### Pharmacogentics Testing: Facilitating Engagement in the Treatment of Co-Occurring Disorders

**Dr. Patricia Allen**  
**Maria Ulmer**  
**Date of Activity: 9/16/2017**

<table>
<thead>
<tr>
<th>Name</th>
<th>Commercial Interests</th>
<th>Relevant Financial Relationships: What Was Received</th>
<th>Relevant Financial Relationships: For What Role</th>
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<tbody>
<tr>
<td>PATRICIA ALLEN</td>
<td></td>
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<td>Employed by SBH</td>
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<tr>
<td>MARIA ULMER</td>
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Pharmacogenetic Testing

Facilitating Engagement in the Treatment of Co-Occurring Disorders

Patricia M. Allen, DNP PMHNP-BC
Maria Ulmer, MA LMFT CAADC
Offered personalized addiction services across a continuum of care in PA, NJ and MA

- Detox, residential, PHP, IOP, outpatient, family, community and alumni programs
- Co-occurring Disorders
- Eating Disorder Program
- Adults, Adolescents and Families
Objectives

1. Apply the principles of evidence-based practice and cost effectiveness in the utilization of genetic testing in the treatment of client with co-occurring disorders.

2. Determine relationship between the use of pharmacogenetics results and treatment engagement outcomes for those with co-occurring disorders.

3. Describe ways in which pharmacogenetic testing can empower the client and support sobriety and resiliency within the co-occurring population.
Overview

- Basics of pharmacogenetics testing
- Criteria for testing
- Case Studies
- Interpreting the test for clients
- Retrospective study results
- Tools of recovery and engagement
Pharmacogenetics & Drug Response

- Pharmacogenetics: the study of DNA sequence variation
- Includes drug metabolism, drug response as well as connect to OTC/herbal
- Genetic variations in drug-metabolizing enzymes can lead to adverse drug reactions (ADRs) and therapeutic failure
- > 50% of U.S. population have gene mutations or variations
- 30 commonly prescribed drugs with high pharmacogenetic risk accounted for 738 million prescriptions in 2013

Evan WE, McLeod HL. NEJM, 2003;348:538-549
Ma Q, LU AYH. Pharmacological Reviews, 2011;63:437-459
# Metabolizer Phenotypes

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Active Drug</th>
<th>Prodrug*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor Metabolizer (PM)</td>
<td>• Require lower dose to avoid side effects and toxicity</td>
<td>• Lack of therapeutic response requires a higher dose</td>
</tr>
<tr>
<td>Intermediate Metabolizer (IM)</td>
<td>• May require lower dose to avoid side effects and toxicity</td>
<td>• Lack of therapeutic response may require a higher dose</td>
</tr>
<tr>
<td>Extensive Metabolizer (EM)</td>
<td>• Standard dose appropriate</td>
<td>• Standard dose appropriate</td>
</tr>
<tr>
<td>Ultra-Rapid Metabolizer (UM)</td>
<td>• Requires higher dose to offset higher rate of metabolism</td>
<td>• May require lower dose to prevent excessive accumulation of active metabolite</td>
</tr>
</tbody>
</table>
Psychiatric drugs whose labels contain PGx information include BUT ARE NOT LIMITED TO:

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>Clomipramine</td>
<td>Fluoxetine</td>
<td>Nefazodone</td>
<td>Protriptyline</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>Clozapine</td>
<td>Fluvoxamine</td>
<td>Nortriptyline</td>
<td>Risperidone</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Desipramine</td>
<td>Iloperidone</td>
<td>Olanzapine</td>
<td>Sertraline</td>
</tr>
<tr>
<td>Atomoxetine</td>
<td>Diazepam</td>
<td>Imipramine</td>
<td>Paroxetine</td>
<td>Thioridazine</td>
</tr>
<tr>
<td>Bupropion</td>
<td>Doxepin</td>
<td>Mirtazapine</td>
<td>Perphenazine</td>
<td>Trimipramine</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Escitalopram</td>
<td>Modafinil</td>
<td>Pimozide</td>
<td>Venlafaxine</td>
</tr>
</tbody>
</table>

Several of these drugs have a boxed warning, which is the FDA’s most serious type of medication labeling.

