Medication Adherence in the Digital Age

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Speakers are paid consultants for Otsuka Pharmaceutical Development & Commercialization, Inc.
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**Despite Guideline-Based Treatment, Suboptimal Outcomes Remain a Challenge in Serious Mental Illness**

### Major Depressive Disorder (MDD)

<table>
<thead>
<tr>
<th>Study</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STAR*D study</strong></td>
<td>Of &gt;3500 patients, 63%-70% patients did not achieve remission</td>
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</tbody>
</table>

### Schizophrenia

<table>
<thead>
<tr>
<th>Study</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CATIE study</strong></td>
<td>Of &gt;1400 patients,</td>
</tr>
<tr>
<td></td>
<td>• 12% attained and maintained remission for 6 months</td>
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<tr>
<td></td>
<td>• 21% attained and maintained remission for at least 3 months</td>
</tr>
<tr>
<td></td>
<td>• 56% had no symptom remission at any visit</td>
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<tr>
<td></td>
<td>• 74% discontinued treatment before 18 months</td>
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</tbody>
</table>

### Bipolar Disorder (BD)

<table>
<thead>
<tr>
<th>Study</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STEP-BD study</strong></td>
<td>Of &gt;1400 patients, less than 1/3 of symptomatic bipolar patients achieved recovery without recurrence over 2 years of follow-up</td>
</tr>
</tbody>
</table>

CATTIE, Clinical Antipsychotic Trials of Intervention Effectiveness; STAR*D, Sequenced Treatment Alternatives to Relieve Depression; STEP-BD, The Systematic Treatment Enhancement Program for Bipolar Disorder.

Outcomes Associated With Poor Adherence in Schizophrenia or Bipolar Disorder

1. ↑Hospitalizations1-5
2. ↑Length of Stay2,4
3. ↑Number of Suicide Attempts4,5
4. ↓Recovery Rate4,6
5. ↑Relapse Rate3,4

In a 2015 analysis of an insurance database encompassing 32,374 patients with bipolar disorder or schizophrenia, adherence decreased total health costs by $19,4977

Nonadherence Starts Early After Discharge From Hospital and Can Increase Over Time In Schizophrenia

- Despite close monitoring, up to 25% of patients diagnosed with schizophrenia were reported as being nonadherent within 7 to 10 days post discharge\(^1\)
- At least 50% of patients diagnosed with schizophrenia became partially adherent or nonadherent within 1 year and 75% within 2 years of discharge\(^1\)

### Illustration of the time course of antipsychotic medication adherence\(^1\)

- Up to 25% of patients are nonadherent within 7 to 10 days post discharge.
- 50% of patients became partially adherent or nonadherent within 1 year of discharge.
- 75% of patients became partially adherent or nonadherent within 2 years of discharge.

**Antipsychotic adherence is not a stable trait; most patients have difficulties with adherence over time\(^2,3\)**

Multiple Factors Influence Nonadherence

**Social/economic factors**
- Lack of social/family support\(^1,2\)
- Caregiver attitudes to medication and illness\(^1,3\)
- Caregiver ability to supervise/remind patient\(^3\)
- Transportation issues\(^1\)
- Unemployment/financial constraints\(^1,2\)
- Homelessness\(^1,2\)
- Lack of daily routines\(^2\)
- Illiteracy/low level of education\(^1\)

**Treatment-related factors**
- Effectiveness\(^1-3\)
- Side effects\(^1-3\)
- Dose frequency, formulation and treatment duration\(^1,3\)
- Financial cost to patient\(^2,3\)
- Co-prescribed drugs and complexity of regimen\(^1,3\)
- Past medication experience\(^1,3\)

**Health care systems/HCT factors**
- Therapeutic alliance\(^2,3\)
- Ease of access/inadequate reimbursement\(^1,3\)
- Availability of resources\(^5\)
- Discharge planning\(^3,6\)
- Poor medication distribution systems\(^1\)

**Patient-related factors**
- Past history of adherence\(^3,4\)
- Stigma about mental illness\(^1,3\)
- Fear of potential side effects\(^1,2\)
- Belief that medications are not needed\(^1,2\)
- Attitudes to medication and illness\(^2,3\)

**Disease-related factors**
- Poor insight\(^2,3\)
- Cognitive impairment\(^2,3\)
- Severity of symptoms\(^1-3\)
- Substance abuse\(^1-3\)
- Comorbid medical or psychiatric conditions\(^1-3\)

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HCT, health care team.

Identifying Reason(s) for Nonadherence Is Key to Tailored Intervention

<table>
<thead>
<tr>
<th>Reasons for nonadherence that require medication monitoring</th>
<th>Additional tailored interventions</th>
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<tbody>
<tr>
<td>Lack of insight</td>
<td>• Patient psychoeducation</td>
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<tr>
<td></td>
<td>• More frequent/longer visits if possible</td>
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<tr>
<td></td>
<td>• Cognitive behavioral therapy</td>
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<tr>
<td></td>
<td>• Family-focused therapy</td>
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<tr>
<td>Persistent symptoms</td>
<td>• Symptom and side effect monitoring</td>
</tr>
<tr>
<td></td>
<td>• More frequent/longer visits if possible</td>
</tr>
<tr>
<td></td>
<td>• Cognitive behavioral therapy</td>
</tr>
<tr>
<td>Substance use</td>
<td>• Patient psychoeducation</td>
</tr>
<tr>
<td></td>
<td>• Involuntary outpatient commitment</td>
</tr>
<tr>
<td></td>
<td>• Integrated dual diagnosis treatment program</td>
</tr>
<tr>
<td>Logistic problems</td>
<td>• Social work targeting logistic problems</td>
</tr>
<tr>
<td>Lack of routines</td>
<td>• Social work targeting logistic problems</td>
</tr>
<tr>
<td></td>
<td>• Interpersonal and social rhythm therapy</td>
</tr>
<tr>
<td>Cognitive deficits</td>
<td>• Social work targeting logistic problems</td>
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<tr>
<td></td>
<td>• Symptom and side effect monitoring</td>
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<td>Poor therapeutic alliance</td>
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<tr>
<td></td>
<td>• Patient psychoeducation</td>
</tr>
<tr>
<td></td>
<td>• Compliance therapy</td>
</tr>
<tr>
<td>Lack of family and social support</td>
<td>• Family-focused therapy</td>
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<tr>
<td></td>
<td>• Social work targeting logistic problems</td>
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</tbody>
</table>

