The PREDICT Program at Vanderbilt: Four Drug – Gene Interactions and Counting

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Professor of Medicine
Pathologist in Chief
Vanderbilt University Hospital
PREDICT
Stands for
Pharmacogenomic Resource for Enhanced Decisions in Care and Treatment
Would it not be great if we could select the right antihypertensive or the right antidepressant or the right antiplatelet agent immediately ---

rather than using the trial and error method and having a poor patient outcome until the drug that works is identified ??
The Need for Pharmacogenomics Testing is Great – How to Practically Implement It Is the Challenge

5.3% of hospital admissions due to adverse drug reactions

Over 200 drug labels now suggest pharmacogenomic testing to guide therapy – and the FDA has mandated testing for 4 of these – 3 are cancer drugs

Adverse drug reactions are 4\textsuperscript{th}-6\textsuperscript{th} leading cause of mortality in the US

Personalized Medicine 8:421, 2011
Outline of the Presentation

Introduction to PREDICT
Warfarin
Plavix
Simvastatin
Azathioprine
Introductory Concepts
DNA extracted from the patient’s blood specimen is genotyped for 184 common polymorphisms within 34 genes associated with drug absorption, distribution, metabolism, and excretion.

Using the Illumina Vera Code ADME Core Panel Assay.
Quick Facts About PREDICT

• Currently no cost to the patient, despite reagent and supply cost of at least $400

• No consent required for test

• Simple blood test

• Average turnaround time for test is 6 days, with a minimum of 3 days

• On hands technologist time is about 14 hours for 30 cases
Warfarin

CYP 2C9 and Vitamin K Epoxide Reductase (VKORC)
Coumadin: Affects the Coagulation Cascade at Multiple Sites

Coumadin:
Reduces Synthesis of II, VII, IX, X –
Does not inhibit any coagulation factors
Monitor with INR
### Recommended Intensity of Oral Anticoagulation for Common Indications
The Treatment Dose and Prophylactic Dose Are the Same

<table>
<thead>
<tr>
<th>Indication</th>
<th>INR</th>
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<tbody>
<tr>
<td>DVT / PE</td>
<td>2.0 - 3.0</td>
</tr>
<tr>
<td>MI</td>
<td>2.0 - 3.0</td>
</tr>
<tr>
<td>Cardiogenic Embolus</td>
<td>2.5 - 3.5</td>
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<tr>
<td>Tissue Heart Valve</td>
<td>2.0 - 3.0</td>
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<tr>
<td>Valvular Heart Disease</td>
<td>2.0 - 3.0</td>
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<tr>
<td>Atrial Fibrillation</td>
<td>2.0 - 3.0</td>
</tr>
<tr>
<td>Mechanical Heart Valve</td>
<td>2.5 - 3.5</td>
</tr>
</tbody>
</table>
INR below 2.0 results in a higher risk of stroke
Risk of Intracranial Hemorrhage in Outpatients on Warfarin

- PTR above 2.0 (INR of 3.7 to 4.3) increases the risk of bleeding
- The estimated odds ratio of subdural hemorrhage increased 7.6 fold as the PTR increased from 2.0 to 2.5 (INR 3.7–4.3 to 5.7–6.8)

Adapted from: Hylek EM, Singer DE, Ann Int Med 1994;120:897-902
Genetic studies – for vitamin k epoxide reductase and cytochrome 2C9 – can be used to identify patients who should receive a lower dose of coumadin to obtain a therapeutic INR.
Off to an Unenthusiastic Start: The Pharmacogenomics of Warfarin

3-7 days to obtain pharmacogenomics test results

INR adjusted into therapeutic range in most cases by that time

The functional clotting test for INR is a low-cost test

What is the benefit of pharmacogenomics testing for warfarin in a patient who is already therapeutically anticoagulated with the drug?
$5 more per day for a year is about $1500/yr more vs warfarin

If 10 million warfarin users change to dabigatran,

it is an additional 1.5 billion dollars EVERY YEAR from the health care system for this one medication switch!
Clopidogrel (Plavix)

CYP 2C19
Following the Warfarin Experience, Pharmacogenomics for Plavix is Introduced to a Skeptical Audience of Potential Users and Laboratory Directors

