Advancing Clinical Implementation of Pharmacogenetics: Progress, Needs, and Opportunities

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Disclosure

• I declare no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

• The University of Florida College of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.
Objectives

• Summarize current national landscape and trends for clinical pharmacogenetics implementation in various practice settings.
• Compare approaches to genetic testing and patient care that may be used in clinical implementation.
• List steps for developing a new clinical pharmacogenetics patient care service.
• Identify factors that influence the successful development of clinical pharmacogenetics services.
Making Progress...
Making Progress...

Pharmacogenomics Implementation Publications
Pharmacogenetics-based therapeutic recommendations — ready for clinical practice?

Julia Kirchheiner, Uwe Fuchs

Abstract: Although considerable progress has been made in basic pharmacogenetic research, less has been done to assess the potential of pharmacogenetics for clinical use.

Pharmacogenetics of antipsychotic therapy: pivotal research issues and the prospects for clinical implementation

Bernard Lerer, MD; Ronald H. Sumner, MD

Putting pharmacogenetics into practice

Michael M Hopkins1, Dolores Ibarreta2, Sibylle Gaisser3, Christien M Enzing4, Jim Ryan5, Paul A Martin6, Graham Lewis7, Symonet Detmar4, M Elske van den Akker-van Marle4, Adam M Hedgewcoe8, Paul Nightingale3, Marielle Dreiling9, K Juliane Hartig9, Wieneke Vuillings1 & Tony Forde2

Genetics is slowly explaining variations in drug response, but applying this knowledge depends on implementation of a host of policies that provide long-term support to the field, from translational research and regulation to professional education.
Prospects for clinical implementation?

Pivotal research Issues?

Ready for clinical practice?

Can we put it into practice?
Implementation of Pharmacogenetics: The University of Maryland Personalized Anti-Platelet Pharmacogenomics Program


Implementation of a multidisciplinary pharmacogenomics clinic in a community health system

Henry M. Dunnberger, Pharm.D., Cancer for Molecular Medicine, Northwestern University Health System, Evanston, IL

Paw Bialkowski, Pharm.D., Medical and Anticoagulation Unit, Northwestern University Health System, Evanston, IL

T. C. Salt, Pharm.D., Pharmacogenetics

Purpose. The development and implementation of a multidisciplinary pharmacogenomics clinic within the framework of an established community-based medical genetics program is described.

Summary. Pharmacogenomics is an important component of precision medicine that holds considerable promise for pharmacotherapy optimization. As part of the development of a health system-wide, integrated...
What is your current practice setting?

- A. Health-system pharmacy
- B. Ambulatory/Primary Care Clinic
- C. Community Pharmacy
- D. Industry
- E. Other
Testing Ground: Interdisciplinary Programs in Academic Health Systems
UF Health Personalized Medicine Program -
Launched June 25, 2012

UF delivers promise of personalized medicine to heart patients

Personalized medicine — a concept in which an understanding of a patient’s genetic makeup is used to enhance treatment — has arrived at UF&Shands, the University of Florida Academic Health […]
UF Health Personalized Medicine Program

Center for Pharmacogenomics

CTSI

Department of Pharmacotherapy and Translational Research

PMP Committee

UF Health PERSONALIZED MEDICINE PROGRAM

UF Pathology Laboratory

Shands Clinical Pharmacy Support

IT / Informatics Team

Optimize Patient Care
Implementation Resources

• Stakeholders
  — Administrators
  — Leadership
  — Clinics and/or clinical services
  — Providers
  — Patients

• Evidence for clinical implementation
  — Process for evidence analysis
  — Oversight body to guide clinical decision making
  — Generate relevant clinical and/or quality improvement data

Implementation Resources

- Personnel
  - Program/service leader
  - Physician champion
  - Frontline clinicians involved in patient care
  - Laboratory specialists
  - Informaticians
  - Educators
  - Patients

