Pharmacogenomics: An Introduction for Practicing Pharmacists and Technicians

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Financial Disclosures

• We have had no financial relationship over the past 12 months with any commercial sponsor with a vested interest in this presentation
Objectives

• Pharmacists
  1. Describe pharmacogenomics and the key areas for current application of personalized medication management
  2. Identify the opportunities to improve healthcare quality and delivery through pharmacogenomics implementation

• Pharmacy Technicians
  1. Identify the basic mechanisms involved in common drug-gene interactions
  2. List common oral medications that have pharmacogenomics dosing guidelines
Personalized Medicine

• **Reduce adverse drug events**
  • Annually, 770,000 injuries and deaths occur due to Adverse Drug Events costing up to $5.6M/hospital
  • Better understand metabolism or inability to metabolize

• **Increase treatment success**
  – Tool for success
  – Hope to reach therapeutic benefit sooner

• **Reduce healthcare costs**

• **Improve healthcare quality**
Pharmacogenomics

“Here's my sequence...”

*The New Yorker*
Targeted Approach
ALL individuals with varying metabolism

* Nursery case
Liver Metabolism Enzymes

- **CYP 2C19**: 10%
  - Antidepressants, Phenytoin, Plavix, PPIs, chemo

- **CYP 2C9**: 15%
  - Warfarin, NSAIDs, diabetes meds, ARBs

- **CYP 2D6**: 25%
  - Pain medications, Zofran, antidepressants, Reglan, antipsychotics, beta blockers, tamoxifen

- **CYP 3A4**: 50%
  - Antipsychotics, pain meds, antibiotics, Statins, benzos, Antiemetics, HIV meds, chemo, Calcium channel blockers, steroids

- **CYP 1A2 and CYP 2B6**
  - Antipsychotics, bupropion, caffeine, naproxen, chemo

Others
- Chemotherapy, Tylenol, anesthetics

CYP 2D6: *4/*41 PM
CYP 2C9: *1/*1
CYP 3A4: *1/*1
CYP 2C19: *1/*2A IM

CYP 2D6: *1/*41
CYP 2C9: *1/*1
CYP 3A4: *1/*1
CYP 2C19: *1/*17 Rapid

Other possible combinations:
- CYP 2D6: *4/*41, *1/*41
- CYP 2C19: *1/*2A, *1/*17, *2A/*17
<table>
<thead>
<tr>
<th>Depression Medications</th>
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<tr>
<td>Fluoxetine (Prozac)</td>
<td>Citalopram (Celexa)</td>
<td>Paroxetine (Paxil)</td>
<td>Sertraline (Zoloft)</td>
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</tr>
<tr>
<td>Fluvoxamine (Luvox)</td>
<td>Venlafaxine (Effexor)</td>
<td>Nortriptyline</td>
<td>Amitriptyline</td>
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<tr>
<td>Bupropion (Wellbutrin)</td>
<td>Escitalopram (Lexapro)</td>
<td>Duloxetine (Cymbalta)</td>
<td>Mirtazapine</td>
<td></td>
</tr>
</tbody>
</table>
CYP 2D6 Dose Adjustments

CYP 2C19 Dose Adjustments

Normal metabolizer

Pharmacist Interpretation

- Pharmacogenomics Results
- Medication List
- Past Adverse Events, Allergies
- Primary Research & Guidelines
- Expert Opinion & Interpretation
Pharmacist Approach

• Is it a prodrug?
  How is it activated? What enzymes are involved?

• Is it an active drug?
  How is it broken down? Is it accumulating?

• What is the therapeutic effect?
  Loss of efficacy?
  Loss of safety?
  Sub therapeutically or Supratherapeutically response?

