A CASE-BASED APPROACH TO IMPROVING LONG-TERM OUTCOMES IN SCHIZOPHRENIA ACROSS THE LIFESPAN

SYMPOSIUM LUNCHEON
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Fairfield, Connecticut
DISCLOSURES

The following faculty has no relevant financial relationship to disclose:

Joyce M. Shea, DNSC, APRN, PMHCNS-BC

The faculty for this activity has disclosed that there will be discussion about the use of products for non-FDA approved indications.
At the conclusion of this activity, participants will do the following:

- Implement motivational interviewing strategies to promote adherence to antipsychotic therapy
- Detail the risk factors for nonadherence to therapy in patients with schizophrenia
- Explain the role of long-acting injectable (LAI) antipsychotic agents in improving adherence
- Identify a patient with schizophrenia who might benefit from LAI therapy
Engaging Patients and Building a Therapeutic Relationship

Introduction to Frank
“Drugs are not always necessary. Belief in recovery always is.”

Norman Cousins
Q1. A new client who has been treated for first episode psychosis tells you that all she needs is "a good rest to feel better." This statement suggests the presence of which predictor of treatment discontinuation?

- Sleep disturbance
- Poor insight
- Lack of family/social support
- Depression
1. A new client who has been treated for first episode psychosis tells you that all she needs is “a good rest to feel better.” This statement suggests the presence of which predictor of treatment discontinuation?

- Sleep disturbance: 10
- Poor insight: 125
- Lack of family/social support: 3
- Depression: 3
Clinical Practice Dilemmas
Dilemma #1

Obtaining a complete assessment and achieving the correct diagnosis for Frank

- Value of a clinical staging model\(^1\)
  - Ultra-high risk, 1st episode, critical period

- DSM-5\(^2,3\)
  - Structure of psychotic disorders classification
  - Dimensional assessment of symptoms

Dilemma #2

Working to establish the relationship between Frank and his illness

- Impact on the person
  - Internalized stigma, role engulfment
    - Personal narrative of illness\(^1\)

- Risks and benefits of lack of awareness of illness
  - Links to issues of “adherence”\(^2\)

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Dilemma #3

Collaborating with Frank’s family members and developing resources

- Provider beliefs about family involvement in therapy
- Education and engagement
- Caregiver role strain and support

Dilemma #4

Shared responsibility + decision-making¹

Finding the right medications²,³

Personal Medicine⁴

Pharmacological Treatments in 1st Episode Psychosis
Evidence and Recommendations

- **Multi-site European study**¹
  - Individuals with first-episode schizophreniform and schizophrenic disorders responded to typical (FGAs) and atypical (SGAs) antipsychotic medications
  - Atypical agents showed some superiority in terms of discontinuation rates and tolerability.

- **International practice guidelines favor the use of SGAs as first-line therapy in early psychosis**²
  - Recognize increased risk of weight gain and metabolic problems with select agents.

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Evidence and Recommendations

- Schizophrenia Patient Outcomes Research Team (PORT) cite evidence supporting the use of either FGAs or SGAs as first-line treatment for patients experiencing their initial positive symptom episode.¹
  - Not clozapine and olanzapine

- No evidence that LAI preparations of FGAs or risperidone offer additional benefits or disadvantages in first-episode patients.²

Evidence and Recommendations

- Individuals with first-episode schizophrenia tend to be more responsive to antipsychotic treatment in general and to be more sensitive to adverse effects.
  - Recommendation is to **start with lower doses** than those used with multi-episode patients
    - FGAs: 300-500 mg CPZ equivalents per day
    - Risperidone and Olanzapine: lower half of daily dosage range for multi-episode patients (1-4 mg and 5-10 mg, respectively)
    - Quetiapine: titrate up to 500-600 mg/day
    - Aripiprazole and Ziprasidone had not been evaluated

Focus on Medication Adherence
Medication Adherence

- Generally defined as the “failure or refusal to comply with treatment recommendations”

- Two types of medication adherence problems:
  - **Complete medication cessation** – “medication refusers”
    - Individuals who do not see the need for or cannot tolerate taking the AP medications.
  - **Partial adherence** – “medication acceptors”
    - Individuals who follow the regimen sporadically or take a lower dose but are not generally opposed to taking AP medications.