Implementation Resources

• Information Technology
  – EHR and clinical decision support
  – Support rapid and accurate communication among implementation team
  – Ensure sharing of timely, easily accessible, and accurate PGx information across a patient’s lifetime and diverse practice settings

• Laboratory Support
  – CAP-CLIA Laboratory with genotyping platform
  – Provide lab test development and validation services
  – Integrate genotype results into the patient care process and electronic health record

Implementation Processes

Program Resources → Develop service workflow and educate all stakeholders → Approval from administration

Optimize the workflow

Program Expansion → Monitor and collect KPI and outcomes data

Launch the service

Develop lab test → Select platform → Validation/verification → Decide upon reporting mechanism for results → Test CDS

Develop CDS → Design alerts → Design algorithm

Education to providers on available PGx testing

Clinical Implementations at UF Health Shands Hospital

# Pharmacogenetic Testing at UF Health

<table>
<thead>
<tr>
<th>Test</th>
<th>Drug</th>
<th>Number of tests</th>
<th>Ordering Service</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2C19</td>
<td>Clopidogrel</td>
<td>1694</td>
<td>Cardiology, UF Health Shands</td>
</tr>
<tr>
<td></td>
<td></td>
<td>634</td>
<td>Cardiology, UF Health Jacksonville</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13</td>
<td>Neurology, Neurosurgery</td>
</tr>
<tr>
<td>TPMT</td>
<td>Thiopurines</td>
<td>43</td>
<td>Hematology/Oncology</td>
</tr>
<tr>
<td></td>
<td></td>
<td>67</td>
<td>Gastroenterology</td>
</tr>
<tr>
<td></td>
<td></td>
<td>42</td>
<td>Other*</td>
</tr>
<tr>
<td>IFNL3</td>
<td>PEG-interferon-α based regimens</td>
<td>96</td>
<td>Gastroenterology</td>
</tr>
<tr>
<td>CYP2D6</td>
<td>Opioids</td>
<td>202</td>
<td>Family Medicine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>33</td>
<td>Internal Medicine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>34</td>
<td>Chronic Pain Clinic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>Adult Oncology</td>
</tr>
<tr>
<td>CYP2D6</td>
<td>SSRIs</td>
<td>12</td>
<td>Psychiatry</td>
</tr>
<tr>
<td>CYP2C19</td>
<td>SSRIs</td>
<td>13</td>
<td>Psychiatry</td>
</tr>
<tr>
<td>CYP2C19</td>
<td>PPIs</td>
<td>40</td>
<td>Gastroenterology</td>
</tr>
</tbody>
</table>

*Dermatology, Rheumatology, Neurology, Internal Medicine, Family Medicine, Surgery

Increasing Collaboration Among Implementing Institutions Supports Further Progress
Increasing Collaboration Among Implementing Institutions Supports Further Progress

Kaplan-Meier Survival Curve

Adjusted Hazard Ratio
LOF-Clopidogrel vs LOF-Alternative: 2.21 (1.13-4.33) p=0.021
LOF-Alternative vs non-LOF: 0.81 (0.48-1.35) p=0.41

Log-rank p=0.016
Log-rank p=0.15

NO. at risk
LOF_CLOP 226 112 89 76 63 39 3
NON-LOF 1243 759 636 677 451 293 28
LOF_ALT 346 245 221 195 161 112 9

LOF = Loss of function

Are you currently providing pharmacogenetic testing to patients in your practice setting?

• No, not at all
• Not yet, but we are planning to in the near future
• We are considering it
• Yes, we are already implementing testing
Emerging Models for Clinical Implementation
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
Northshore University Health System: Multidisciplinary Pharmacogenomics Clinic

Visit 1

- Genetic counselor or nurse practitioner obtains medication history and other pertinent data using specially designed guide
- Medical geneticist or pharmacist discusses benefits, limitations, and risks of pharmacogenomic testing with patient

Patient decides whether to have pharmacogenomic testing

- Yes: Patient fills out forms for results disclosure and identifies clinicians who may review results
- No: End of visit

