Pharmacogenetics

IMProving America’s Communities Together

WEST PALM BEACH, FL • THURSDAY, JUNE 21, 2018

BENJAMIN BLUML, RPH
SENIOR VICE PRESIDENT, RESEARCH AND INNOVATION
Improve health by inspiring philanthropy, research and innovation that advances pharmacists’ patient care services

Innovative Practice Model Designs with Consistently Improved Outcomes

- Adherence
- Osteoporosis
- Alzheimer’s
- Diabetes
- Depression
- Hypertension
- Osteoporosis

Our Research and Innovation Axioms

Do the right things well.


Align the Incentives, Improve the Outcomes, Control the Costs.

Net Annual Savings in Chronic Disease

- The Asheville Project: $3,356
- Patient Self-Management Program: $918
- Diabetes Ten City Challenge: $1,079
- Project ImPACT: Depression: $983

"The best way to predict the future is to invent it.” – Alan Kay
Creating the Basis for a Preferred Future

Immunizations
Diabetes

APhAFoundation.org/our-work
Where we’re going…
Best way to get there…

<table>
<thead>
<tr>
<th>Empowered patients</th>
<th>Put patients first</th>
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<tbody>
<tr>
<td>Increased collaboration</td>
<td>Optimize medication use</td>
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<tr>
<td>Enhanced safety</td>
<td>Improve communication</td>
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<td>Improved outcomes</td>
<td>Manage information</td>
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<td>Reduced costs</td>
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“*Patient-centered, team-based care is the best way to invent a preferred future.*”
Patient Credentialing

*Meeting Patients Where They Are With Their Care*

Empowering people to be effective in their own self-management...

- **Assessment Domains**
  - Knowledge*
  - Skills
  - Performance

- **Achievement Levels**
  - Beginner
  - Proficient
  - Advanced

Evaluation/planning underway:
- Piloting collaboration with PCMHs
- Potential inclusion with
  - New eMeasures in development
  - Health plan benefits integration
IMPACT Database Explorer

Meeting Providers Where They Are With Their Data

Innovative Data Management Systems designed to...

◦ Build on the Foundation’s successful patient-centered, team-based care research and innovation history
◦ Aggregate key information (assessment, clinical, economic, and humanistic data) for meaningful evaluation and use
◦ Provide clinicians and researchers with integrated data dashboards and reporting utilizing secure technology infrastructure
◦ Accommodate use of information across the clinician care continuum utilizing appropriate, de-identified, aggregated display framework consistent with APhA Foundation privacy and confidentiality principles
American Pharmacists Association

Pharmacist Distribution by Geography*

**APHA MEMBERS**

- Northeast: 35%
- Midwest: 18%
- South: 28%
- West: 1%
- U.S. Territories: 18%

**PROFESSION**

- Northeast: 38%
- Midwest: 23%
- South: 19%
- West: 19%
- U.S. Territories: 19%

*Source: APhA Database (Nov-14), US BLS (May-13)
Our Research and Innovation
20+ Years of Imagining What is Possible…

- 1996 – Point-of-Care testing in community pharmacies?
- 1999 – At-risk screening, identification, and referral?
- 2004 – 11 National Pharmacy orgs agree on MTM?
- 2006 – Monitoring depression status qualitatively?
- 2009 – Home BP/Activity monitoring for hypertension?
- 2010 – Translate employer successes to underserved?
- 2014 – 3D printing of customized medications at POC?
- 2016 – Arming providers with registry data at POC?
- 2017 – Process workflow optimizations for prevention?
- 2018 – PGx decision making integrated into MTM?

- Cholestech LDXs / Point-of-Care testing now across US
- HRAs, practice level screenings commonly used now
- Definition in Federal regulations, MTM is a standard
- PHQ-9 / PHQ-2 assessments now frequently utilized
- Enhanced accountability and discovery in patient care
- Evidence that individualized, team-based care works
- Proof of concept / FDA approval for printing tablets
- Improved identification/resolution of unmet needs
- Federally supported model in multi-state/year grant
- Active work on resources w/Pgx to enhance safe use
Imagining What Might Be Possible

...Pharmacogenomics, Team-Based Care

15-Mar-10
- Coriell Institute for Medical Research/APhA Foundation NIH Research Proposal Collaboration
  - Reinvigorating the Biomedical Research Community by forging a new collaborative relationship to study the role of the pharmacist

24-Feb-11
- APhA Foundation / Coriell – Institute Council of Applied Pharmacogenomics  http://cpmc.coriell.org
  - First 12 pharmacists trained as part of a pharmacists coaching team within the Coriell Personalized Medicine Collaborative