Partial Adherence in Schizophrenia Begins Early and Prevalence Increases Over Time

![Graph showing adherence over time](slide_theory.png)

- **10-14 Days**: 25%
- **1 Year**: 50%
- **2 Years**: 75%

Slide courtesy of PJ Weiden, MD

Impact of Non-Adherence

COSTS + RISKS
$290bn/year$^{1}$

- Acute symptom relapse
- Suicide
- Arrest
- Prolonged hospitalization$^{2}$

Factors Influencing Adherence

Conflicting Evidence About Adherence

- Poor insight possibly linked to nonadherence\(^1\)

- Opposing effects on QoL\(^2\)
  - More adherence = fewer psychotic symptoms + higher QoL
  - More adherence = more med SEs + lower QoL

- Relapse common among med-adherent patients, especially with co-occurring substance abuse\(^3\)

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Q2. A 30-year-old woman with schizophrenia has been on an oral antipsychotic agent for the past 5 years. At this visit, she tells you, "I'm done taking these pills because they make me tired." What response from you is most likely to support medication adherence?

- "You know that if you don’t take your medication you might have a relapse."
- "Have you thought about taking physical exercise and changing your diet?"
- "You’re concerned that the pills are making you feel tired. Would you like to discuss other options?"
- "That’s not good. We should change your medication to an injectable drug."
Peer Responses from Live Event

2. A 30-year-old woman with schizophrenia has been on an oral antipsychotic agent for the past 5 years. At this visit, she tells you, “I’m done taking these pills because they make me tired.” What response from you is most likely to support medication adherence?

“You know that if you don’t take your medication you might have a relapse.”

“Have you thought about taking physical exercise and changing your diet?”

“You’re concerned that the pills are making you feel tired. Would you like to discuss other options?”

“That’s not good. We should change your medication to an injectable drug.”

Votes:
1. 1
2. 2
3. 4
4. 223

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Note: The bar graph shows the number of votes for each response option.
Motivational Interviewing

A Strategy to Enhance Adherence and Support Recovery
Motivational Interviewing

- Based on a model of change that focuses on one’s attitudes with respect to treatment and insight over time\(^1\)
- A “client-centered counseling style for eliciting behavior change by helping clients to explore and resolve ambivalence”\(^2\)
- Incorporates 5 basic principles that allow the person to “discover the advantages and disadvantages of their behaviors for themselves”\(^3\)

Principles of MI

- Express empathy
- Develop discrepancy
- Avoid arguing
- Roll with resistance
- Support self-efficacy

Steps for Information Provision with MI

ASK the CLIENT:

- What do you already know about X?
- Could I provide you with new information about X?
- What do you think/feel about this new information?

MI Outcomes

- More persuasive and supportive than coercive and argumentative
- Better outcomes with longer and more numerous sessions of MI\(^1\)
  - Can be effective with even 15 minute sessions
- Better relationship between clinician and client\(^2\)

MI Outcomes

- Clearly within the nurse’s scope of practice\(^1\)
- Limited research on the effectiveness of MI in increasing medication adherence among those with schizophrenia\(^2\)
- MI can allow those with schizophrenia “to explore their own goals and to take a more active role in treatment”\(^3\)

Patient Preferences in Therapy Selection

The Role of Long-Acting Injectable Antipsychotic Agents in Preventing Relapse

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Disclosures

Leslie Citrome, MD, MPH
Consultant: Alexza, Alkermes, Bristol-Myers Squibb, Eli Lilly, Forest, Forum (Envivo), Genentech, Janssen, Jazz, Lundbeck, Merck, Medivation, Mylan, Novartis, Noven, Otsuka, Pfizer, Reckitt Benckiser, Reviva, Shire, Sunovion, Takeda, Teva

Speakers Bureau: AstraZeneca, Forest, Lundbeck, Novartis, Otsuka, Sunovion, Takeda, Teva

Shareholder: Bristol-Myers Squibb, Eli Lilly, Johnson & Johnson, Merck, Pfizer

The faculty for this activity has disclosed that there will be discussion about the use of products for non-FDA approved indications.
Six Years Later: What’s New? What’s Different? What’s Next?