For patients being treated with Plavix, there is an opportunity to reduce the risk for thrombosis by performing pharmacogenomics testing to determine if Plavix is likely to be effective

and

the change to a more effective antiplatelet agent can be performed at no extra cost
INDIVIDUAL RESPONSE TO PLAVIX IS VARIABLE

• Patients exhibit variable response to clopidogrel

• Patients may also experience variable return of platelet function after clopidogrel is withdrawn prior to surgery

Serebruan et al. J Am Coll Cardiol 2005;45:246-51
Hochholzer et al. Circulation 2005; 111:2560-4
EFFECTIVENESS OF CHRONIC PLAVIX THERAPY

response to Plavix

Clopidogrel nonresponsiveness is associated with increased risk of thrombotic events and correlates to poorer clinical outcomes

% Patients with Recurrent CVS Events at 6 Months

CV Events at 6 Months (%)

0% 10% 20% 30% 40% 50% 60%

1st 2nd 3rd 4th

LOW

HIGH

INHIBITION OF PLATELETS BY CLOPIDIGREL: INHIBITION AT THE ADP RECEPTOR

CLOPIDIGREL

LIVER

CYP2C19

CLOPIDIGREL METABOLITE

ADP Receptor

PLATELET
Genetic Studies

for Cyp2C19 loss of function alleles in the liver –

that convert Plavix to its active metabolite – can identify patients who do not have an anti-platelet effect from Plavix

There are multiple tests to assess platelet function, but they are expensive and do not always agree –

and the logistics of performing platelet function tests are often complex
Who is Being Tested for CYP2C19 at Vanderbilt?

All patients who are receiving a coronary artery stent by interventional cardiology

and now in addition

Patients seen in primary care who are expected to require a coronary artery stent – and will need Plavix after it is placed – so that the appropriate antiplatelet drug is selected in advance

Patients chosen for this testing qualify by a complex formula based upon clinical and laboratory findings
Perform testing for CYP 2C19

Considering only the loss of function alleles, if homozygous, switch from Plavix to Prasugrel or Ticagrelor

Considering only the loss of function alleles, if heterozygous, switch to Prasugrel or Ticagrelor

If loss of function alleles are accompanied by gain of function alleles, the switch away from Plavix may or may not be recommended
<table>
<thead>
<tr>
<th>Metabolizer Status</th>
<th>Examples of Alleles Responsible</th>
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<tr>
<td>Intermediate</td>
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<tr>
<td>Hyper</td>
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<tr>
<td>Hypo</td>
<td><em>2</em>2</td>
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<tr>
<td>Allele Name</td>
<td>Comments</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------------------------------------------------------------------</td>
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<tr>
<td>CYP 2C19*1</td>
<td>Wild-type/normal</td>
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<tr>
<td>CYP 2C19*2</td>
<td>nonfunctional</td>
</tr>
<tr>
<td>CYP 2C19*2B</td>
<td>nonfunctional</td>
</tr>
<tr>
<td>CYP 2C19*3</td>
<td>poor metabolism of compounds like proguanil - with implications for malaria prophylaxis</td>
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<tr>
<td>CYP 2C19*4</td>
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<td>CYP 2C19*5</td>
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<tr>
<td>CYP 2C19*6</td>
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<tr>
<td>CYP 2C19*7</td>
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</tr>
<tr>
<td>CYP 2C19*8</td>
<td>nonfunctional</td>
</tr>
<tr>
<td>CYP 2C19*17</td>
<td>ultra-rapid metabolizer</td>
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</table>

Many Alleles for CYP 2C19 – Plavix metabolism May Be Difficult to Assess

SNPedia, 2011
If the data from pharmacogenomics testing becomes part of a patient specific, expert driven narrative by an expert in coagulation, approximately $30 can be collected for each case for a professional interpretation which is far less than the cost of the test.
After Education of Physician Users at Vanderbilt, Who Responds to Questions About Pharmacogenomics Test Results?

The first responder is a pharmacy resident with a fact sheet who is reached by calling 875-GENE.

The second responder is a content expert in the field related to the drug gene interaction -- this expert is available to the first responder for more complex questions.
INHIBITION OF PLATELETS BY PRASUGREL: INHIBITION AT THE P2Y12 ADP RECEPTOR

PRASUGREL \rightarrow \text{LIVER} \rightarrow \text{PRASUGREL METABOLITE}

PRASUGREL \rightarrow \text{CYP3A4 and 2B6}

\text{P2Y12 ADP Receptor}

\text{PLATELET}
Ticagrelor is an allosteric reversible antagonist of the ADP receptor.
What Happens When Plavix Becomes Generic and Costs Only $1.00 per day versus $6.00 per day for Prasugrel or Ticagrelor?