24-Dec-12
- APhA Foundation Committee to Advance PGx in Pharmacy Practice
  http://www.APhAFoundation.org/pharmacogenomics
  - Strategic Plan for Advancing Pharmacogenomics in Pharmacy Practice; outlined key areas of focus:
    - Research / Evidence
    - Practice / Business Models
    - Standards / Policies
    - Education / Awareness / Advocacy
    - Health Information Technology
Imagining What Might Be Possible
…3D Printing, PGx, Nanotechnology

16-Sep-14
- APhA Foundation assertion that we would see 3D printing in the future capable of producing medications customized to an individual's genome at the point of care. Furthermore, imagine what might be possible if components could be added to those “printed medications” to provide live, real-time monitoring.

25-Oct-14
- Proof of concept reported in Medical News Today -- University of Central Lancashire produced a new 3D printer that can “print” a tablet with a precise quantity of medicine suitable for administration to patients.

1-Dec-14
- MIT report in Technology Review, “3-D-Printing Bio-Electronic Parts,” indicated that researchers were able to print light emitting diodes for the first time with new “inks” that contain semiconductors.

Other Converging Innovation
- University of California San Diego scientists have presented Nanoscale 3D printing and tissue engineering applications
- Swiss researchers have produced wireless remote monitoring of glucose levels using nanostructures and biosensors

INTEGRATING PHARMACOGENETIC TESTING IN REAL-WORLD PRACTICE

Invited Presentation at CIAPM, Los Angeles, 26-Aug-16

Joshua N. Liberman, PhD, Sutter Health
Benjamin M. Bluml, RPh, APhA Foundation
Matthew Rutledge, Rxight/MD Labs
% of Population for which Particular Drug is Ineffective…

- 38% Anti-Depressants
- 40% Asthma Drugs
- 43% Diabetes Drugs
- 50% Arthritis Drugs
- 70% Alzheimer’s Drugs
- 75% Cancer Drugs

Efficiently integrating PGx testing into the selection and treatment process

- Research to employ a very broad and comprehensive PGx panel
  - 60 target alleles
  - 18 genes
  - Potentially covering over 200 medications from 14+ therapeutic categories
- Patient medication preferences will be categorized using red/yellow/green flagging system
- A patient genetic consultation or “Personalized Medication Review™ (PMR)” from a trained pharmacist included with every test
- Recommendations communicated to prescribing physician(s) for action.
Center for Translational Medicine / DoD Partnership Vision and Goals

- **Vision:** Forge a consortium of leading public and private sector health leaders to provide a holistic end-to-end Precision Medicine Demonstration

- **Goal:** Demonstrate immediate readiness benefits and cost savings from a rapid *Precision Medicine* pilot focused on key military and public health issues

- **Expected outcomes:**
  - Better Care, Access
  - Improved Health
  - Lower Cost
The Clinical Pharmacogenetics Implementation Consortium (CPIC®) is an international consortium of individual volunteers and a small dedicated staff who are interested in facilitating use of pharmacogenetic tests for patient care.

One significant barrier to implementation of pharmacogenetic testing in the clinic is the difficulty in translating genetic laboratory test results into actionable prescribing decisions for affected drugs.

CPIC’s goal is to address this barrier to clinical implementation of pharmacogenetic tests by creating, curating, and posting freely available, peer-reviewed, evidence-based, updatable, and detailed gene/drug clinical practice guidelines (https://cpicpgx.org/publications/).

CPIC guidelines follow standardized formats, include systematic grading of evidence and clinical recommendations, use standardized terminology, are peer-reviewed, and are published in a leading journal (in partnership with Clinical Pharmacology and Therapeutics) with simultaneous posting to cpicpgx.org, where they are regularly updated.
PGx tools for practice:

- Guidelines
- Genes-Drugs
- Alleles
- Publications
- Meetings
- Resources
- Informatics
CPIC guidelines are designed to help clinicians understand HOW available genetic test results should be used to optimize drug therapy, rather than WHETHER tests should be ordered. A key assumption underlying the CPIC guidelines is that clinical high-throughput and pre-emptive (pre-prescription) genotyping will become more widespread, and that clinicians will be faced with having patients’ genotypes available even if they have not explicitly ordered a test with a specific drug in mind. CPIC’s guidelines, processes and projects have been endorsed by several professional societies.