- 25 years old
- Many episodes
- Used different medications
- Factors that influence effective treatment
- Best strategies for involving Frank in treatment choices
What is Evidence-Based Medicine?
What Is Evidence-Based Medicine?

Clinical Judgment

Relevant Scientific Evidence

Patients’ Values and Preferences

EBM

Sackett DL et al. BMJ. 1996;312(7023):71-72
What Is Evidence-Based Medicine?

Sackett DL et al. BMJ. 1996;312(7023):71-72
Consider Side Effect Profile

- Side effects may:\(^1\)
  - Contribute to treatment nonadherence
  - Limit return to maximal levels of social functioning
  - Potentially contribute to long-term morbidity
- SGAs are generally better tolerated than FGAs regarding EPS\(^2\)
- Differences exist among SGAs regarding adverse effect profiles
  - Metabolic effects, sedation, akathisia, etc.
  - May impact treatment adherence and long-term outcomes\(^1,2\)

Reverberations from Side Effects
How Patient and Clinician Responses May Differ

Therapeutic Features of Antipsychotics

All Drugs are Different
Comparative Efficacy and Tolerability of 15 Antipsychotic Drugs in Schizophrenia

Rank Order for Efficacy

Figure 3: Forest plot for efficacy of antipsychotics drugs compared with placebo

Treatments are ranked according to their surface under the cumulative ranking (SUCRA) values (appendix p 98).

SMD=standardised mean difference. CrI=credible interval.

Different Rank order for Weight Gain

…And Different for EPS

...And Different for Prolactin Elevation

![Graph showing prolactin increase SMD (95% CI) for various drugs.]

- Risperidone: 1.23 (1.06 to 1.40)
- Paliperidone: 1.30 (1.08 to 1.51)
- Other drugs listed with their prolactin increase SMD (95% CI)

"Risperidone and Paliperidone Boundary"

...And Different for QTc Prolongation

…And Different for Sedation

Q3. According to clinical evidence in schizophrenia, which statement concerning LAIs is correct?

- LAIs have shown noninferiority in efficacy compared to placebo.
- There are no differences in efficacy among first- and second-generation LAIs.
- LAIs have been shown to reduce the time to relapse.
- LAIs are noninferior to oral antipsychotics in reducing time to relapse.
3. According to clinical evidence in schizophrenia, which statement concerning LAIs is correct?

- LAIs have shown noninferiority in efficacy compared to placebo.  
- There are no differences in efficacy among first- and second-generation LAIs.  
- LAIs have been shown to reduce the time to relapse.  
- LAIs are noninferior to oral antipsychotics in reducing time to relapse.

**Votes:**
- 2 for the first statement
- 11 for the second statement
- 182 for the third statement
- 27 for the fourth statement
What About Long-Acting Injectable Antipsychotics?
Advantages of LAI Antipsychotics

- Reduces dosage deviations\(^1\)
- Eliminates guessing about adherence status\(^2,3\)
- Shows start date of nonadherence\(^2,3\)
- Disentangles reasons for poor response to medication\(^3\)
- Eliminates need for the patient to remember to take a pill daily\(^1\)
- Enables prescribers to avoid first-pass metabolism + establish a better relationship between dose and blood level\(^1\)
- Results in predictable and stable plasma levels\(^1\)
- Eliminates abrupt loss of efficacy if dose missed\(^1,3\)
- Some patients may prefer them, especially if already receiving LAIs\(^4\)

Potential Obstacles

- Lack of infrastructure in outpatient settings
- Need to refrigerate, store, reconstitute, etc
- Overburdened public agencies
- Frequency of injections and consequent inconvenience for staff and patients
- Need to take concomitant medications orally
- Anti-shot sentiment

LAIIs Are Infrequently Used

- Most clinicians report using long-acting injectable atypical antipsychotics in <10% of patients\(^1\)
- Psychiatrists have not offered an LAI antipsychotic to nearly two-thirds of their patients\(^2\)
- Only 12.4% of patients who were not taking oral therapies as prescribed were switched to a LAI antipsychotic formulation during a 3-year prospective study\(^3\)

Reasons for Not Prescribing LAI Atypical Antipsychotics

- Sufficient Adherence to Oral: 86%
- Patient Refusal: 80%
- Antipsychotic Not Available as LAI: 75%
- Costs of Drug: 71%
- Not Appropriate Option After Relapse: 68%
- Poorer Control of Effect Compared to Oral Drug: 58%
- High EPS Risk With LAI: 31%

EPS=extrapyramidal symptom; LAI=long-acting injectable.