The requirement is $5.00 more per day for a drug taken for the rest of the patient’s life.

$5.00 per day for every 1 million users amounts to 5 million dollars per day or $1.825 billion per year to the national health care budget.

This will raise major questions about the need to switch from Plavix to Prasugrel or Ticagrelor and may require pharmacogenomics data to permit payment for the more expensive drug.
A Vanderbilt Anecdote

Shortly after the pharmacogenomics testing for Plavix was introduced, a shipment of reagents was received but one reagent was missing.

Because of that, testing for CYP 2C19 in real time for a patient receiving Plavix and a new drug eluting stent was not performed.

During the two weeks when testing could not be performed, this patient had an in-stent thrombosis.
A Vanderbilt Anecdote

When the test was performed on this patient after the thrombotic event, the result showed that two loss of function alleles for CYP 2C19.

This convinced most of the interventional cardiologists of the value of pharmacogenomics testing for Plavix because the stent thrombosis was likely to have been prevented by using Prasugrel instead of Plavix.
Release of the Results in EMR

Results in Molecular Diagnostics Tab

Clopidogrel DGI Result

PREDICT DNA Testing Comment
Clopidogrel *2/*2 Decision Support

**Clopidogrel Poor Metabolizer Rules**

Genetic testing has been performed and indicates this patient may be at risk for inadequate anti-platelet response to clopidogrel (Plavix) therapy. This patient has been tested for CYP2C19 variants, and the presence of the *2/*2 genotype has identified this patient as a poor metabolizer of clopidogrel. Poor metabolizers treated with clopidogrel at normal doses exhibit higher rates of stent thrombosis/other cardiovascular events.

**Treatment modification is recommended if not contraindicated:**
- Prescribe prasugrel (EFFIENT) 10mg daily and stop clopidogrel (PLAVIX) startdate, 10 AM

Due to increased risk of bleeding compared to clopidogrel, prasugrel should not be given to patients:
- that have a history of stroke or transient ischemic attack ***Not known; please check StarPanel***
- that are greater than 75 years of age
- whose body weight is less than 60 kg

Click here for more information.

If prasugrel (EFFIENT) not selected, please choose desired action:
- increase maintenance dose of clopidogrel (PLAVIX) 150 mg daily, startdate, 10 AM
- Maintain requested daily dose of clopidogrel (PLAVIX) 75 mg daily, startdate, 10AM

If not using prasugrel, please select a reason:
- Contraindicated for prasugrel
- Potential side effects
- Patient opts for clopidogrel
- Other (Specify): [ ]

Click here for more information.

**NOTE:** The Vanderbilt P&T Committee has recommended that prasugrel (if not contraindicated) should replace clopidogrel for poor metabolizers; if this is not possible consider doubling the standard dose of clopidogrel (or, use standard dose clopidogrel). However, there is not a national consensus on drug/dose guidance in this population.

Ticagrelor-new alternative to be added soon.
Clopidogrel *1/*2 Decision Support

Clopidogrel Intermediate Metabolizer Rules

Genetic testing has been performed and indicates this patient may be at risk for inadequate anti-platelet response to clopidogrel (Plavix) therapy.

This patient has been tested for CYP2C19 variants, and the presence of the *1/*2 genotype has identified this patient as an Intermediate metabolizer of clopidogrel. Intermediate metabolizers treated with clopidogrel at normal doses exhibit higher rates of stent thrombosis/other cardiovascular events.

Treatment modification is recommended if not contraindicated:
- Prescribe prasugrel (EFFIENT) 10 mg daily and stop clopidogrel (PLAVIX), start date 10 AM

Due to increased risk of bleeding compared to clopidogrel, prasugrel should not be given to patients:
- that have a history of stroke or transient ischemic attack
- that are greater than 75 years of age
- whose body weight is less than 60 kg

***Not known; please check StarPanel

Click here for more information

If prasugrel (EFFIENT) not selected, please choose desired action:
- Increase maintenance dose of clopidogrel (PLAVIX) 150 mg daily, start date 10AM
- Maintain requested daily dose of clopidogrel (PLAVIX) 75 mg daily, start date 10AM

If not using prasugrel, please select a reason:
- Contraindicated for prasugrel
- Potential side effects
- Patient opts for clopidogrel
- Other (Specify) [ ]

Click here for more information

Cancel Order
StarPanel Testing Prompts

Click Here

Order Window will appear
Evaluation of Pharmacogenomics Success with Plavix

The primary outcome is to determine the number of prescription changes away from Plavix when loss of function alleles are detected.