• Action – Alternate therapy, dose decrease, dose increase, increased monitoring, etc.
Interactions

• Drug-Drug Interaction (DDI)
  An interaction solely caused by drug response to a coadministered drug

• Drug-Gene-Interaction (DGI)
  An interaction solely caused by drug response to CYP450 genetics
  Example: citalopram and CYP2C19

• Drug-Drug-Gene Interaction (DDGI)
  An interaction that is a cumulative effect of both a DDI and DGI
  Example: CYP2D6 PM on metoprolol and fluoxetine
• Verbeurgt et al study
  n= 1143 patients
  - genotyped for CYP2C9, CYP2C19 and CY2D6
  - 34% of all potentially clinically significant drug interactions were due to DGI (14.7%) or DDGI (19.2%).
Impact of Phenoconversion

Changes in phenotype after clinical interpretation

Where can I find high quality PGx information?

• Canadian Pharmacogenomics Network (CPNDS)
  • http://cpnds.ubc.ca/

• Clinical Pharmacogenomics Implementation Consortium (CPIC)
  https://cpicpgx.org/guidelines/

• Dutch Pharmacogenetics Working Group
  https://www.knmp.nl/

• Pharmacogenomics Knowledge Base (PharmGKB)
  • https://www.pharmgkb.org/
Guidelines and Implementation

• CPIC = Clinical Pharmacogenomics Implementation Consortium
  • International consortium to facilitate the use of PGx in patient care
    “One 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”

• Guidelines are published (open access) and indexed in Pubmed
  • Endorsed by American Society of Health-System Pharmacists (ASHP) and American Society for Clinical Pharmacology & Therapeutics (ASCPT)
  • Recognized by College of American Pathologists (CAP)

https://cpicpgx.org
CPIC Guidelines

- CPIC guidelines are designed to help clinicians understand **HOW** available genetic test results should be used to optimize drug therapy.
  - Not WHETHER tests should be ordered.

- Key Assumption:
  - Clinical high-throughput and pre-emptive genotyping will become more widespread.
  - Clinicians will be faced with having patients’ genotypes available even if they did not order test with drug in mind.
CPIC guideline genes and drugs, January 2018

- **TPMT**
  - MP, TG, azathioprine
- **CYP2D6**
  - Codeine, tramadol, hydrocodone, oxycodone, TCAs, SSRIs, ondansetron, tropisetron, atomoxetine
- **CYP2C19**
  - TCAs, clopidogrel, voriconazole, SSRIs, PPIs (in progress)
- **VKORC1**
  - Warfarin
- **CYP2C9**
  - Warfarin, phenytoin, celecoxib (in progress)
- **CYP4F2**
  - Warfarin
- **HLA**
  - Allopurinol, CBZ, abacavir, phenytoin
- **CFTR**
  - Ivacaftor
- **DPYD**
  - 5FU, capecitabine, tegafur
- **G6PD**
  - Rasburicase
- **UGT1A1**
  - Atazanavir
- **SLCO1B1**
  - Simvastatin
- **IFNL3 (IL28B)**
  - Interferon
- **CYP3A5**
  - Tacrolimus
- **CYP2B6**
  - Efavirin (in progress)
- **RYR1**
  - Inhaled anesthetics
What is CPIC?

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 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 (click here for all CPIC 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 cpcpgx.org, where they are regularly updated.
Guidelines

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 – read more.

Each CPIC guideline adheres to a standard format, and includes a standard system for grading levels of evidence and phenotypes, how to assign phenotypes to clinical genotypes, prescribing recommendations based on genotypes, and a standard system for assigning strength to each prescribing recommendation. The SOP for guideline creation has been published on Current Drug Metabolism: Incorporation of Pharmacogenomics into Routine Clinical Practice: The Pharmacogenetics Implementation Consortium (CPIC) Guideline Development Process. The CPIC authorship guidelines were updated in June 2014.