The FDA labeling for these drugs includes warnings and precautions based upon PGx information which may be associated with dose adjustments, risk for adverse events, or clinical response variability.
Numerous medications are available for the management of psychiatric disorders, such as anxiety, depression and PTSD.

However,
- Many patients do not have symptom relief yet they suffer from side effects
- A patient may start an anti-depressant and not be seen for a follow-up appointment for as long as 4-6 months
- As a result, patients frequently stop their medication due to lack of efficacy or side effects which significantly increases the risk of harm or suicide
The STAR*D Study is a Landmark Study Demonstrating the Impact of Treating Depression

- In the STAR*D study, patients with depression were treated with Celexa for 14 weeks (1st).
- Patients who did not achieve remission* were changed to a new treatment strategy (2nd).
- Patients who still did not achieve remission (after a 14-week trial) could try up to 2 additional successive treatment strategies (14 weeks each 3rd and 4th).

* Remission, or complete recovery from depression, was defined as a score of 7 or less on the 17-item Hamilton Rating Scale for Depression (HAM-D17).

Co-Occurring Disorders

- Over 65% of SUD are co-occurring
  - Substance Use Disorders are often accompanied by MDD, BAD, GAD
- 70-75% of Summit Behavioral Health’s patients present with co-occurring disorders across the continuum of services
- Identification, treatment and engagement are critical for long term recovery outcomes
- Recovery tools - MAT and Pharmacogenetics testing

NIDA, 2015
Delivery of Client Centered Treatment

- Personalized treatment starts with the clinical biopsychosocial assessment
  - Pharmacogenetics testing
  - Medication Assisted Treatment
  - Family involvement
  - Quality of life
Tools of Engagement

- Integrative treatment approach
  - Cohesion, collaboration and coordination
  - “TEAM”
- Environment
  - Trust
  - Safety
  - Sense of community
- Therapeutic strategies
  - Person-centered
  - Comprehensive assessment and evaluation … reevaluation
- Diverse Therapeutic Modalities
- Pharmacology and Pharmacogenetics
So… what works?

➢ “Meet them where they are”

➢ Everything *and* the Kitchen Sink
  ➢ Evidence-based and Measurable
  ➢ Creative and Innovative

➢ Breath of Hope
When presented with the idea of PG testing, we recognized the opportunity to offer cutting-edge and medically driven resources that truly exemplified individualized care.

- Nearly 4 years of testing
- Stats, 2016 132 tests (one location) over one year period
- Of those 132 clients 44% had gene variances
  - 18 genes analyzed, 8 mutations per client
- Prozac, Lexapro, Seroquel and Motrin most common variation
Cost

- Covered by insurance companies
- Typical financial aid
  - $25-$200
- Look at client’s income vs family
- Option of cash payment
Performance Improvement

The journey from anecdotal case studies to Retrospective Review.
Case Study 1

- Client is a 23 year old single male living with parents
- Opiate Use Disorder, Cocaine Use Disorder, MDD and GAD
- DOC: Heroin - 10 bags daily
- Polysubstance abuse from the age of 12
- Longest period of sobriety 7 months
- Supportive family
### Interpreting Test Results

<table>
<thead>
<tr>
<th>Gene</th>
<th>Metabolism Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP1A2</td>
<td>IM</td>
<td>Slightly lower drug metabolism</td>
</tr>
<tr>
<td>CYP 2C 19</td>
<td>UM</td>
<td>Rapid drug metabolism → decrease therapeutic response</td>
</tr>
<tr>
<td>CYP3A5</td>
<td>PM</td>
<td>Very slow metabolism → increase drug toxicity</td>
</tr>
<tr>
<td>HTR2A</td>
<td></td>
<td>Serotonin receptor mutation → impacts medication response</td>
</tr>
<tr>
<td>HTR2C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COMT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTHFR 677C</td>
<td></td>
<td>Methylation</td>
</tr>
</tbody>
</table>
APPLICATION

➢ Stopped Lexapro
➢ Started
  ➢ Neurontin (discontinued after 6 months)
  ➢ Wellbutrin XL 150 mg
  ➢ Vistaril 25 mg BID prn (was 50 mg and TID)

➢ Seroquel 100 mg for sleep (discontinued at 9 months)

