been slow, momentum is building for newer practice models
• We are making progress - multigene panels, NGS are here to stay

• Policy Initiatives to facilitate adoption:
  • Improve the evidence base
  • Address uncertainty
  • Facilitate implementation
  • Continue to estimate value

Assessment Questions

1. In the future, it is likely that genetic information will be:

   A. Decreasingly available to individual patients

   B. Increasingly used to guide population health decisions

   C. Increasingly restricted by patients’ primary care providers

   D. Decreasingly used to guide a patient’s individual medical care

**Objective 1:** Describe the basics of pharmacogenomics and pharmacogenomic testing
Assessment Questions

2. The Clinical Pharmacogenetics Consortium (CPIC) guidelines:

   A. Provide guidance on using pharmacogenetic test results in practice
   
   B. Recommend whether a test should be ordered
   
   C. Recommend when to order a test

   D. Are available for the majority of medications

Objective 2: Recognize the impact of genetic testing on therapy plan development
Assessment Questions

3. The cost of testing, value of a pharmacogenomics test, and insurance reimbursement for testing have implications for:

A. Which drugs have pharmacogenomic information in the FDA labeling

B. Which drugs are regulated by the European Medicines Agency

C. Public policy regarding pharmacogenomic testing

D. Whether a drug is approved by FDA

*Objective 3: *Discuss the economic impact of pharmacogenomic testing and future implications for policy development.
Thank You!

Questions?