Search:

<table>
<thead>
<tr>
<th>GUIDELINES</th>
<th>DRUGS</th>
<th>GENES</th>
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<td>ivacaftor</td>
<td>CFTR</td>
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<tr>
<td>CYP2C19 and Clopidogrel</td>
<td>clopidogrel</td>
<td>CYP2C19</td>
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<tr>
<td>CYP2C19 and Voriconazole</td>
<td>voriconazole</td>
<td>CYP2C19</td>
</tr>
<tr>
<td>CYP2C9, HLA-B and Phenytoin</td>
<td>phenytoin</td>
<td>HLA-B CYP2C9</td>
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</table>
### Table 1b Assignment of CYP2C19 predicted phenotypes

<table>
<thead>
<tr>
<th>Likely phenotype</th>
<th>Genotypes</th>
<th>Examples of CYP2C19 diplootypes</th>
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</thead>
<tbody>
<tr>
<td>Ultrarapid metabolizer (~5–30% of patients)</td>
<td>An individual carrying two increased function alleles or one normal function allele and one increased function allele</td>
<td>*1/*17, *1/*17</td>
</tr>
</tbody>
</table>

### Table 3 Dosing recommendations for CYP2C19 and SSRIs

#### Table 3a Dosing recommendations for citalopram and escitalopram based on CYP2C19 phenotype

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Implication</th>
<th>Therapeutic recommendation</th>
<th>Classification of recommendation</th>
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<tr>
<td>CYP2C19 Ultrarapid metabolizer</td>
<td>Increased metabolism when compared to extensive metabolizers. Lower plasma concentrations will increase probability of pharmacotherapy failure.</td>
<td>Consider an alternative drug not predominantly metabolized by CYP2C19.</td>
<td>Moderate</td>
</tr>
<tr>
<td>CYP2C19 Extensive metabolizer</td>
<td>Normal metabolism</td>
<td>Initiate therapy with recommended starting dose.</td>
<td>Strong</td>
</tr>
<tr>
<td>CYP2C19 Intermediate metabolizer</td>
<td>Reduced metabolism when compared to extensive metabolizers.</td>
<td>Initiate therapy with recommended starting dose.</td>
<td>Strong</td>
</tr>
<tr>
<td>CYP2C19 Poor metabolizer</td>
<td>Greatly reduced metabolism when compared to extensive metabolizers. Higher plasma concentrations may increase the probability of side effects.</td>
<td>Consider a 50% reduction of recommended starting dose and titrate to response or select alternative drug not predominantly metabolized by CYP2C19.</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
The CYP2C19 gene has several known functional variants:
- Functional (*1)
- No function (*2, *3, others)
- Increased function (*17) – promoter variant, increased transcription

Individuals have 2 copies of CYP2C19.

Different combinations of these alleles cause five different metabolizing phenotypes:

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Genotype</th>
<th>Prevalence (approximate)</th>
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</thead>
<tbody>
<tr>
<td>Ultrarapid Metabolizer (UM)</td>
<td>*17/*17</td>
<td>5%</td>
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<tr>
<td>Rapid Metabolizer (RM)</td>
<td>*1/*17</td>
<td>25%</td>
</tr>
<tr>
<td>Normal Metabolizer (NM)</td>
<td>*1/*1</td>
<td>40%</td>
</tr>
<tr>
<td>Intermediate Metabolizer (IM)</td>
<td>*1/*2, *1/*3, *2/*17</td>
<td>25%</td>
</tr>
<tr>
<td>Poor Metabolizers</td>
<td>*2/*2, *2/*3, *3/*3</td>
<td>2%</td>
</tr>
</tbody>
</table>
Mechanisms and Annotations

- PharmGKB® = Pharmacogenomics Knowledge Base
  - Financially supported by NIH; managed at Stanford University
  - Provides information about how human genetic variation affects response to medications

- Available resources on PharmGKB
  - Mechanism diagrams
  - Annotations of Drug Labels (FDA) and Guidelines (CPIC, Dutch Guidelines)
  - Prescribing information related to pharmacogenomics
  - Genes of interests and gene variants

https://www.pharmgkb.org/
Clinical Annotations

Clinical annotations summarize all of PharmGKB’s annotations of published evidence for the relationship between a particular genetic variant and a medication. They are given a rating by PharmGKB depending on how much published evidence there is to support the relationship and the quality of that evidence.

