Improving Treatment Adherence in Schizophrenia
How Common Is Nonadherence?

- Nonadherence is estimated to be as high as 60%.
- 40% of annual costs for rehospitalization are due to nonadherence.
- 75% of patients who discontinue their medication experience significant symptom exacerbation over 1 year compared to 25% of those who adhere to their medication.
- Treatment nonadherence is associated with up to a 7-fold increased risk of suicide attempt.

Assessing Nonadherence

- **Patient self-report**
  - Unreliable

- **Physician report**
  - Overly optimistic

- **Pill counts**
  - Easily manipulated

- **Rx renewals**
  - Medication must be obtained from a single source

- **Microelectric monitoring of pill caps**
  - Expensive

- **Physiological monitoring**
  - Invasive

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Factors That May Affect Medication Adherence

- Poor illness insight
- Cognitive deficits
- Positive symptoms
- Doctor/patient relationship
- Treatment efficacy
- Side effects
- Treatment regimen
- Drug abuse

Relationship Between Symptoms and Adherence

- Increased adherence
- Decreased symptoms
- Decreased adherence
- Increased symptoms
Progressive Gray Matter Loss in Adolescent Patients With Schizophrenia Over 5 Years

Gray Matter Loss in Adult Patients With Schizophrenia at Baseline and 5-Year Follow-Up

Excessive gray matter loss was related to an increased number of hospitalizations (increased psychotic episodes).

Psychosis and Brain Volume Changes During the First 5 Years of Schizophrenia

Consequences of Nonadherence on Functional Outcomes

• Nonadherence is associated with:
  – Alcohol-related problems
  – Reduced mental functioning
  – Reduced satisfaction with life
  – Psychiatric hospitalizations
  – Use of emergency psychiatric services
  – Arrests
  – Violence
  – Victimization
  – Substance use

Nonadherence Is Associated With Increased Hospitalization

Partial Nonadherence

- Patient reduces dose of drug or fails to take drug from time to time
- Can lead to unexplained and unanticipated adverse events
- Suboptimal treatment increases risk of relapse
  - A 20% reduction in treatment compliance predicts a 3.1 point increase in PANSS total score

Even Partial Nonadherence Is Detrimental

- Nonadherent patients defined here are those who miss <50% of their medication for 2 weeks or more.
- Missing even <25% of medication for >2 weeks increases the risk for psychotic relapse.

How to Improve Adherence

• Minimize side effects and increase drug efficacy
  – By switching to another antipsychotic

• Utilize long-term depot formulations

• Psychosocial interventions

• Maximize cognitive functioning
Strategies to Improve Adherence

• Basic communication
  – Take the patient's preferences into account
  – Explain the benefits and hazards of treatment options

• Strategy-specific interventions
  – Adjusting medication timing and dosage for least intrusion
  – Minimize adverse effects and maximize effectiveness

• Reminders (psychosocial interventions)

• Evaluate adherence regularly

## Long-Acting Injectable (LAI) Antipsychotics to Improve Medication Adherence

### Advantages
- Assured medication delivery
- Continuous antipsychotic coverage
- No need to remember to take medication every day
- Drug remains in system for 1-2 weeks after a missed dose
- Reduced risk of relapse and rehospitalization
- Avoidance of first-pass metabolism
- Peak plasma level is lower and occurs less often (less side effects?)
- More frequent contact with treatment team
- Increasing number of options available

### Disadvantages
- Cost/insurance coverage
- More appointments
- Oral to LAI conversion
- Perceived stigma
- Negative perceptions by clinicians

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Atypical Antipsychotics With Long-Acting Depot Formulations

- **Iloperidone**: 4 wk in trials
- **Aripiprazole**: 4 wk in trials
- **Paliperidone**: 4 wk, 12 wk in trials
- **Risperidone**: 2 wk, 4 wk in trials
- **Olanzapine**: 2 wk, 4 wk

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Depot Injections Are Associated With a 50-65% Lower Risk of Rehospitalization Compared to Their Oral Counterparts

