Genomics and Patient Safety: Practical Applications for Pharmacogenomics

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“All I’m saying is _now_ is the time to develop the technology to deflect an asteroid.”
Overview

• Evaluate opportunities to evolve CME delivery amidst genomic advances and ongoing health care transformation

• Describe regional and national KP efforts to implement genomic medicine that optimizes patient safety and provider satisfaction

• Produce actionable takeaways based on these experiences thus far...
IOM Genomics Roundtable

• Recent workshop in August, 2014
• “Improving Genetics Education in Graduate and Continuing Health Professional Education: Workshop Summary"

- Challenges in reaching providers
- Just-in-time education
- Innovative education models
- Building evidence to reduce mistakes
- How to be ‘interprofessional’
Takeaways: How to Evolve

• More effective means – such as just-in-time learning – are available and increasingly relevant

• CME should be more interprofessional

• Should leverage existing initiatives (i.e., PROCEED, MedEdPortal)

• David Davis, Senior Director, Continuing Education and Performance Improvement, AAMC
Takeaways: Just-in-time Approach

• Benjamin Raby, Section Editor – Genetics, UpToDate
• Associate Professor of Medicine
• Channing Division of Network Medicine and the Division of Pulmonary and Critical Care Medicine,
• Director, Brigham and Women’s Hospital Pulmonary Genetics Center Harvard Medical School

• Critical need to incorporate disease-specific genetic information rapidly
• UpToDate makes educational information accessible through electronic medical records
• Biggest challenge is the ‘lag’ between reports of translational findings and integration into practice
Takeaways: IPE

• Diane C. Seibert, Professor, Chair & Director, Family Nurse Practitioner Program

• Uniformed Services University

• The concept of IPE is to learn about what another profession does, with other professionals in the same environment, and taught from different professions

• IPE is useful because health care systems are so complex that different perspectives are needed to get the best outcomes
Medical Practice Realities

Most physicians deliver only 55% of recommended care

▪ 42% report not enough time with their patients

Pharmacist protocols for approval of medication refills free up physician time

Providers spend 13% of their day on care coordination

▪ Only half of their time on activities using their medical knowledge.

▪ MTM telepharmacy services during transitions of care improve physician efficiency
Time demands on primary care physicians...

2500 Patients

Chronic Care Management (6.7 hrs/day)
Level A & B Recommended Preventive Care Services (7.4 hrs/day)
Acute Care (4.6 hrs/day)

18.7 hours per day

Cutting panel size to 1250 = 9.35 hours per day

And that doesn’t count phone call, charting, and other paperwork or other administrative tasks.

KP National Program – By the numbers...

- 7 regions serving 8 states and the District of Columbia
- Over 9 million members
- 174,000 employees
- Over 16,000 physicians
- Over 48,000 nurses
- 38 hospitals
- 611 medical offices and other facilities
- $50 billion operating revenue (2012)
A little history on the KP’s Genetic Strategy

Genetics Services Vision Statement

Kaiser Permanente provides clinical genetic and testing services to guide personalized evidence-based care decisions and care delivery. Our team-based approach enlists clinical expertise, information technology and cross regional collaboration to support high quality, reliable and efficient human genetic testing.

3 Strategic Pillars to Realize the Vision

Evidence-based Quality Care
Establish the highest standard of care and strive for continuous improvement

Collaboration and Affordability
Ensure that high quality, affordable care is consistent across regions

IT and Enabling Infrastructure
Create IT solutions and infrastructure that support high quality, affordable care
### Why are we here?

**We need a team based approach to genetic testing and selection in Oncology**

<table>
<thead>
<tr>
<th>Themes</th>
<th>Oncologists</th>
<th>Geneticists</th>
<th>Laboratory</th>
<th>Pharmacy</th>
</tr>
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<tbody>
<tr>
<td>Multiple areas of specialization</td>
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<td>Some help</td>
<td>The FDA continues to pair genetic tests with cancer treatments</td>
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<tr>
<td>Hundreds of clinical trials</td>
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<td>Laboratory panels and tests changing rapidly</td>
<td>Need pathology and molecular testing experts to help us select the right tests and panels</td>
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**David Baer, MD** – “We (oncologists, lab directors, geneticists, pathologists, pharmacists) have to all stop saying it’s not our job and start working collaboratively to figure this stuff out.”
Interregional Genetic Testing Resource Plan