Curated Pathways

Curated pathways are evidence-based diagrams of how a medication is metabolized in your body or how a medication works in the body. Pathway diagrams are accompanied by a written description.

Drug Label Annotations

Medication labels that contain pharmacogenomic (PGx) information are annotated on the PharmGKB website. We currently provide annotations on relevant American, Canadian, European and Japanese labels. Drug label annotations are assigned a level of PGx information including whether they recommend or require genetic testing for a patient before prescribing the medication.
Clinical Guideline Annotations

PharmGKB annotates PGx-based drug dosing guidelines published by the Clinical Pharmacogenetics Implementation Consortium (CPIC), the Royal Dutch Association for the Advancement of Pharmacy - Pharmacogenetics Working Group (DPWG), the Canadian Pharmacogenomics Network for Drug Safety (CPNDS) and other professional societies. PharmGKB annotations present a brief summary of the genotype-based dosing recommendations.

We welcome any information regarding published PGx dosing guidelines - please contact us.

Guideline Videos. PharmGKB has recorded short video introductions of some CPIC dosing guidelines. The full video overview of a guideline can be seen on the individual guideline page, when available.

Filter for Source: All

<table>
<thead>
<tr>
<th>Drug</th>
<th>CPIC</th>
<th>DPWG</th>
<th>CPNDS</th>
<th>Other</th>
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<td>HLA-B 08/10/2011</td>
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<td>acenocoumarol</td>
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<td>CYP2C9 08/10/2011</td>
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<td>allopurinol</td>
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<td>HLA-B 10/01/2012</td>
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<td>amitriptyline</td>
<td>CYP2C19, CYP2D6 11/15/2018</td>
<td>CYP2D6 08/10/2011</td>
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<td>aripiprazole</td>
<td>CYP2D6 08/10/2011</td>
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<td></td>
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</tr>
<tr>
<td>atazanavir</td>
<td>UGT1A1 09/18/2015</td>
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<td></td>
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</tbody>
</table>
Annotation of DPWG Guideline for citalopram and CYP2C19

PharmGKB ID: PA166104977

Summary

For CYP2C19 ultrarapid metabolizers, monitor citalopram plasma concentration and titrate dose to a maximum of 150% in response to efficacy and adverse drug event, or select an alternative drug.

Annotation

The Royal Dutch Pharmacists Association - Pharmacogenetics Working Group has evaluated therapeutic dose recommendations for citalopram based on CYP2C19 genotype [Article:2141232]. They conclude to monitor plasma concentration and titrate dose to a maximum of 150% in response to efficacy and adverse drug event or select alternative drug (e.g. fluoxetine, paroxetine) for the CYP2C19 UM phenotype.
Pharmacokinetics of the selective serotonin reuptake inhibitor citalopram.

Pathways
### Resource list

<table>
<thead>
<tr>
<th>Reference Name</th>
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<tr>
<td>PharmGKB</td>
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<td>FDA’s Pharmacogenetic website</td>
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<td>St. Jude’s PG4KDS Implementation ToolKit for Professionals</td>
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<td>IGNITE and SPARK toolkit</td>
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<td>EMERGE</td>
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Implementing Pre-emptive Pharmacogenomics in a Rural Health System
## Choosing an Approach

### Targeted vs Panel Testing
- **Targeting one disease state or several?**
- **Seeking insurance reimbursement?**
- **Is a particular medical specialty asking for PGx?**

### Preemptive vs Reactive
- **How wide is the “buy-in” from providers and administration?**
- **Is your EMR capable to handle discrete PGx results?**
- **Do providers know what to do with PGx results?**