Each CPIC guideline adheres to a standard format, and includes a standard system for grading levels of evidence linking genotypes to phenotypes, how to assign phenotypes to clinical genotypes, prescribing recommendations based on genotype/phenotype, and a standard system for assigning strength to each prescribing recommendation. The SOP for guideline creation has been published in Current Drug Metabolism: Incorporation of Pharmacogenomics into Routine Clinical Practice: The Pharmacogenetics Implementation Consortium (CPIC) Guideline Development Process. The CPIC authorship guidelines are updated regularly.
CPIC assigns CPIC levels to genes/drugs with

1. PharmGKB Clinical Annotation Levels of Evidence of 1A, 1B, 2A and 2B, or
2. A PharmGKB PGx level for FDA-approved drug labels of “actionable pgx”, “genetic testing recommended”, or “genetic testing required”, or
3. Based on nomination to CPIC for consideration.

Process for assigning CPIC levels

Levels for genes/drugs

Process for prioritizing CPIC guidelines
## Level Definitions for Genes/Drugs

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<th>CPIC Level</th>
<th>Clinical Context</th>
<th>Level of evidence</th>
<th>Strength of Recommendation</th>
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<tr>
<td>A</td>
<td>Genetic information should be used to change prescribing of affected drug</td>
<td>Preponderance of evidence is high or moderate in favor of changing prescribing</td>
<td>At least one moderate or strong action (change in prescribing) recommended.</td>
</tr>
<tr>
<td>B</td>
<td>Genetic information could be used to change prescribing of the affected drug because alternative therapies/dosing are extremely likely to be as effective and as safe as non-genetically based dosing</td>
<td>Preponderance of evidence is weak with little conflicting data</td>
<td>At least one optional action (change in prescribing) is recommended.</td>
</tr>
<tr>
<td>C</td>
<td>There are published studies at varying levels of evidence, some with mechanistic rationale, but no prescribing actions are recommended because (a) dosing based on genetics makes no convincing difference or (b) alternatives are unclear, possibly less effective, more toxic, or otherwise impractical or (c) few published studies or mostly weak evidence and clinical actions are unclear. Most important for genes that are subject of other CPIC guidelines or genes that are commonly included in clinical or DTC tests.</td>
<td>Evidence levels can vary</td>
<td>No prescribing actions are recommended.</td>
</tr>
<tr>
<td>D</td>
<td>There are few published studies, clinical actions are unclear, little mechanistic basis, mostly weak evidence, or substantial conflicting data. If the genes are not widely tested for clinically, evaluations are not needed.</td>
<td>Evidence levels can vary</td>
<td>No prescribing actions are recommended.</td>
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As of May, 2018 there are 49 level A Drug/Gene pairs and over 350 total...

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<th>Drug/Gene Pair</th>
<th>CPIC Level</th>
<th>PharmGKB Level of Evidence</th>
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<th>Testing Required/Recommended</th>
<th>Testing Information</th>
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Inventing a Preferred Future…

Patient Access to Needed Medications & Pharmacy Services

Interoperability of Pharmacy & Health Information Technology

Medication Use
Quality & Safety

*Align the Incentives, Improve the Outcomes, Control the Costs*™
Team-Based Care Contributions in Pharmacy Practice

**Health Promotion**
- Health Risk Assessment
- Immunizations
- Oral Health
- Wellness Programs

**Health Management**
- Asthma
- Cardiovascular Disease (Dyslipidemia, Hypertension)
- Coagulation Disorders
- Congestive Heart Failure
- Depression
- Diabetes
- Osteoporosis

*Selection Criteria:*
- High prevalence
- High risk
- High cost
- Problem prone

...all with MTM
Imagine What Might Be Possible
...in Patient-Centered, Team-Based Care if...

Together we make Pharmacogenetic data transferrable and usable in community practice within the context of well-established guidelines?

1. Would the world be a better place if each patient had an accurate, up-to-date listing of their medications that they were able to share with each healthcare provider at every visit?

*Pharmacogenetic information is a patient characteristic that is difficult to transfer across care settings; not a single number easily recalled like height, weight, or other metrics...*

2. Is it possible and does it make sense that a pharmacogenetic record would be a part of a comprehensive medication record/list that patients control and share with their healthcare providers?

3. Could we facilitate optimized medication use and therapeutic decision making with a Web Service/API that allows healthcare providers to access continuously updated CPIC pharmacogenetic content at the point-of-care?
Imagine What Might Be Possible
…in Patient-Centered, Team-Based Care if…

PGx Data (Minimum Data Set)
+
Current Medication List
+
Actionable Guidelines (e.g., CPIC A/B)

... available at the point-of-care