Advancements in the Assessment of Medication Adherence: A Panel Discussion and Case Study

Finding Clarity in the Midst of Uncertainty
Agenda

• Medication adherence in serious mental illness
• Consequences of non-adherence
• Effectiveness of medication monitoring tools
• New Research in medication monitoring solutions
• Case Study: The Center for Health Care Services in Bexar County, Texas
Medication Use in Serious Mental Illness
Adherence Over Time

Estimated Percentage of Patients with Schizophrenia Partially Adherent, Following Discharge (missing 20% - 80% of medications prescribed)

Keith, S., Kane, J. J Clin Psych. 2003;64(11): 1308-3015
Consequences

- Higher likelihood of relapse
- Higher rates of hospitalization
- Increased severity of community violence
- Increased risk of suicide attempts
- Higher rates of comorbid substance abuse

Partial Adherence and Psychiatric Hospitalization in Schizophrenia

Valenstein M., et al; Medical Care 2002; 40(8), 630-639
Substance Use in People with Psychotic Disorders

• Rates: substantial, poorly defined
  – about 50% have recent harmful alcohol or drug use (cannabis, cocaine, stimulants)
  – cannabis makes psychotic symptoms worse
  – plus prescription drug abuse (opiates, benzos, stimulants)

• Self-report is not accurate when substance use is a focus of treatment
Economic Burden

• In 2005, national costs for re-hospitalization related to patients not taking their prescribed antipsychotic medications was an estimated $1.479 billion\textsuperscript{1}

• The Healthcare Cost and Utilization Project calculated $16.1 billion in costs in 2011 for mood disorder-related hospitalizations\textsuperscript{1}

• Improving adherence in schizophrenia could save $1,600 per patient per year in Medicaid and criminal justice costs\textsuperscript{2}

\textsuperscript{1} Sun SX, et al., Curr Med Res Opin. 2007;23(10):2305-12
Effectiveness of medication monitoring tools
Goals of Medication Monitoring

• Identify patients who may not be taking their prescribed medications, *to allow for early intervention*

• Identify possible use of non-prescribed medications or illicit drugs that could interfere with treatment goals

• *Prescribe the right drug, at the right dose, at the right time*
Adherence Monitoring Methods

- Patient self-report
- Pill counts/med refills/MPR
- Clinician impression
- Electronic monitoring
- Plasma levels
- Pharmacy records
- Office-based testing options
- New Tools for Psychotropic Urine Drug Monitoring
Clinical Assessment of Medication Compliance in Schizophrenia

- Patient Self-Report: 86%
- Physician Impression: 66%
- Pill Count: 75%
- Electronic Monitoring: 63%
- Plasma Levels: 49%

Antipsychotic Drugs Detected in a Population with Mental Illness

- Approximately 6% of all the samples had a non-prescribed antipsychotic drug found.
  - 6% of samples that had the prescribed antipsychotic drug present had an additional non-prescribed antipsychotic drug found.
  - 6% of the samples that were missing the prescribed antipsychotic drug had a different antipsychotic drug found.

The Proportion of Prescribed Antipsychotic Medications Found in Urine

N = 7,700

Illicit Substances Found in a Population with Mental Illness


N = 7,700

<table>
<thead>
<tr>
<th>Substance</th>
<th>% of samples</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids</td>
<td>20.2%</td>
<td><strong>1.43</strong> (1.25-1.63)</td>
</tr>
<tr>
<td>Cocaine</td>
<td>6.1%</td>
<td><strong>1.7</strong> (1.35-2.14)</td>
</tr>
<tr>
<td>THC</td>
<td>20.1%</td>
<td><strong>1.4</strong> (1.26-1.57)</td>
</tr>
<tr>
<td>Any Combo</td>
<td>39.9%</td>
<td><strong>1.7</strong> (1.35-2.14)</td>
</tr>
</tbody>
</table>

OR, 1.43; 95% CI, 1.25-1.63
OR, 1.17; 95% CI, 1.02-1.33
OR, 1.4; 95% CI, 1.26-1.57
New Research in medication monitoring solutions
Detection of Aripiprazole in Urine (Dretchen, 2013)