Focus on expanding the value to Oncologists

- Pharmacogenomics
- Oncology
- Regular updates

- Intuitive to use
- Establish access
- Incorporate its use

- Improve decision making
- Speed the application of new evidence for patients
- Improve the consistency of care
Oncologists may want to see only cancer related tests and all test lists have the capability to search for a specific test of interest.
The KP Research Bank will have samples from 500k members

**General Cohort** [410,000]

Enables research of relevance to all KP members across a broad spectrum of common diseases and builds on existing 200,000 samples

**Pregnancy Cohort** [60,000]

Will be among the largest and richest pregnancy research cohorts in the world

**Cancer Cohort** [30,000]

Linked to tissue banks; Oncology is an early adopter of genomic medicine; over half of KP researchers focus on cancer

KP Biobank [500,000]

Goal: 500K

Enrolled & Sampled
KP National Program – Building Connections

Goals for 2015

• Draft a “roadmap” of resources and champions in each KP region for pharmacogenomics

• Provide content expertise to help guide implementation and research
Kaiser Permanente Colorado

• Colorado's largest nonprofit health plan
• 28 Medical Offices
  • 6,000+ staff and physicians
  • 635,000 members
• Recognized by the National Committee for Quality Assurance (NCQA) as the top-ranked private health plan in Colorado and No. 13 in the entire nation for 2013-2014
• 22 KPCO clinics and more than 300 individual physicians have earned the top-level Patient-Centered Medical Home designation from the National Committee for Quality Assurance (NCQA)
Precision Medicine

• Includes applied Pharmacogenomics (PGx)
• Part of a systematic approach to optimizing pharmacotherapy
• Recent comments by President Obama during SOTU address augment current translational efforts
KPCO Regional Goals

Promulgate use of evidence-based technology to optimize patient safety:

1. Prevent avoidable adverse drug reactions
2. Promote and increase medication adherence
3. Provide targeted educational information to front-line clinical providers about impact of pharmacogenomics
KPCO Implementation Roadmap

- 2011
  - Became National KP Co-Lead for PGx
- 2012
  - Implemented targeted CYP2C19 genotyping for clopidogrel
- 2013
- 2014
  - Developed proposal for embedded just-in-time education for front-line clinicians re: CYP2C19-clopidogrel interaction
KPCO Implementation Roadmap

- Expanding Clinical Testing with PGx Panel (6 genes, pre-emptive screening) to identify impact on healthcare related utilization and provider satisfaction
- Developing proposal for front-line provider education to increase engagement and collaboration
Interim Data Summary for KPCO

• 219 patients approached for CYP2C19 genotyping (post-ACS, stent implantation)
• 149 patients completed testing
• 77 (~52%) of patients had an actionable genotype (e.g. carried at least one gain-of-function or loss-of-function allele)
• Clinical Pharmacy recommendations accepted 100% of the time.
Interim Data Summary for KPCO

- 37 patients diagnosed with inherited Long QT Syndrome (LQTS)
- 13 (~35%) of patients had an active Rx for a drug with known QT-prolongation effects
- Comprehensive medication reviews for all patients, with consult/recommendations forwarded to all downstream providers
- Problem list updated for all patients
Examples of Outside Resources

Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C9 and VKORC1 Genotypes and Warfarin Dosing

JA Johnson¹, L Gong², M Whirl-Carrillo³, BF Gage³, SA Scott⁴, CM Stein⁵, JL Anderson⁶, SE Kimmel⁷,⁸,⁹, MTM Lee¹⁰, M Pirmohamed¹¹, M Wadelius¹², TE Klein¹³ and RB Altman¹²,¹³

Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Codeine Therapy in the Context of Cytochrome P450 2D6 (CYP2D6) Genotype

KR Crews¹, A Gaedigk², HM Dunnenberger³, TE Klein⁴, DD Shen⁵,⁶, JT Callaghan⁷,⁸, ED Kharasch⁹ and TC Skaar⁷

Clinical Pharmacogenetics Implementation Consortium Guidelines for Cytochrome P450-2C19 (CYP2C19) Genotype and Clopidogrel Therapy