➢ Stopped smoking
➢ Stopped ginseng Red Bull
➢ Stopped grapefruit juice

➢ Initiated Vivitrol, committed to 12 months completion
Treatment Outcomes

- Sober 19 months sober
- Mood stabilized
  - “I never thought any medication would help me, I have more energy, my mood is even and I’m getting my life on track”
- Accepted in a graduate program for fall
- Back to work
  - “I bought a boat, that wouldn’t have happened if I were still using”
- Remains engaged in aftercare: individual, aftercare group (weekly)
- AA, sponsor, commitments
- Yoga
Case Study 2

➢ The client is a 25 year old single female living in a sober living home

➢ Dxs: Opiate Use Disorder, Alcohol Use Disorder, Cocaine Use Disorder, MDD, GAD, ADHD.

➢ Trauma history including near death alcohol OD at 14, sexual abuse

➢ History of SI, SIB: cutting and burning

➢ Tx hxs: Rehab, residential, mental health inpatient, PHP, outpatient
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<th>Description</th>
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<tbody>
<tr>
<td>CYP1A2</td>
<td>UM</td>
<td>Rapid drug metabolism → decrease therapeutic response</td>
</tr>
<tr>
<td>CYP 3CA4</td>
<td>IM</td>
<td>Slightly slower drug metabolism → adjust dose</td>
</tr>
<tr>
<td>CYP3A5</td>
<td>PM</td>
<td>Very slow drug metabolism → increased risk of drug toxicity</td>
</tr>
<tr>
<td>COMT</td>
<td>A/A</td>
<td>Impacts mood regulation, associated with efficacy of ADHD meds</td>
</tr>
<tr>
<td>MTHFR</td>
<td>677C</td>
<td>Methylation → important for neurotransmitter production, homocysteine levels</td>
</tr>
</tbody>
</table>
APPLICATION

- Stopped Seroquel
- Stopped Trazodone
- Continued Lamictal 200 mg BID
- Lowered Lexapro 10 mg
- Increased Neurontin 600 QID
- Added Remeron 7.5 mg
- Added pre-natal vitamin
Treatment Outcomes

- Sober over 18 months
  - Longest sobriety was 90 days while in inpatient treatment
- Mood stabilized
- No SI, SIB
- Working
- Active in AA, sponsor, taking commitments
- Engagement increased throughout recurrence of symptoms
Determine if stabilization of the co-occurring opiate and mental health disorder supports engagement and abstinence.

To identify and support best practices leading to sustained engagement and abstinence.

Overall goal of identifying best practices in the care of those we treat with co-occurring disorders.
Outcomes

- Retrospective analysis
- MAT
  - Engagement, sobriety
- Pharmacogenetics testing
  - Stabilization
- Preliminary results
  - Engagement at 30, 60, 90 days
12 months period of time
Males and females 18 or older admitted to outpatient continuum primary opiate use disorder
Clients with a co-occurring psychiatric disorder in addition to the opiate addiction were included in the sample.
Exclusionary criteria include clients with a primary mental health disorder as well as any client with a severe mental health disorder.
Clients with a primary diagnosis other than opiate use disorder were excluded.
Outcomes of Clients with Co-Occurring Disorders and ID Genetics Testing
Results

MAT at 30, 60 and 90 Days

Suboxone

Vivitrol

No MAT
Results

MAT Breakdown

78 clients received No MAT

30 clients were treated with Suboxone

50 clients were treated with Vivitrol
Summary of Findings

➢ Clients receiving MAT (65%) remained engaged longer than those not receiving MAT 37%).

➢ Clients using Vivitrol were nearly equal with Suboxone.

➢ Clients with co-occurring disorders who benefited from pharmacogenetics testing remained engaged longer than those without guided treatment.
Next Steps

➢ Continue evaluation of data: characteristics of those with sustained engagement as well as those that fell off during the 1st 90 days.
➢ Evaluate aspects of engagement
➢ Expand data collection to include evaluation at 12 months
  ➢ Continue to incorporate SBH values of providing client centered, innovative, holistic and evidenced-based treatment to support engagement and recovery.
➢ Reduce the long standing stigma of substance dependence and mental illness, empowering the client
Without Engagement
there can be no Best Practice.