### In-house vs Outsourced
- **Does your lab have the capabilities/ capacity for PGx?**
- **Do you have the financial resources to support PGx testing?**
Sanford Imagenetics

• Established in 2014 after a $125 million gift from philanthropist Denny Sanford

• Goal: to integrate genomics into primary care
  • IM and genetics

• Scope: Implement CPIC guidelines into electronic medical record to drive drug-gene alerts for all prescribers
Sanford “Chip”

- Laboratory developed test (LDT)
  - BeadChip technology – 100,000s of SNPs
- Designed specifically for genetic screening
- Uses a small sample of blood
- Used to evaluate risk for several potential health conditions + pharmacogenomics

SNP = Single Nucleotide Polymorphism
Types of Genetic Screening

**PHARMACOGENETICS:**
Returns genetic variants known to impact an individual’s ability to metabolize certain medications

**DISEASE PREDISPOSITION:**
Returns genetic variants from a set of genes defined by the ACMG known to increase risk for conditions known to have medical actionability.

*The American College of Medical Genetics and Genomics (ACMG) has selected a set of 59 genes (ACMG 59) with medically actionable steps can be taken to minimize risk*
PGx Testing Options

• Focused, single gene PGx
  • CYP2C19 - clopidogrel
  • CYP2D6/CYP2C19 – antidepressants

• Pre-emptive panel PGx
  • 8-gene panel: CYP2C9, CYP2C19, CYP2D6, CYP3A5, DPYD, TPMT, SLCO1B1, VKORC1
  • 10-gene panel awaiting validation; planning 15-gene soon

• PGx + ACMG 59 = Sanford Chip
# Drug-Gene Pairs from CPIC guidelines

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Drug Class</th>
<th>Common Clinical Use(s)</th>
<th>Gene(s)</th>
</tr>
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<tbody>
<tr>
<td>Amitriptyline</td>
<td>TCA (tricyclic antidepressant)</td>
<td>Depression, neuropathic pain</td>
<td>CYP2C19, CYP2D6</td>
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<tr>
<td>Azathioprine</td>
<td>Immunosuppressant</td>
<td>Crohn’s disease, lupus</td>
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<tr>
<td>Capetitabine</td>
<td>Fluoropyrimidine</td>
<td>Solid tumors, including colorectal cancer</td>
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<tr>
<td>Citalopram</td>
<td>SSRI (selective serotonin reuptake inhibitor)</td>
<td>Major depressive and anxiety disorders</td>
<td>CYP2C19</td>
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<tr>
<td>Clomipramine</td>
<td>TCA (tricyclic antidepressant)</td>
<td>Depression, neuropathic pain</td>
<td>CYP2C19, CYP2D6</td>
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<tr>
<td>Clopidogrel</td>
<td>Anticoagulant</td>
<td>Coagulopathy</td>
<td>CYP2C19</td>
</tr>
<tr>
<td>Codeine</td>
<td>Opioid analgesic</td>
<td>Pain, cough</td>
<td>CYP2D6</td>
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<td>Desipramine</td>
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<td>Escitalopram</td>
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<td>Fluoxetine</td>
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<th>Gene(s)</th>
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<td>Simvastatin</td>
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<td>Tacrolimus</td>
<td>Immunosuppressant</td>
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<td>CYP3A5, TPMT</td>
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<td>Warfarin</td>
<td>Anticoagulant</td>
<td>Thromboembolism</td>
<td>CYP2C9, VKORC1</td>
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</table>

Prepared in June 2018 by Anna Alhoub, PharmD, April Schulz, PharmD, and Russ Weihe, MD

Potential Adverse Outcomes: Patient specific drug metabolizer phenotypes can cause a patient to experience therapeutic failures and/or increased side effects to any of the medications listed above.
PGx results workflow

PGx Results Workflow

- Not actionable
- Note entered into chart
- Phone call to provider
- Clinical note in chart
- Therapy changed as determined by provider. If requested, pharmacist will contact patient.