The secondary outcome is to determine the number of in-stent thromboses or major adverse coronary events in patients originally treated with Plavix and then switched to a different antiplatelet agent.
Recommendations for Medication Change: Plavix

*From March 2011 to February 2012 at Vanderbilt –*

3312 patients tested

707 patients with a CYP 2C19 actionable genotype

149 patients with CYP 2C19 actionable genotype and a drug eluting stent

131 recommendations for medication change

48 medication changes made
<table>
<thead>
<tr>
<th>Metabolizer Status</th>
<th>Number of Cases</th>
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</thead>
<tbody>
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<td>Intermediate</td>
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<td>Indeterminate</td>
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<td>Hypo</td>
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<tr>
<td>Week Number</td>
<td>Test Volume</td>
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</tr>
<tr>
<td>1</td>
<td>60</td>
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<tr>
<td>2</td>
<td>80</td>
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<td>85</td>
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<td>4</td>
<td>113</td>
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<tr>
<td>5</td>
<td>164</td>
</tr>
<tr>
<td>6</td>
<td>213</td>
</tr>
</tbody>
</table>
Simvastatin

SLCO1B1

(solute carrier organic anion transporter family, member 1B1)
After the Experience With Plavix, There is Now a More Receptive Audience for Pharmacogenomics Testing of Patients Receiving Statin Drugs at High Doses

The gene is SLCO1B1 - and the drug is Simvastatin at an 80 mg daily dose

The adverse consequence is myopathy

Treatment recommendations when this drug gene interaction is present typically involves reduction of dose
Myopathy Occurs with High Doses of Statins, Particularly Simvastatin at 80 mg daily

SLCO1B1 is a transporter protein on the plasma membrane of the hepatocyte involved in the uptake of simvastatin into the cell

Myopathy occurs when the Simvastatin does not enter the hepatocyte, and is present in high circulating drug concentrations, which impairs cholesterol synthesis in myocytes
Simvastatin – Drug Gene Interactions by Effect at Vanderbilt

<table>
<thead>
<tr>
<th>Metabolizer Status</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal risk</td>
<td>3146</td>
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<td>Intermediate risk</td>
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<tr>
<td>High risk</td>
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### Release of the Results in EMR

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel DGI</td>
<td>POOR METABOLIZER, REDUCED ANTI-PLATELET EFFECT - gene: CYP2C19 - gene result: *2/*2</td>
</tr>
<tr>
<td>Simvastatin DGI</td>
<td>NORMAL MYOPATHY RISK, MAJOR ALLELE HOMOZYGOUS (T:T) - gene: SLC01B1 - gene result: *1B HET</td>
</tr>
</tbody>
</table>

- **Results in Molecular Diagnostics Tab**
- **Simvastatin DGI Result**
- **Clopidogrel DGI Result**
- **PREDICT DNA Testing Comment**

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**DNA METHOD**

DNA extracted from this specimen was genotyped for 184 common polymorphisms within 34 genes associated with drug absorption, distribution, metabolism and excretion using the Illumina Vera Code ADME Core Panel Assay. Genes analyzed using this bead array technology include: ABCB1; ABC2C; ABCG2; CYP1A1; CYP1A2; CYP2A6; CYP2B6; CYP2C19; CYP2C8; CYP2C9; CYP2D6; CYP2E1; CYP3A4; CYP3A5; DPYD; GSTM1; GSTP1; GSTT1; NAT1; NAT2; SLC15A2; SLC22A1; SLC22A2; SLC22A6; SLC01B1; SLC01B3; SLC02B1; SULT1A1; TPMT; UGT1A1; UGT2B15; UGT2B17; UGT2B7; VKORC1.