Long-Acting Injectable Antipsychotics Reduce Relapse in Long-Term Studies

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Depot Events</th>
<th>Oral Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arango 2005</td>
<td>10</td>
<td>6</td>
<td>26</td>
<td>5.2%</td>
<td>1.28 [0.56, 2.93]</td>
<td></td>
</tr>
<tr>
<td>Barnes 1983</td>
<td>3</td>
<td>3</td>
<td>19</td>
<td>1.9%</td>
<td>0.89 [0.21, 3.85]</td>
<td></td>
</tr>
<tr>
<td>Del Guidice 1975</td>
<td>21</td>
<td>30</td>
<td>31</td>
<td>22.8%</td>
<td>0.80 [0.65, 0.99]</td>
<td></td>
</tr>
<tr>
<td>Falloon 1978</td>
<td>8</td>
<td>5</td>
<td>20</td>
<td>4.2%</td>
<td>1.92 [0.74, 4.95]</td>
<td></td>
</tr>
<tr>
<td>Gaebel 2010</td>
<td>54</td>
<td>102</td>
<td>355</td>
<td>18.6%</td>
<td>0.53 [0.39, 0.71]</td>
<td></td>
</tr>
<tr>
<td>Hogarty 1979</td>
<td>22</td>
<td>32</td>
<td>55</td>
<td>14.8%</td>
<td>0.63 [0.43, 0.92]</td>
<td></td>
</tr>
<tr>
<td>Li 1996</td>
<td>32</td>
<td>52</td>
<td>155</td>
<td>15.1%</td>
<td>0.54 [0.37, 0.79]</td>
<td></td>
</tr>
<tr>
<td>Potapov 2008</td>
<td>4</td>
<td>8</td>
<td>20</td>
<td>3.6%</td>
<td>0.50 [0.18, 1.40]</td>
<td></td>
</tr>
<tr>
<td>Rifkin 1977</td>
<td>2</td>
<td>3</td>
<td>23</td>
<td>1.4%</td>
<td>0.81 [0.15, 4.45]</td>
<td></td>
</tr>
<tr>
<td>Schooler 1979</td>
<td>26</td>
<td>35</td>
<td>143</td>
<td>12.4%</td>
<td>0.76 [0.49, 1.20]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) | 843 | 829 | 100.0% | 0.70 [0.57, 0.87] |
Total events | 182 | 276 |

Heterogeneity: Tau² = 0.04; Chi² = 15.35, df = 9 (P = 0.08); I² = 41%
Test for overall effect: Z = 3.32 (P = 0.0009)

**Long-Acting Injectable Antipsychotics Not Different Regarding Adverse Event Drop-Out Rate in Long-Term Studies**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Depot Events</th>
<th>Oral Events</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arango 2005</td>
<td>0</td>
<td>26</td>
<td></td>
<td>Not estimable</td>
</tr>
<tr>
<td>Barnes 1983</td>
<td>1</td>
<td>19</td>
<td>5.4%</td>
<td>0.89 [0.06, 13.23]</td>
</tr>
<tr>
<td>Del Guidice 1975</td>
<td>0</td>
<td>27</td>
<td></td>
<td>Not estimable</td>
</tr>
<tr>
<td>Falloon 1978</td>
<td>0</td>
<td>20</td>
<td></td>
<td>Not estimable</td>
</tr>
<tr>
<td>Gaebel 2010</td>
<td>8</td>
<td>355</td>
<td>28.3%</td>
<td>0.80 [0.32, 2.00]</td>
</tr>
<tr>
<td>Hogarty 1979</td>
<td>5</td>
<td>55</td>
<td>4.8%</td>
<td>10.02 [0.57, 176.70]</td>
</tr>
<tr>
<td>Potapov 2008</td>
<td>3</td>
<td>20</td>
<td>15.0%</td>
<td>1.00 [0.23, 4.37]</td>
</tr>
<tr>
<td>Rifkin 1977</td>
<td>8</td>
<td>23</td>
<td>15.5%</td>
<td>4.87 [1.14, 20.72]</td>
</tr>
<tr>
<td>Schooler 1979</td>
<td>10</td>
<td>143</td>
<td>31.0%</td>
<td>1.03 [0.44, 2.39]</td>
</tr>
</tbody>
</table>