Methods for Measuring Adherence

Subjective Methods
- Patient or Provider Report

Objective Methods
- Serum Drug Levels
- Pill Counting
- Pharmacy Records
- Technology-Assisted Monitoring

Rx, prescription.
Physicians May Tend to Underestimate Adherence Problems in Their Own Clinical Practice

Rates of Nonadherence Assessed in Patients Diagnosed With Schizophrenia by Various Assessment Methods

<table>
<thead>
<tr>
<th>Adherence assessment method</th>
<th>Nonadherence (%) in a 12-week study (N = 52)</th>
<th>Nonadherence (%) in a 6-month study (N = 61)</th>
<th>Nonadherence (%) in a 12-month study (N = 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotic plasma level</td>
<td>51</td>
<td>57</td>
<td>39</td>
</tr>
<tr>
<td>Electronic monitoring</td>
<td>37</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Physician impression</td>
<td>34</td>
<td>Physician impression</td>
<td></td>
</tr>
<tr>
<td>Pill count</td>
<td>25</td>
<td>5</td>
<td>Claims data (MPR)</td>
</tr>
<tr>
<td>Patient self-report</td>
<td>14</td>
<td>Patient self-report</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Physician impression</td>
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Assessing Optimum Benefit From Antipsychotic Medication: the NOB checklist

<table>
<thead>
<tr>
<th>Individuals Not Receiving Optimum Benefit From Antipsychotic Medication (NOB) Checklist</th>
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</thead>
<tbody>
<tr>
<td>1. Based upon the patient’s report, caregiver report, or your prescribing record, the patient has missed doses since the last visit</td>
</tr>
<tr>
<td>2. Patient is currently on more than 1 antipsychotic (not during a switch)</td>
</tr>
<tr>
<td>3. Patient has been on more than 2 antipsychotics in the past 12 months</td>
</tr>
<tr>
<td>4. Patients has been hospitalized or had a crisis visit in the past 12 months</td>
</tr>
<tr>
<td>5. Patient is not satisfied with current level of symptom control</td>
</tr>
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</table>

Yes responses are indicative of suboptimal benefit and may alert to need for treatment modification.

Digital Technology Is Poised to Become the Fourth Wave of Evolution in Mental Health Care

1890s
Psychoanalysis

1952
Psychopharmacology

1980s-1990s
Evidence-based practice in mental health care

2015
Digital psychiatry

Suboptimal treatment response remains an ongoing concern

Examples of Adherence Technologies in Psychiatry: Smartphone, Tablets, and Computers

- **Calendar-based alarms on phones**¹
  - Can alert patients to take required medication dosages at specific times of day

- **Video chat**²
  - Can allow care provider to directly monitor medication taking

- **Email and text notifications**³
  - Can provide scheduled reminders to take medication

- **Smartphone and tablet apps**¹
  - May include:
    - Reminders for taking and refilling medications
    - Alerts for doctor or pharmacy appointments
    - Pharmacy contact info and/or medication information

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Examples of Adherence Technologies in Psychiatry: Devices

1. **Event marker-signaling devices**
   - Smart pills equipped with sensors or cameras

2. **Facial recognition**
   - Combines with motion-sensing technology to detect pill taking

3. **Breath-based devices**
   - Patient blows into device after taking medication and device detects ingestion

4. **Smart packaging and pill dispensers**
   - Electronic devices that can monitor the opening of a lid or tablet strip

5. **Wearable devices**
   - Detects when medicine is taken and alerts users when it is not

6. **Voice recognition systems**
   - Can request medication refills from pharmacy, remind patients to take medications, track food intake, etc.

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### Potential Pros and Cons of Using Digital Technology in Assessing Adherence

#### Pros*
- Can reduce cost\(^1\)
- Can reduce user effort required\(^1\)
- Can enhance accuracy of adherence measures\(^1\)
- Can communicate adherence measures to the provider\(^1\)\(^†\)
- Can issue reminders and alert messages\(^1\)\(^†\)
- Portable/doesn’t restrict user mobility\(^1\)
- Can monitor in real-time in natural environment\(^1\)
- Most patients with SMI have access to the internet or a smartphone\(^2\)

#### Cons*
- Security and privacy issues\(^1\)
- Certain technologies can be expensive\(^1\)
- System accuracy and data fidelity\(^1\)
- Battery consumption/lifetime\(^1\)
- Acceptability and user comfort (usability)\(^1\)
- Tampering and active non-compliance\(^1\)

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\(*\) Versus manual approaches.

\(^†\) When connected to healthcare systems.

SMI, serious mental illness.

Research is still needed to determine:

- Efficacy of technologies in improving adherence
- Determination of which technology is right for each patient
- Patient satisfaction with technologies
- Outcomes of technology options added to in-person care or combined with other forms of technology

Additionally, there is a need for evidence-based guidelines on the use of such technologies.
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