SA Scott¹, K Sangkuhl², EE Gardner³, CM Stein⁴,⁵, J-S Hulot⁶,⁷, JA Johnson⁸,⁹,¹⁰, DM Roden¹¹,¹², TE Klein² and AR Shuldiner¹³,¹⁴

The Clinical Pharmacogenomics Implementation Consortium: CPIC Guideline for SLCO1B1 and Simvastatin-Induced Myopathy

RA Wilke¹,², LB Ramsey¹, SG Johnson¹,², WD Maxwell⁶, HI McLeod⁷, D Voora⁵, RM Krauss⁹, DM Roden¹,², Q Feng¹,², RM Cooper-DeHoff⁷,⁹, L Gong¹¹, TE Klein¹¹,¹², M Wadelius¹³ and M Niemi¹⁴

CPIC Informatics: Supporting Guideline Implementation

Overall, a tremendous opportunity to align/meld just-in-time education for front-line clinicians

Johnson SG. KP Colorado CYP2C19 Algorithm

CYP2C19 Genotyping

Ultra-rapid and Extensive Metabolizer
*1/*1
*1/*17
*17/*17

Intermediate Metabolizer
*1/*2

Poor Metabolizer
*2/*2

Normal or increased antiplatelet effect

ACS
(Strong)

IS
(Weak)

Reduced antiplatelet effect; increased risk for adverse cardiac outcomes

ACS
(Moderate)

IS
(Weak)

Significantly reduced antiplatelet effect; increased risk for adverse cardiac outcomes

IS
(Weak)

Dipyridamole AND ASA

Prasugrel OR Ticagrelor

Dipyridamole AND ASA

ACS, IS: Acute Coronary Syndrome, Ischemic Stroke

Johnson SG. KP Colorado CYP2C19 Algorithm
Clinical Pharmacogenetics Implementation: Approaches, Successes, and Challenges


Current challenges exist to widespread clinical implementation of genomic medicine at the University of Florida (UF), including lack of evidence, cost-effectiveness, patient acceptance, and regulatory approval. Herein we describe the processes for development of the program, the challenges faced, and the clinical acceptance by clinicians of the genomic medicine implementation. The UF Pharmacogeneomic Medicine Program (UF-PMP) implemented in 2011 at the UF Clinical Translational Science Institute. The UF-PMP was established to catalyse the translation of genomics into practice by providing clinicians with access to actionable genotypes, drug therapy changes implemented in 56 individuals, average turnaround time from blood draw to genotype result entry in the medical record was 3.5 business days. Seven different third party payors, including Medicare, reimbursed for the test during the first month of billing, with an 85% reimbursement rate for outpatient claims that were submitted in the first month. These data highlight multiple levels of success in clinical implementation of genomic medicine. © 2014 Wiley Periodicals, Inc.

KEY WORDS: pharmacogenetics, genomic medicine, implementation; CYP2C19, personalized medicine
All clinical genotype results are posted in EMR
Clinical Pharmacogenomics Consult Entered into EMR

<table>
<thead>
<tr>
<th>PKN Tests</th>
<th>TPMT Genotype Clinical Consult</th>
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<tbody>
<tr>
<td>Thiopurine S Methyl Genotype Result: *1/*3A</td>
<td>f Abnormal</td>
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</tbody>
</table>

***PHARMACOKINETICS CONSULT FOR***

*TPMT GENOTYPE*

Sample for TPMT genotype obtained 06/11/12.
Thiopurine S Methyl Transferase Genotype Result: *1/*3A.

This result means the genotype is heterozygous. Heterozygous means intermediately low TPMT activity. This patient may be at risk for toxicity with 6-mercaptopurine and should receive no more than 60 mg/m²/day of 6-mercaptopurine pending further evaluation by a clinical pharmacist and attending Hematology/Oncology physician. If myelosuppression occurs, this result suggests that the 6-mercaptopurine dose be titrated based on WBC and ANC. Every effort should be made to keep other anticancer agent doses at protocol levels.

Time/date of Consult: 06/15/2012 15:18    Jane Smith, Pharm.D.