**Total (95% CI)**

- Total events: 35
- Total: 688
- 100.0%
- Risk Ratio: 1.34 [0.70, 2.58]

Heterogeneity: Tau² = 0.17; Chi² = 6.84, df = 5 (P = 0.23); I² = 27%
Test for overall effect: Z = 0.88 (P = 0.38)

Controversy: An Expanded Meta-analysis Found No Differences in Study-Defined Relapse/All-Cause Discontinuation Between LAIs and Oral Antipsychotics…

| Fluphenazine | 8 | 826 | 0.79 | 0.02 |
| Haloperidol | 1 | 25  | 0.99 | 0.97 |
| Olanzapine LAI | 2 | 1,445 | 1.08 | 0.65 |
| Risperidone LAI | 9 | 2,608 | 0.98 | 0.88 |
| Zuclopenthixol | 1 | 46  | 1.28 | 0.56 |
| **Total** | 21 | 4,950 | 0.93 | 0.35 |

| Fluphenazine | 7 | 721 | 1.00 | 0.98 |
| Haloperidol | 1 | 29  | 0.79 | 0.52 |
| Olanzapine LAI | 2 | 1445 | 1.24 | 0.25 |
| Risperidone LAI | 9 | 2641 | 1.00 | 0.98 |
| Zuclopenthixol | 1 | 46  | 0.51 | 0.44 |
| **Total** | 20 | 4,882 | 1.03 | 0.65 |

AP, antipsychotic; CI, confidence interval; LAI, long-acting injectable antipsychotic; RR, relative risk

...Perhaps Because LAIs Were Not Superior to Oral Antipsychotics Regarding Adherence in RCTs?

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>LAI Events</th>
<th>OAP Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (95% CI)</td>
<td>955</td>
<td>1063</td>
<td>100.0%</td>
<td>0.77 [0.49, 1.22]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>55</td>
<td>73</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.19; Chi² = 14.90, df = 9 (P = 0.09); I² = 40%
Test for overall effect: Z = 1.10 (P = 0.27)
Test for subgroup differences: Chi² = 3.00, df = 2 (P = 0.22), I² = 33.3%

OAP, oral antipsychotic; CI, confidence interval; LAI, long-acting injectable antipsychotic; RR, relative risk

In “Mirror-Image” Studies, LAIs reduce risk of hospitalization compared with oral antipsychotics

AP, antipsychotic; CI, confidence interval; LAI, long-acting injectable antipsychotic; RR, relative risk

Real-World Studies Favor Use of LAI Antipsychotics

As study design shifts toward real-world populations, LAI formulations display significant advantages.

LAI=long-acting injectable antipsychotic; RCT=randomized controlled trial; RR=risk ratio.
LAI Antipsychotics

Is there a case for earlier use?
Potential Advantages of Enhanced Adherence

- Potentially decrease the percentage of time spent experiencing psychotic symptoms
  - In the first 2 years experiencing psychotic symptoms is the **strongest predictor** of long-term symptoms and disability\(^1\)

- Potentially decrease number of psychotic episodes
  - Patients experience *a decrease in treatment response* with subsequent exacerbations\(^2\)
  - Neuropathological *brain changes often progress* with subsequent clinical episodes\(^3\)

- LAI antipsychotics allow for *swift identification of overt nonadherence* and eliminate covert nonadherence\(^4\)

The Case for Earlier Use

“A paradigm shift is afoot in which the "last shall be first," namely, use of long-acting injectable (LAI) antipsychotics, rather than being reserved for use only at the last stages of schizophrenia, may be shifting to first-line treatment of early episodes of this illness.”

