Pharmacogenomics in Practice and Training: Opportunities and Challenges

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Inaugural ACCP-AACP Institute of Medicine Anniversary Fellow in Pharmacy, 2012-2014
Learning Objectives

• Describe clinical implementation efforts across different settings (e.g., integrated health system, behavioral health clinic, and within pharmacy student curricula)

• Analyze potential benefits -- and possible detriments -- for clinical pharmacogenomic testing

• Recognize and resolve potential barriers to clinical implementation in different settings
Precision Medicine

• Applied Pharmacogenomics (PGx)

• The “Holy Grail” the Pharmacy Profession must own

• Integrating Genomic Medicine Into Pharmacy Practice
ASHP Pharmacy Forecast 2014-2018

• Need for PGx expertise growing

• New ASHP Policy Statement on Pharmacists’ role in PGx

“There will be at least one pharmacist in at least 25% of hospitals who is charged with becoming a departmental expert on applying pharmacogenomics knowledge in patient care.”

42% of Pharmacy Practice Leaders Agree

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 earned the top-level Patient-Centered Medical Home designation from the National Committee for Quality Assurance (NCQA)
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)
KPCO Implementation Roadmap

- 2010
  - CPS position approved
- 2011
  - MD collaborator identified
  - CPS PharmD hired (July)
- 2012
- 2013

- Baseline assessment of genetic testing utilization
KPCO Implementation Roadmap

- Attached to IOM Genomics Roundtable
- Landscape survey of PGx implementation at other institutions (St. Jude’s, Geisinger, etc.)
- Granted IRB approval for pilot study (May)
KPCO Implementation Roadmap

- 2011
  - Became National KP Co-Lead for PGx
- 2012
  - Implemented targeted \( CYP2C19 \) genotyping for clopidogrel
- 2013
  - First IPPE and APPE offering focused on PGx
- 2014
KPCO Implementation Roadmap

2012 - 2013 - 2014 - 2015

• National Lead for Pharmacogenomics Sub-Committee
• Initiating Clinical Testing with PGx Panel
• First APPE student rotations
Examples of Outside Resources

Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C9 and VKORC1 Genotypes and Warfarin Dosing
JA Johnson¹, L Gong³, M Whirl-Carrillo², BF Gage³, SA Scott¹, CM Stein⁵, JL Anderson⁶, SE Kimmel⁷,¶,§,¶, MTM Lee⁹, M Pirmohamed¹¹, M Wadelius¹², TE Klein² and RB Altman²,†,∥

Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Codeine Therapy in the Context of Cytochrome P450 2D6 (CYP2D6) Genotype
KR Crews¹, A Gaedigk², HM Dunnenberger¹, TE Klein⁴, DD Shen⁵,¶, JT Callaghan⁷,¶, 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,¶, J-S Hulot⁶,¶, JA Johnson⁷,¶,§,¶,¶, 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 Ramsey³, SG Johnson⁴,¶, WD Maxwell⁶, HL McLeod⁷, D Voora⁸, RM Krauss⁹, DM Roden¹¹,², Q Feng¹,², RM Cooper-DeHoff¹⁰, L Gong¹¹, TE Klein¹¹,¹², M Wadelius¹³ and M Niemi¹⁴

CYP2C19 Genotyping

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

  Normal or increased antiplatelet effect

  - ACS (Strong)
  - IS\(^{\text{a}}\) (Weak)

    - Clopidogrel

- Intermediate Metabolizer
  *1/*2

  Reduced antiplatelet effect; increased risk for adverse cardiac outcomes

  - ACS (Moderate)
  - IS\(^{\text{a}}\) (Weak)

- Poor Metabolizer
  *2/*2

  Significantly reduced antiplatelet effect; increased risk for adverse cardiac outcomes

  - ACS (Strong)
  - IS\(^{\text{a}}\) (Weak)

    - Prasugrel OR Ticagrelor\(^{\text{b}}\)
    - Dipyridamole AND ASA

Johnson SG. KP Colorado CYP2C19 Algorithm
Pharmacist Competency Map
Genetics and Genomics Competency Center. Available at: http://g-2-c-2.org/competency/pharmacist

**E: 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 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: PHARMACOCINETICS/PHARMACODYNAMICS**

- **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)

**F: 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
Emerging Roles for Pharmacists in Clinical Implementation of Pharmacogenomics

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

1The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, New York; 2Pharmacy Department, The Mount Sinai Hospital, New York, New York; 3Division of General Internal Medicine, Icahn School of Medicine at Mount Sinai, New York, New York; 4UF Health Personalized Medicine Program, Gainesville, Florida; 5Department of Pharmacotherapy and Translational Research, Center for Pharmacogenomics, College of Pharmacy, University of Florida, Gainesville, Florida; 6Clinical & 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
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.
All clinical genotype results are posted in EMR

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Cerner Millenium v2010.02. Powerchart application

Courtesy of Clinical Pharmacogenetics Service at St. Jude Pediatric Research Hospital
Discussion Questions

• Where does pharmacogenomics fit within pharmacy practice? Is it a stand-alone specialty? Integrated with comprehensive medication management?

• What are some of the challenges and barriers to clinical implementation in your practice setting?

• How should we be training the future pharmacist workforce to use pharmacogenomics in clinical practice?