PGx Results

Actionable
PGx results workflow

• Pharmacist reviews 100% of PGx samples
  • 3 FTE clinical pharmacists

• PGx demographics (since Jan 2018)
  • ~3900 total PGx panels reviewed
  • 14% of PGx panels contain an actionable drug-gene interaction (per CPIC guideline)

• Documentation and Education
  • Pharmacist clinical note on all PGx panels*
  • Notes forwarded to prescribers; education provided to patients if specifically requested
Example of a PGx report ("traffic light" report) sorted by drug class vs recommendation for use

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>DRUG CLASS</th>
<th>STANDARD PRECAUTIONS</th>
<th>USE WITH CAUTION</th>
<th>CONSIDER ALTERNATIVES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticancer Agents</td>
<td>Dihydropyrimidines</td>
<td>Capetitabine (Celebrex) Fluorouracil (Adrucil, peth; Carac (topical); Eludex (topical))</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thiopurines</td>
<td>Azathioprine (Azasan, Imuran) Mercaptopurine (Purinethol, Purinex)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Anticoagulants</td>
<td>Warfarin (Coumadin)</td>
<td>Clopidogrel (Plavix)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Antiplatelets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Statins</td>
<td>Simvastatin (Zocor)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>Opioids</td>
<td>Codeine (Codeine; Fioricet with Codeine) Tramadol (Ultrace)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotropic</td>
<td>Antidepressants</td>
<td>Citalopram (Celexa) Desipramine (Norpramin) Escitalopram (Lexapro) Fluoxetine (Prozac, Sarafem) Fluvoxamine (Luvox) Nortriptyline (Pamelor) Paroxetine (Paxil, Bricelle) Sertraline (Zoloft)</td>
<td>Amitriptyline (Elavil) Clomipramine (Anafranil) Doxepin (Silenor) Imipramine (Tofranil) Trimipramine (Surmontil)</td>
<td></td>
</tr>
<tr>
<td>Transplantation</td>
<td>Immunosuppressants</td>
<td>Tacrolimus (Prograf)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Clinical Decision Support (CDS)

- Lab results/reports available as discreet data in EMR
- Best Practice Advisories (BPA's) programmed to fire for providers as appropriate
- In 2018, acceptance rate for PGx BPAs was 45%
Local laboratory, Sioux Falls

- State-of-the-Art Genetics Laboratory
- Multidisciplinary team
- Clinical laboratory with CLIA and CAP for the entire Avera footprint
- Research and service laboratory for national and international partners and collaborators

- Pharmacogenetics
- Twins work, complex diseases
- Cancer genetics, etc.
• **Pain Panel ≤24 hour turnaround time**
  • Consider for patients with acute pain from injury, procedure or surgery not responding to current pain regime.

• **Plavix (CYP2C19) Panel ≤24 hour turnaround time**
  Consider for patients taking or newly prescribed clopidogrel (Plavix) for ACS with PCI, past Major Adverse Cardiovascular Events, stroke or TIA

• **Transplant Genotyping Panel ≤24 hour turnaround time**

• **CYP3A5 for immunosuppressants, Pain, etc.**

• **Comprehensive Genefolio ~5 day turnaround, up to 14 business days at highest volumes (includes a full pharmacist consultation)**
  • **All Psychotropics**
  • **Warfarin**
  • **Pain**
  • **Statins**
  • **Clopidogrel**
  • **ADHD meds**
  • **Others**
  • **Over 1,000 meds evaluated, all home meds included**
Process

Consent Blood Sample

Genetics Lab DNA Extraction Processing

CLINICAL DECISION SUPPORT IN THE EMR AT THE TIME OF PRESCRIBING

Physician uses Report to make Medication Decisions

Report Generated Recommendations

Results to Pharmacists
Current Medications (12/22/16)