• Metabolite OPC3373 was detected more frequently than aripiprazole and dehydroaripiprazole
  – Aripiprazole detected: 50% of samples
  – Dehydroaripiprazole detected: 8% of samples
  – OPC3373 detected: all samples

• SUMMARY: The detection of OPC3373 should be considered the most reliable indicator of aripiprazole medication use

Quantitative levels of aripiprazole parent drug and metabolites in urine: Methods

• 150 adults, clinically assessed as compliant with a stable aripiprazole regimen had observed dosing for 5 consecutive days.

• Urine specimens, obtained on days 1, 4, and 5
  – Analyzed for pH, creatinine, specific gravity
  – Analyzed for aripiprazole, OPC3373, and dehydroaripiprazole.

• Linear regression was used to assess the association between unadjusted urine levels of each drug/metabolite and dose taken

• Linear stepwise multiple regression was performed to identify variables that added to the explanation of the variance.
Quantitative levels of aripiprazole parent drug and metabolites in urine: Results

OPC3373 was found in 97% of urine samples, whereas unchanged aripiprazole and dehydroaripiprazole were found in only 58 and 39% of samples, respectively.
Quantitative levels of aripiprazole parent drug and metabolites in urine: Results

Quantitative levels of aripiprazole parent drug and metabolites in urine: Results

Predicted ln dose from multiple regression equation vs. ln dose

Quantitative levels of aripiprazole parent drug and metabolites in urine: Conclusions

• Urine levels of aripiprazole and metabolites, when combined with key variables, yields a strong relationship between measurable urine parameters and dose taken.

• By defining the expected range of adjusted urine levels for each dose, the potential exists for a clinical test to identify partially nonadherent individuals who would not have been identified by conventional “present vs. absent” urine drug testing.

Case Study: The Center for Health Care Services
San Antonio, Texas
About The Center for Health Care Services

Serving Adults and Children in Bexar County, Texas at over 14 locations.

In 2014, utilizing 1115 funds, The Center:

- Served 35,000 patients with 712,000 services
- Employed 1,100 social service professionals and administrators with a total payroll of $47 million
Goal of Med Monitoring Program

- Objectively assess the likelihood that patients are taking prescribed medications, so that Prescribers may make clinical decisions with confidence.

- Identify patients who may have problems related to substance abuse and route them to the appropriate care.

- Determine which patients may be at risk for negative clinical outcomes, and provide care accordingly.
Monitoring Protocol

First Six Months:

• Initial assessment of all patients

Ongoing Protocol:

• All new patients

• All walk-in appointments

• All post-hospitalization appointments

• Risk-based monitoring, as determined by the Provider, based on review of previous report and clinical assessment
Testing Panel

Detects the following antipsychotic medications:

- Aripiprazole  
- Quetiapine  
- Risperidone

Also detects:

- Antidepressants
- Stimulants
- Opioids/synthetic opiates

- Clozapine  
- Haloperidol  
- Lurasidone

- Olanzapine  
- Paliperidone  
- Ziprasidone

- Benzodiazepines
- Sedatives/hypnotics
- Illicit drugs
  - Designer drugs
- Alcohol (EtG/EtS biomarker)
Partial Adherence Reference Data

Aripiprazole, Quetiapine XR, Risperidone, and Opioid Medications:

Normalized laboratory results are compared to a database of results from patients who have been clinically assessed as adherent, providing additional information about the likelihood of adherence.
Implementation Process

- Vendor’s Account Executives (AEs) partner with CHCS leadership to ensure the introduction of Medication Monitoring Program is seamless and coordinated throughout the organization.

AE supports Medical team in determining site-specific monitoring protocols and Patient communication.

AE meets with Clinical Leadership to develop workflows that fit with facility’s existing processes.

AE provides training and education to all stakeholders in the Monitoring Program workflow.