Not All Studies Show Superiority of Depot Antipsychotics

### Characteristics That May Affect Adherence

<table>
<thead>
<tr>
<th>Atypical Antipsychotic</th>
<th>Dosing Schedule of Oral Formulation</th>
<th>Alternative Formulations</th>
<th>Side Effects*</th>
<th>Additional Caveats</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sedating</td>
<td>Weight Gain</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>1X day</td>
<td>4 wk in trials</td>
<td>10 and 15 mg oral disintegrating tablets; 9.75 mg/1.3 injection</td>
<td>unusual</td>
</tr>
<tr>
<td>Asenapine</td>
<td>2X day</td>
<td>Only available in 5 and 10 mg sublingual tablets</td>
<td>common</td>
<td>not unusual</td>
</tr>
<tr>
<td>Iloperidone</td>
<td>2X day</td>
<td>4 wk in trials</td>
<td>common</td>
<td>common</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>1X day</td>
<td>2 wk 4 wk</td>
<td>Oral disintegrating tablet</td>
<td>common</td>
</tr>
<tr>
<td>Paliperidone</td>
<td>1X day</td>
<td>4 wk 12 wk in trials</td>
<td>Only available in extended release formulation</td>
<td>common</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>2X day</td>
<td>12 wk in trials</td>
<td>common</td>
<td>common</td>
</tr>
<tr>
<td>Quetiapine XR</td>
<td>1X day</td>
<td></td>
<td>common</td>
<td>common</td>
</tr>
<tr>
<td>Risperidone</td>
<td>1X day</td>
<td>2 wk 4 wk in early trials</td>
<td>0.5, 1, and 2 mg oral disintegrating tablets; 1 mg/mL liquid</td>
<td>common</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>2X day</td>
<td>10-20 mg IM formulation available</td>
<td>not unusual</td>
<td>unusual</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>1X day</td>
<td></td>
<td>common</td>
<td>common</td>
</tr>
</tbody>
</table>

*Side effects scale: Unusual = reported in few patients, Not unusual = occurs in a significant minority, Common = many experienced or can be in significant amount, Problematic = occurs frequently, can be in a significant amount, and may be a health problem in some patients.
Psychosocial Interventions

- Supported employment
- Cognitive behavioral therapy (CBT)
- Cognitive adaptation therapy (CAT)
- Cognitive remediation therapy (CRT)
Pharmacy-Based Intervention

Valenstein et al. Schizophr Bull 2009; Epub ahead of print.
Cognitive Remediation Therapy

ACT Now!
Recovery Is Going Fast!
Elements of ACT

• Developed in the 1970s

• Goal
  – Replace crisis-oriented clinical care with intensive community-based intervention

• Design
  – Integrative care is continuous and offered for as long as it is needed
  – Care is available 24/7
  – Team approach to care
The ACT Team

ACT leader
Psychiatrists
Psychiatric nurses
Employment specialist
Substance abuse specialist
Peer specialist
Additional mental health professionals
Program assistant

• The team meets regularly to discuss each case
• At least one team member visits the patient on a regular basis to assess medication efficacy, treatment adherence, medication side effects, physical health, and other issues that could potentially affect recovery

### ACT Services

- Medication prescription, administration, and monitoring
- Illness management and recovery skills
- Continuous assessment and intervention

### Element of Recovery

#### Symptom management

- Crisis assessment and intervention
- Illness management and recovery skills
- Medication prescription, administration, and monitoring

#### Physical health

- Illness management and recovery skills
- Medication prescription, administration, and monitoring
- Individual supportive therapy

#### Reduced hospitalization

- Substance abuse treatment
- Illness management and recovery skills
- Individual supportive therapy

#### Reduced criminal activity

- Housing support services
- Employment-support services
- Transportation

#### Reduced substance abuse

- Intervention with support networks
- Transportation

#### Stable housing

- Intervention with support networks
- Individual supportive therapy

#### Employment

- Frequent interaction with ACT team members
- Integration of patient’s wishes in treatment planning

#### Community involvement

- Individual supportive therapy
- Assistance with activities of daily living
- Case management

#### Family involvement

- Integration of patient’s wishes in treatment planning
- Incorporation of recovering patients as peer specialists on ACT team

#### Treatment alliance

- Cognitive ability

#### Empowerment

- RECOVERY
Is ACT Worth It?

• Direct and indirect costs of treating schizophrenia are ~$60 billion
  – 2/3 of these costs are from hospitalizations

• Increased cost of ACT-based care is offset by:
  – Reduced hospitalizations
  – Reduced use of emergency services
  – Reduced criminal activities and justice system use
  – Increased engagement in the workforce
  – Decreased use of welfare services
  – Reduced death from suicide

• May be most cost-effective for patients who are severely disabled by their illness, have numerous hospitalizations, or are at high risk for relapse