Cindy L. Vnencak-Jones, Ph.D.
ABMG-Certified Molecular Geneticist
Director, Molecular Diagnostics Lab
Genes analyzed using this technology include:

ABCB1; ABCC2; ABCG2; CYP1A1; CYP1A2; CYP2A6; CYP2B6; CYP2C19; CYP2C8; CYP2C9; CYP2C6; CYP2E1; CYP3A4; CYP3A5; DPYD; GSTM1; GSTP1; CSTT1; NAT1; NAT2; SLC15A2; SLC22A1; SLC22A2; SLC22A6; SLC01B1; SLC01B3; SLC02B1; SULT1A1; TPMT; UGT1A1; UGT2B15; UGT2B17; UGT2B7; VKORC1
Simvastatin (ZOCOR) High Risk for Muscle Toxicity Rules

Genetic testing has been performed and indicates this patient may be at High risk for myopathy with simvastatin therapy.

This patient has been tested for SLCO1B1 variants, and the presence of the *5 homozygous (CC) genotype has identified this patient at a High risk for simvastatin-related myopathy. There is a strong association between genetic variation in SLCO1B1 and simvastatin-induced myopathy risk.

Treatment modification is recommended if not otherwise contraindicated:
- *PREFERRED* Prescribe atorvastatin (LIPITOR) 20 mg daily and stop simvastatin (ZOCOR), startdate 10 AM
- Prescribe pravastatin (PRAVACHOL) 80 mg daily and stop simvastatin (ZOCOR), startdate 10 PM

Other statin therapy considerations include:
- Use caution when prescribing statin therapy in patients with predisposing risk factors for myopathy: Age >65 years (Patient's age: 36 years), renal impairment (Patient's Scr: 0), or other acute medical or surgical conditions which predispose the patient for renal failure.
- Monitor for evidence of muscle injury: elevated Creatine Kinase (CK) level in the absence of a cardiac event, muscle pain, muscle weakness or tenderness, or Rhabdomyolysis.

Click here for more information.

If simvastatin is not discontinued, please choose desired action:
- Maintain requested daily dose of simvastatin (ZOCOR) 40 mg at bedtime, startdate 10PM with routine CK monitoring
- Decrease requested daily dose to simvastatin (ZOCOR) 20 mg at bedtime, startdate 10PM with routine CK monitoring
- Decrease requested daily dose to simvastatin (ZOCOR) 10 mg at bedtime, startdate 10PM with routine CK monitoring

NOTE: The Vanderbilt P&T Committee has recommended that atorvastatin (if not contraindicated) should replace simvastatin for patients with High risk for myopathy, if this is not possible continue simvastatin and regular CK monitoring. However, there is not a national consensus on drug/dose guidance in this population.
Simvastatin (ZOCOR) Intermediate Risk for Muscle Toxicity Rules

Genetic testing has been performed and indicates this patient may be at Intermediate risk for myopathy with simvastatin therapy.

This patient has been tested for SLC01B1 variants, and the presence of the *5 heterozygous (CT) genotype has identified this patient at an Intermediate risk for simvastatin-related myopathy. There is a strong association between genetic variation in SLC01B1 and simvastatin-induced myopathy risk.

**Treatment modification is recommended if not otherwise contraindicated:**

- **PREFERRED** Prescribe atorvastatin (LIPITOR) 20 mg daily and stop simvastatin (ZOCOR), startdate 10 AM
- Prescribe pravastatin (PRAVACHOL) 30 mg daily and stop simvastatin (ZOCOR), startdate 10 PM

**Other statin therapy considerations include:**

- Use caution when prescribing statin therapy in patients with predisposing risk factors for myopathy: Age >65 years (This patient's age: 46 years), renal impairment (This patient's Scr: UNAVAILABLE), or other acute medical or surgical conditions which predispose the patient for renal failure.
- Monitor for evidence of muscle injury: elevated Creatine Kinase (CK) level in the absence of a cardiac event, muscle pain, muscle weakness or tenderness, or Rhabdomyolysis.