Patient Acceptance of LAI Antipsychotic Therapy

- In a survey of psychiatrists, patient refusal was cited as a primary reason for not prescribing LAI antipsychotics¹
- BUT, in a survey of patients without LAI antipsychotic experience, 79% cited they had never been informed about the option by their psychiatrist²
- In a survey of patients with ≥3 months of LAI antipsychotic experience:
  - Injectable antipsychotics were the preferred formulation³
  - 70% of patients felt better supported in their illness by virtue of regular contact with the doctor or nurse who administered their injection³

<table>
<thead>
<tr>
<th></th>
<th>RLAI</th>
<th>OLAI</th>
<th>PLAI</th>
<th>ALAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year approved</td>
<td>2003</td>
<td>2009</td>
<td>2009</td>
<td>2013</td>
</tr>
<tr>
<td>Other indications?</td>
<td>Bipolar disorder</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Injection sites</td>
<td>Deltoid or gluteal</td>
<td>Gluteal</td>
<td>Deltoid or gluteal</td>
<td>Gluteal</td>
</tr>
<tr>
<td>Needle gauge</td>
<td>20G or 21G</td>
<td>19G</td>
<td>22G or 23G</td>
<td>21G</td>
</tr>
<tr>
<td>Injection volume</td>
<td>~2 mL</td>
<td>1.0 to 2.7 mL</td>
<td>0.25 to 1.5 mL</td>
<td>2 mL (400 mg)</td>
</tr>
<tr>
<td>Injection frequency</td>
<td>Every 2 weeks</td>
<td>Every 2 or 4 weeks</td>
<td>Every 4 weeks</td>
<td>Every 4 weeks</td>
</tr>
<tr>
<td>Starting dose</td>
<td>25 mg</td>
<td>Varies from 210 mg q2wk or 405 mg q4wk to 300 mg q2wk</td>
<td>234 mg Day 1 + 156 mg Day 8 in deltoid</td>
<td>400 mg</td>
</tr>
<tr>
<td>Maintenance dose</td>
<td>25 mg (max 50 mg)</td>
<td>Varies from 150 mg q2wk or 300 mg q4wk to 300 mg q2wk</td>
<td>117 mg (range 39 to 234 mg)</td>
<td>300 or 400 mg (adjust for CYP2D6 or CYP3A4 issues)</td>
</tr>
<tr>
<td>Oral supplementation?</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Reconstitution needed?</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Refrigeration needed?</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Requires observation?</td>
<td>No</td>
<td>3 hours</td>
<td>No</td>
<td>No</td>
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## Curious About Cost?

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Cost to Hutchings Psychiatric Center, NY</th>
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<tbody>
<tr>
<td>Fluphenazine</td>
<td>$68 per 5-mL vial (25 mg/mL)</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>$18 for 1 mL 50 mg/mL; $34 for 1 mL 100 mg/mL</td>
</tr>
<tr>
<td>RLAI</td>
<td>$128 for 12.5 mg, $257 for 25 mg, $385 for 37.5 mg, $514 for 50 mg</td>
</tr>
<tr>
<td>PLAI</td>
<td>$256 for 39 mg, $513 for 78 mg, $771 for 117 mg, $1,028 for 156 mg, $1,542 for 234 mg</td>
</tr>
<tr>
<td>OLAI</td>
<td>$540 for 210 mg, $772 for 300 mg, $1,042 for 405 mg</td>
</tr>
<tr>
<td>ALAI</td>
<td>$1,050 for 300 mg, $1,408 for 400 mg</td>
</tr>
</tbody>
</table>

Avoidance of Relapse…
How to Choose a LAI Agent
How to Choose a Long-Acting Injection

1. Is the patient demonstrating adequate efficacy and tolerability on oral fluphenazine, haloperidol, risperidone, paliperidone, olanzapine, or aripiprazole?
   - Switch to the corresponding depot formulation
   - For patients receiving oral risperidone, can consider using paliperidone palmitate for convenience
     - No requirement for oral supplementation upon initiation, less frequent injections, supplied in prefilled syringes, smaller needle bore, lower injection volume, no refrigeration required
   - For patients receiving oral fluphenazine or haloperidol, need to weigh the potential disadvantages of using concomitant oral anticholinergics for the management of motoric adverse effects
     - These agents add complexity to the regimen (an oral tablet/capsule)
     - Anticholinergic agents can interfere with memory and other cognitive functions