Buccal sample collected and sent to laboratory

Northshore University Health System: Multidisciplinary Pharmacogenomics Clinic

Visit 2

Patient leaves with clinical summary report

Pharmacist or medical geneticist 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

All documentation is added to EHR and forwarded to previously selected clinicians
### Duke University Health System: Pharmacist-Led MTM Services in Outpatient Cardiology Clinic

<table>
<thead>
<tr>
<th>MTM Visit 1</th>
<th>MTM Visit 2</th>
</tr>
</thead>
</table>
| • Complete medication history  
• Review of pharmacogenetic testing with patient  
• Collect blood sample | • Review pharmacogenetic test results with patient  
• Discuss recommended treatment changes based on results |

Between Visits

• Pharmacist reviews results  
• Discuss recommendations with cardiologist

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Cleveland Clinic Health System: Provider-Requested Pharmacogenomics Consultation Service

- 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 code

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

similar but Different
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
Needs and Opportunities for Pharmacist Implementations
Continue Current Efforts

• Build the evidence
  • Clinical outcomes, implementation
• Develop novel research and patient care models
• Improve practice-based resources and clinical guidelines
• Educate providers and patients
• Support efforts to secure reimbursement for preemptive panel-based testing
• Refine and develop new strategies to overcome system-wide barriers to implementation (e.g., CDS, point-of-care resources)
Increase Collaboration

Established interdisciplinary PGx Programs in Academic Health Systems

- Experience building and sustaining successful programs
- In-depth knowledge of PGx evidence and clinical actionability
- Extensive experience with clinical resources and laboratory testing
- Established provider and patient education programs and materials

Emerging PGx Programs in Community-Based Practice Settings

- Experience partnering with commercial laboratories
- Practical awareness of provider/pharmacist preferences for education and communication
- Access to and relationships with patients and providers
- Experience with existing pharmacist compensation models

Learn From Each Other
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
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 mos
- Return on Investment (ROI) analysis demonstrated positive net gain of $2,644 and an ROI of 38.1%

### Table 2. MRPs Identified During AWV and CMM Follow-up Visits

<table>
<thead>
<tr>
<th>Type of MRP</th>
<th>AMV (n = 139)</th>
<th>CMM Visit at Three Months (n = 59)</th>
<th>CMM Visit at Six Months (n = 80)</th>
<th>All Three Visits (n = 278)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect drug</td>
<td>58 (41.7)</td>
<td>14 (23.7)</td>
<td>19 (23.8)</td>
<td>91 (32.7)</td>
</tr>
<tr>
<td>Insufficient therapeutic monitoring</td>
<td>35 (25.2)</td>
<td>12 (20.3)</td>
<td>23 (28.7)</td>
<td>70 (25.2)</td>
</tr>
<tr>
<td>Inappropriate dose, frequency, or administration</td>
<td>19 (13.7)</td>
<td>10 (16.9)</td>
<td>15 (18.6)</td>
<td>44 (15.8)</td>
</tr>
<tr>
<td>Undertreatment of chronic condition</td>
<td>22 (15.8)</td>
<td>15 (25.4)</td>
<td>10 (12.5)</td>
<td>47 (16.9)</td>
</tr>
<tr>
<td>Nonadherence</td>
<td>5 (3.6)</td>
<td>8 (13.6)</td>
<td>13 (16.3)</td>
<td>26 (9.4)</td>
</tr>
</tbody>
</table>

*MRP = medication-related problem, AWV = annual wellness visit, CMM = comprehensive medication management.

Enhance Education and Training in Clinical Pharmacogenomics

• Reimbursable pharmacist business models
• Steps to choose among commercial laboratories
• Developing skills for clinical use of practice-based pharmacogenomics resources
• How to assess evidence of clinical utility when CPIC guidelines are not available
• How to discern and interpret actionable pharmacogenetic test results in a lab report
• Networking opportunities among pharmacists who are implementing PGx across diverse practice settings
• Equip pharmacists with knowledge and skills to succeed