Click here for [more information](#)

**If simvastatin is not discontinued, please choose desired action:**

- Maintain requested daily dose of simvastatin (ZOCOR) 40 mg at bedtime, startdate 10PM with routine CK monitoring
- Decrease requested daily dose to simvastatin (ZOCOR) 20 mg at bedtime, startdate 10PM with routine CK monitoring
- Decrease requested daily dose to simvastatin (ZOCOR) 10 mg at bedtime, startdate 10PM with routine CK monitoring

**NOTE:** The Vanderbilt P&T Committee has recommended that atorvastatin (if not contraindicated) should replace simvastatin for patients with Intermediate risk for myopathy; if this is not possible continue simvastatin and regular CK monitoring. However, there is not a national consensus on drug/dose guidance in this population.
Azathioprine

TPMT
(Thiopurine Methyltransferase)
Expecting a Very Receptive Audience, Pharmacogenomics Testing for the Enzyme TPMT for Patients Receiving the Drug Azathioprine Will Shortly be Introduced

Azathioprine is commonly used for treatment of inflammatory bowel disease, transplant rejection, rheumatoid arthritis, multiple sclerosis, atopic dermatitis, and acute lymphocytic leukemia.

Severe TPMT enzyme deficiencies can cause severe sometimes life-threatening myelosuppression in patients treated with azathioprine — even if intermediate TPMT activity there is increased risk.
Goals for Pharmacogenomics Testing at Vanderbilt

To optimize the decision about the selection of a specific drug

Example: The choice of Plavix versus Prasugrel or Ticagrelor

To optimize the decision about avoidance of a specific drug

Example: Azathioprine
Goals for Pharmacogenomics Testing at Vanderbilt

To optimize the decision about the use of a drug at a specific dose

Example: Simvastatin

To optimize a decision about the initial dose of a drug

Example: Warfarin
Where Does PREDICT Go From Here?
New Drug-Gene Interactions Coming to Vanderbilt Pharmacogenomics

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<tr>
<th>Drug</th>
<th>Gene</th>
<th>Adverse Outcome</th>
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<tbody>
<tr>
<td>Tacrolimus</td>
<td>CYP 3A5</td>
<td>Acute Organ Rejection</td>
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<tr>
<td>Tamoxifen</td>
<td>CYP 2D6</td>
<td>Cancer Recurrence Skin Hypersensitivity</td>
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<tr>
<td>Abacavir</td>
<td>HLA – B* 57012</td>
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</tr>
</tbody>
</table>

All Estimated to go Live between Fall 2012 and Spring 2013
Essentially All Enzymes for Drug Metabolism Exhibit Common Polymorphisms

Estimated Adverse Events Prevented over 5 years

<table>
<thead>
<tr>
<th>Drug</th>
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<td>Abacavir</td>
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## FDA Labels With Pharmacogenomic Biomarkers

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<td>Tiotropium</td>
<td>CYP2D6</td>
</tr>
<tr>
<td></td>
<td>Tamoxifen</td>
<td>CYP2D6</td>
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<tr>
<td></td>
<td>Tacrolimus</td>
<td>CYP3A5</td>
</tr>
<tr>
<td>Other</td>
<td>Simvastatin</td>
<td>SLCO1B1</td>
</tr>
<tr>
<td></td>
<td>Azathioprine</td>
<td>TPMT</td>
</tr>
<tr>
<td></td>
<td>Warfarin</td>
<td>VKORC1</td>
</tr>
</tbody>
</table>
There is Often More Than 1 Variant Allele

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number of Variants</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2C19</td>
<td>9</td>
<td>Plavix</td>
</tr>
<tr>
<td>SLCO1B1</td>
<td>6</td>
<td>Simvastatin</td>
</tr>
<tr>
<td>VKORC1</td>
<td>1</td>
<td>Warfarin</td>
</tr>
<tr>
<td>CYP2C9</td>
<td>13</td>
<td>Warfarin</td>
</tr>
<tr>
<td>TPMT</td>
<td>1</td>
<td>Azathioprine</td>
</tr>
</tbody>
</table>
After Experience at Vanderbilt with Two Drug Gene Interactions, and the Near-Term Implementation of Several More ...

Can this program be profitable?

*Can this program be scalable?*

What are the roadblocks to success?

**What is the value to patient outcome?**

There is still a level of uncertainty about this central question!
It takes so long to get the result that an activity assay is used to direct the choice of drug and drug dose

The test is so expensive that no insurance company, no hospital, and few patients can pay for the test

No medical decision making is associated with the test result
Summary of the Presentation

Introduction to PREDICT
Warfarin – CYP2C9 / VKORC
Plavix – CYP2C19
Simvastatin – SLCO1B1
Azathioprine - TPMT