- Implementation of monitoring at 9 clinic locations completed in 2 months.
- Report Review training with Medical team to ensure familiarity with Results Reports and ease of interpretation.
- Vendor provides ongoing analytics to Clinical Leadership.
1. Illicit Drugs
   (Cocaine) Benzoylecgonine

2. Medications Or Metabolites Detected But Not Listed On Requisition

<table>
<thead>
<tr>
<th></th>
<th>Hydrocodone</th>
<th>Norhydrocodone</th>
<th>Amphetamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methamphetamine</td>
<td></td>
<td>Ethyl Glucuronide</td>
<td>Ethyl Sulfate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Methamphetamine D/L isomer</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>D Isomer (MS)</td>
<td></td>
<td>91.2%</td>
<td></td>
</tr>
<tr>
<td>L Isomer (MS)</td>
<td></td>
<td>8.8%</td>
<td></td>
</tr>
</tbody>
</table>

**RESULTS EXPLANATION**

The d/l (dextrorotatory /levorotatory) isomer differentiation is a follow-up test to a positive methamphetamine MS confirmation result. The d/l isomer result is reported as a percentage. Greater than 20% concentration of d-isomer methamphetamine can result from either illicit methamphetamine use, use of certain d-methamphetamine containing prescription drugs, or as a metabolite of certain prescription drugs (e.g. benzphetamine).
Monitored Patient Case Study: First Test, 9/14

3. Medication Monitoring Results

<table>
<thead>
<tr>
<th>Medication Prescribed</th>
<th>Test Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATIVAN TABLET</td>
<td>Positive</td>
</tr>
<tr>
<td>SEROQUEL TABLETS EXTENDED RELEASE</td>
<td>Positive</td>
</tr>
<tr>
<td>HALDOL TABLETS</td>
<td>Negative</td>
</tr>
</tbody>
</table>

4. Rx Guardian CD Standard Scores (Current)

The Genesis Summary Report displays Standard Scores and Historical Trends for the following prescribed drugs: Morphine (extended release formulations and Kadian), Hydrocodone (immediate release formulations), Oxycodone (immediate and extended release formulations), Oxymorphone (immediate and extended release formulations), Methadone, Aripiprazole, Quetiapine (extended release formulation) and Risperidone.

Quetiapine (7-Hydroxyquetiapine)

![Graph showing standard score distribution with a cut-off at 2.64]

Less than 5% of patients clinically assessed as adherent in the Rx Guardian CD database have Standard Scores less than -2.0 or greater than +2.0. Less than 1% of patients clinically assessed as adherent in the Rx Guardian CD database have Standard Scores less than -3.0 or greater than +3.0.
Monitored Patient Case Study: Follow-up 5/15

1. Illicit Drugs
   No illicit drugs detected based on provider order.

2. Medications Or Metabolites Detected But Not Listed On Requisition
   No unlisted medications detected.
Monitored Patient Case Study: Follow-up 5/15

3. Medication Monitoring Results

<table>
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</tr>
<tr>
<td>SEROQUEL TABLETS EXTENDED RELEASE</td>
<td>Positive</td>
</tr>
<tr>
<td>KLOPINOPI TABLETS</td>
<td>Positive</td>
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Early Results: Center for Health Care Services

Adult Behavioral Health patients with Standard Scores **outside of +/- 2** for prescribed Antipsychotic

![Standard Score Distribution Graph](image)

Northwest Clinic
Average 300 patients/mth

- August: 40%
- September: 20%
- October: 17%

Zaramora
Average 600 patients/mth

- August: 42%
- September: 14%
- October: 17%

Harvard Place
Average 300 patients/mth

- August: 41%
- September: 25%
- October: 17%

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Average 300 patients/mth

Average 600 patients/mth

Average 300 patients/mth
Early Results: Center for Health Care Services

Adult Behavioral Health patients positive for illicit drugs

Northwest Clinic
Average 300 patients/mth

- August: 20%
- September: 20%
- October: 18%

Zaramora
Average 600 patients/mth

- August: 22%
- September: 19%
- October: 17%

Harvard Place
Average 300 patients/mth

- August: 21%
- September: 19%
- October: 17%
Questions, Discussion