2. Is the patient being treated acutely?
   - Consider depot antipsychotics that do not require oral supplementation and where the clinical trials have demonstrated acute efficacy, either paliperidone palmitate or olanzapine pamoate

3. Are weight gain and metabolic adverse effects a concern for this individual patient?

- Consider aripiprazole monohydrate, paliperidone palmitate, or risperidone microspheres among the SGAs, in that order
- Can consider the first-generation long-acting injectable antipsychotics as well

4. Is prolactin elevation a clinical concern for this individual patient?

- Consider aripiprazole monohydrate
- Avoid paliperidone palmitate, risperidone microspheres, or the first-generation long-acting injectable antipsychotics

5. Is cost the primary concern?

- The first-generation depot antipsychotics may be the only option available

6. Are any of the following people or entities NOT enrolled in the Olanzapine Pamoate Patient Care Program: patient, prescriber, health care facility, pharmacy?

- Olanzapine pamoate cannot be used

Q4. A 19-year-old student who recently experienced first episode psychosis is being treated with daily oral fluphenazine 6 mg. He develops akathisia, which he finds distressing, and his medication is switched to a second-generation LAI. Which statement best describes the rationale for this switch?

- LAIs reduce side effects that are known to be risk factors for non or partial adherence.
- LAIs improve ease of administration and reduce clinic appointments.
- Dose adjustments can be made easily with LAIs to address the side effects.
- LAIs are more efficacious than oral antipsychotic formulations.
4. A 19-year-old student who recently experienced first episode psychosis is being treated with daily oral fluphenazine 6 mg. He develops akathisia, which he finds distressing, and his medication is switched to a second generation LAI. Which statement best describes the rationale for this switch?

- LAIs reduce side effects that are known to be risk factors for non or partial adherence: 143
- LAIs improve ease of administration and reduce clinic appointments: 3
- Dose adjustments can be made easily with LAIs to address side effects: 6
- LAIs are more efficacious than oral antipsychotic formulations: 8
Treatment Is a Dynamic Process

- Switches offer both *opportunity* and *risk*
- A medication does not have to be perfect
  - Does it relieve symptoms well enough?
  - Is it tolerated well enough?
  - Is the patient willing to take it?
- Shared decision-making and patient “buy-in”
  - Symptoms
  - Tolerability
Switch or Stay?

- Past history of efficacy of drug response
- Nature of psychiatric condition, acuity
- Target signs and symptoms
- Patient preference, history of adherence
- Need for special monitoring
- Amenable to other interventions to address tolerability?
  - Diet, exercise, and statins for obesity and dyslipidemia
  - Beta-blockers for akathisia
  - Anticholinergic medications for EPS
Sustaining Therapy Across the Lifespan

Frank: Ten Years Later at 35

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Loganville, Georgia
Georgia State University
College of Health and Human Sciences
Atlanta, Georgia
Disclosures

Kimberly Littrell, MS, APRN, PMHCNS-BC
Speakers Bureau Forest, Sunovion

The faculty for this activity has disclosed that there will be discussion about the use of products for non-FDA approved indications.
Practice Guidelines and Algorithms

- Emerged in the 1990s to provide a system of uniform clinical care, estimate health care costs, and evaluate health care benefits
- Professional Associations and Clinical Experts
- Mental Health Systems
  - Public and Private
  - Local, State, and Federal Levels
    - The Texas Medication Algorithm Project
    - Schizophrenia PORT (Patient Outcomes Research Team) Recommendations
    - Surgeon General’s Report on Mental Health
- Insurance Carriers and Health Benefit Administrators
Psychiatric Rehabilitation
Collaborative Care

Residential

Educational

Medications

Spiritual

Psychiatry

Medical

Dental

Advocacy

Vocational

12-Step Dual Diagnosis

Impact of Collaborative Care

- Recovery of a normal life in the community
- Reduce impairments, disabilities, and handicaps
- Active family involvement
- Build on patients’ strengths, interests, and capabilities
- Integrate + coordinate services
- Requires time, patience, and resilience

Individualization of treatment is a fundamental pillar of rehabilitation.