- aspirin
- biaxin
- calcium carbonate
- cholecalciferol
- colcortol
- fish oil
- fludrocortisone (nasal)
- insulin aspart
- levothyroxine
- losartan
- metformin
- metoprolol
- multivitamin
- omeprazole
- rosuvastatin
- venlafaxine
- vitamin complex

Current Medication Considerations:

1. Metoprolol has a significant drug-drug-gene interaction because of the patient's poor CYP2D6 function. The patient would be expected to have lower than normal blood levels of metoprolol due to reduced metabolism of the medication. It would be fine to continue using metoprolol as long as it is well tolerated but it would be recommended to be conservative with the dose and to monitor closely for hypotension and bradycardia.

2. Losartan has a moderate drug-drug-gene interaction because of the patient's reduced CYP2C9 function. The patient would be expected to have higher than normal blood levels of losartan due to reduced metabolism of the medication. It would be fine to continue using losartan as long as it is well tolerated but it would be recommended to be conservative with the dose and to monitor closely for adverse effects.

3. Omeprazole has a moderate drug-drug-gene interaction because of the patient's reduced CYP2C19 function. The patient would be expected to have higher than normal blood levels of omeprazole due to reduced metabolism of the medication. It would be fine to continue using omeprazole as long as it is well tolerated but it would be recommended to be conservative with the dose and to monitor closely for adverse effects.

4. Venlafaxine has a moderate drug-drug-gene interaction because of the patient's reduced CYP2D6 function. Venlafaxine is metabolized through CYP2D6 to an active metabolite that contributes to efficacy. It would be fine to continue using venlafaxine as long as it is well tolerated and effective but it would be recommended to monitor closely for effectiveness. If venlafaxine is not effective it would be suggested to try another SSRI such as vilazodone (Viibryd®) or an SNRI such as duloxetine (Cymbalta®), duloxetine (Cymbalta®), or levomilnacipran (Reboxetine®).
Female in her 50's, developmental disorder due to mother's fall in 7th month of pregnancy, intellectual disability, bizarre behaviors
Institutionalized since age 4

Started on antipsychotics many years ago
Antipsychotics cause many side effects, this patient has abnormal movements and cholesterol issues

Treat abnormal movement side effects with a medication
New medication for side effects causes constipation

Add additional medications to treat constipation
Patient exhibits more behaviors due to constipation, non-verbal expression
Pharmacogenomics panel run, realize patient doesn’t metabolize antipsychotic well (CYP 2D6 PM) and drug accumulates in her body → side effects

Blood level of drug = looks like patient taking 16mg/day instead of 6mg/day, decrease dose by 75%

New blood level still high, discontinue drug, side effects start to diminish

All realized due to running a PGx panel
Final thoughts on preemptive PGx

• Several approaches to implementing pharmacogenomics
  • One approach isn’t necessarily better than another; different strengths/weaknesses
• Clinical Decision Support conveys a significant advantage in preemptive PGx
  • Clinical data supports several drug-gene interactions/guidelines
  • Cost efficiency with gene panels
  • Paucity of data supporting outcomes with prospective
Pharmacist Question #1

The use of pharmacogenomics can benefit a health system or clinic in what ways?

A. Shorten the amount of time before therapeutic benefit of a medication is realized
B. Reduce treatment costs for both patient and provider
C. Improve quality of care and the patient experience
D. All of the above
Pharmacist Question #2

Pharmacogenetic results (genotype/phenotype) always give clinicians a clear “yes/no” indication about whether or not a specific medication is appropriate for a given individual?

A. True
B. False
Technician Question #1

Which of the following organs is most closely associated with drug metabolism?

A. Pancreas
B. Liver
C. Lymph nodes
D. Skin
Technician Question #1

Which of the following oral medications has a pharmacogenomics dosing guideline?

A. Aspirin
B. Citalopram
C. Metformin
D. Lisinopril
References


• Others on slides