Management Discipline View

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<th>Annotated Display</th>
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<td>06/04/2010</td>
<td>HIM Summary</td>
<td>Active</td>
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<td>TPMT - Thiopurine methyltransferase deficiency</td>
<td>06/11/2010</td>
<td>Medical</td>
<td>Active</td>
</tr>
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</table>

Courtesy of Clinical Pharmacogenetics Service at St. Jude Pediatric Research Hospital
Clinical Decision Support an Integral Component

If a clinician selects a medication that is linked to the pharmacogenomic alert, a Warning Box will appear with a brief description of the potential problem. The clinician is then directed to select an appropriate action before proceeding.

Courtesy of Clinical Pharmacogenetics Service at St. Jude Pediatric Research Hospital
Emerging Roles for Pharmacists in Clinical Implementation of Pharmacogenomics

Aniwa Owusu-Obeng,1,2,3,7 Kristin W. Weitzel,4,5,6,8,9 Randy C. Hatton,7 Benjamin J. Staley,7 Jennifer Ashton,7 Rhonda M. Cooper-Dehoff,4,5,8,9 and Julie A. Johnson,4,5,6,8,9

1The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, New York; Pharmacy Department, Mount Sinai Hospital, New York, New York; Division of General Internal Medicine, Icahn School of Medicine at Mount Sinai, New York, New York; UF Health Personalized Medicine Program, Gainesville, Florida; 7Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville, Florida; 8Clinical & Translational Science Institute, University of Florida, Gainesville, Florida; 7Pharmacy Department, UF Health Shands Hospital, Gainesville, Florida; 8Department of Medicine, University of Florida, Gainesville, Florida

Pharmacists are uniquely qualified to play essential roles in the clinical implementation of pharmacogenomics. However, specific responsibilities and resources needed for these roles have not been defined. We describe roles for pharmacists that emerged in the clinical implementation of genotype-guided clopidogrel therapy in the University of Florida Health Personalized Medicine Program, summarize
Pharmacist Competency Map
Genetics and Genomics Competency Center. Available at: http://g-2-c-2.org/competency/pharmacist

B: BASIC GENETIC CONCEPTS

- B1: To demonstrate an understanding of the basic genetic/genomic concepts and nomenclature
- B2: To recognize and appreciate the role of behavioral, social, and environmental factors (lifestyle, socioeconomic factors, pollutants, etc.) to modify or influence genetics in the manifestation of disease
- B3: To identify drug and disease associated genetic variations that facilitate development of prevention, diagnostic and treatment strategies and appreciate there are differences in testing methodologies and are aware of the need to explore these differences in drug literature evaluation
- B4: To use family history (minimum of three generations) in assessing predisposition to disease and selection of drug treatment

G: GENETICS AND DISEASE

- G1: To understand the role of genetic factors in maintaining health and preventing disease
- G2: To assess the difference between clinical diagnosis of disease and identification of genetic predisposition to disease (genetic variation is not strictly correlated with disease manifestation)
- G3: To appreciate that pharmacogenomic testing may also reveal certain genetic disease predispositions (e.g., the Apo E4 polymorphism)

P: PHARMACOGENETICS/PHARMACOGENOMICS

- P1: To demonstrate an understanding of how genetic variation in a large number of proteins, including drug transporters, drug metabolizing enzymes, direct protein targets of drugs, and other proteins (e.g., signal transduction proteins) influence pharmacokinetics and pharmacodynamics related to pharmacologic effect and drug response
- P2: To understand the influence (or lack thereof) of ethnicity in genetic polymorphisms and associations of polymorphisms with drug response
- P3: Recognize the availability of evidence based guidelines that synthesize information relevant to genomic/pharmacogenomic tests and selection of drug therapy (e.g., Clinical Pharmacogenomics Implementation Consortium)

E: ETHICAL, LEGAL AND SOCIAL IMPLICATIONS (ELSI)

- E1: To understand the potential physical and/or psychosocial benefits, limitations and risk of genomic/pharmacogenomic information for individuals, family members and communities, especially with genomic/pharmacogenomic tests that may relate to predisposition to disease
- E2: To understand the increased liability that accompanies access to detailed genomic patient information and maintain confidentiality and security
- E3: To adopt a culturally sensitive and ethical approach to patient counseling regarding genomic/pharmacogenomic test results
- E4: To appreciate the cost, cost-effectiveness, and reimbursement by insurers relevant to genomic or pharmacogenomic tests and test interpretation, for patients and populations
- E5: To identify the need to refer a patient to a genetic specialist or genetic counselor