Relevant Terminology: Recovery

- Process of managing one’s illness and disability
  - Least amount of interference with normal life
  - May still have symptoms + be receiving treatment
- Requires increasing competency in:
  - Psychosocial functioning
  - Management of the illness and associated impairments
  - Cognitive functioning

Collaborative Care Model
Collaborative Care Model

Assessment

- Systematic approach to collecting baseline data to identify strengths, capabilities, and aptitudes as well as current and future needs
- Degree of enduring symptoms including the cognitive impact of the illness
- Patient’s level of knowledge about schizophrenia, prescribed medications, possible side effects
- Current stressors, response to stress, and coping style
- Readiness to set rehabilitation goals
- Necessary skills and overall functionality
  - Self-care
  - Nutritional habits
  - Money management
  - Problem solving
- Basic resources and supports

Planning

During the planning process several important functions are performed:

- Setting priorities and goals
- Appraising strengths
- Selecting appropriate interventions
- Determining resources

Everyone works together to:

- Clarify personal choices
- Identify environmental options
- Clarify personal values
- Identify personal interests

Littrell KH, Littrell SH. *Psychiatric Annals*. 1998;28(7):
Implementation

- The actual “carrying out” of the rehabilitation plan
- The patient, family (if available), and treatment team assume JOINT RESPONSIBILITY in setting the plan in motion

Implementing Vocational Strategies

- The return to work should be a major focus of the rehabilitative process for anyone who identifies this as a goal\(^1\).

- In the CATIE Trial, baseline data from 1,400 patients was collected prior to entry. In the month before the baseline assessment\(^2\):
  - 14.5% of the patients reported participating in competitive employment
  - 12.6% reported other (noncompetitive) employment activity
  - 72.9% reported no employment activity

- A review of 9 controlled trials showed that employment rates for people with schizophrenia, even with optimal support, range from only 30% to 80%, with a median of 60% across studies\(^3\).

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\(^1\)The President’s New Freedom Commission on Mental Health. *Achieving the Promise: Transforming Mental Health Care in America*. Rockville, MD: US Department of Health and Human Services; 2003. DHHS Publication SAM-03-3832;


Evaluation

- Determine the degree to which our initial goals have been accomplished or have failed...and why?
- Do we modify the goals or develop new ones?
- Ongoing and integral element of the entire process

If there is failure to meet an established goal, especially a consistent failure, we must look closely to evaluate potential barriers to recovery.
Q5. A 26-year-old man with schizophrenia recently secured part-time employment. He is adamant that he no longer needs antipsychotic medication. Which response is most likely to support medication adherence?

- Suggest an immediate psychiatric consult for your client.
- Tell your client he should not stop his medication.
- Remind your client how well he has been doing and how important it is to stick with treatment.
- Explore with your client his long-term goals.
5. A 26-year-old man with schizophrenia recently secured part-time employment. He is adamant that he no longer needs antipsychotic medication. Which response is most likely to support medication adherence?

- Suggest an immediate psychiatric consult for your client: 1
- Tell your client he should not stop his medication: 3
- Remind your client how well he has been doing and how important it is to stick with treatment: 37
- Explore with your client his long-term goals: 113
Metabolic Monitoring
Metabolic Changes

- Hyperglycemia
- Dyslipidemia
- Weight gain

In 2003, the Food and Drug Administration (FDA) required all manufacturers of atypical antipsychotics to change their labeling to include a warning about the risks of hyperglycemia and diabetes with atypical antipsychotics.
## Monitoring Metabolic Side Effects

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Conclusions

- New antipsychotics have demonstrated enhanced efficacy for a wide range of schizophrenia symptoms.
- Safety and tolerability of antipsychotic medications is important for short-term acceptance and long-term adherence.
- These newer antipsychotics improve the landscape of recovery and require diligent efforts to capture their benefits.
- There is a crushing need to incorporate Collaborative Team approaches which enhance adherence and foster true recovery.