

The Under Utilization of Long-Acting Injectable Antipsychotics in the Treatment of Schizophrenia and Bipolar Disorder in Kentucky

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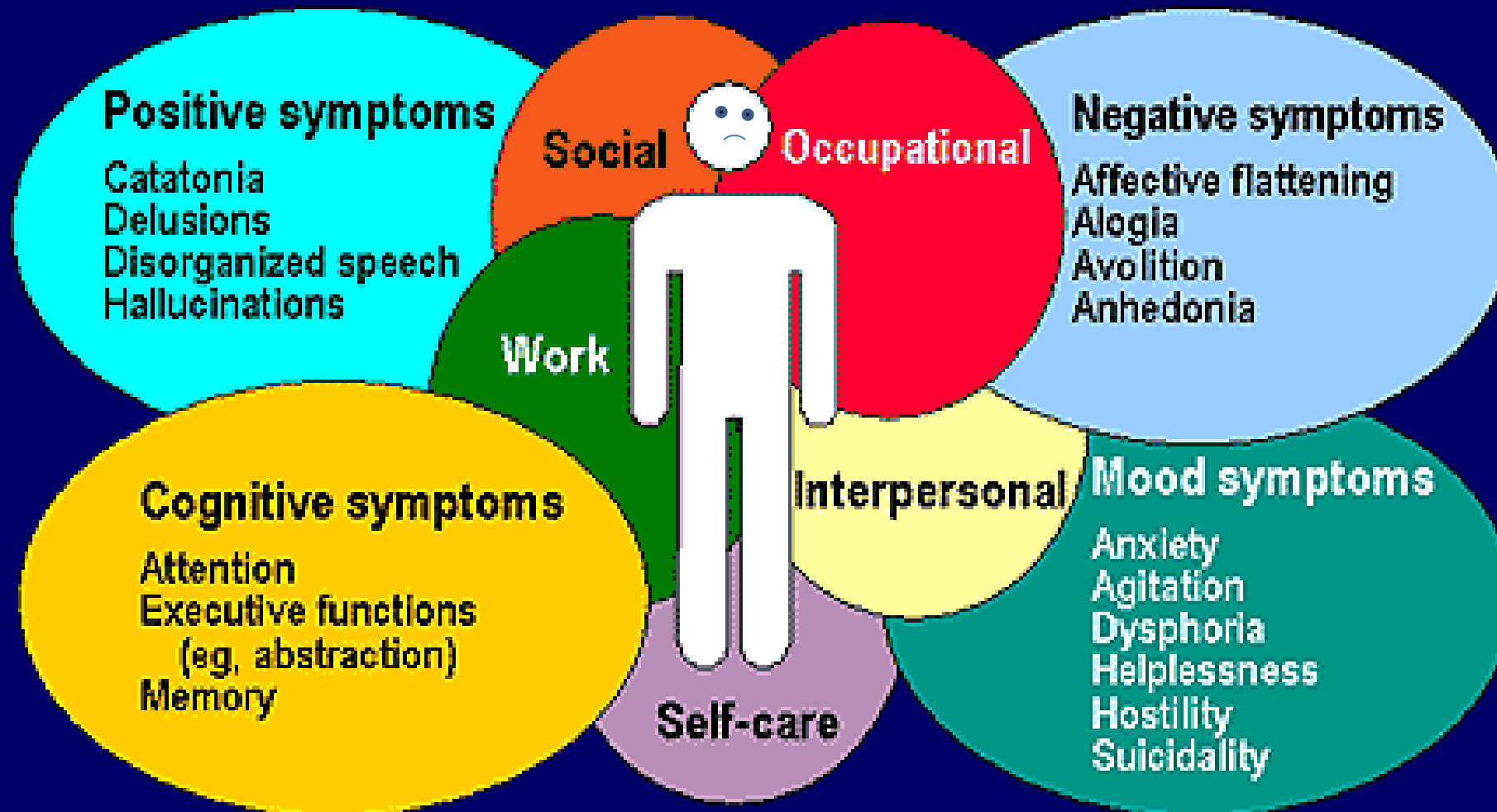
Board Certified Psychiatrist

- **Communicare, Elizabethtown, KY**
 - **1993 to present**
 - **Medical director - ACT team**
 - **Medical Director – AOT team**
- **University of Louisville – Assistant Clinical Professor**

Schizophrenia

- **A genetic psychiatric disorder associated with multiple dysregulated neurotransmitter systems that leads to dysfunction in multiple brain regions, leading to mental and physical symptoms.**
- **The condition is reactive to environmental influences and in most cases is chronic, debilitating and deteriorating.**

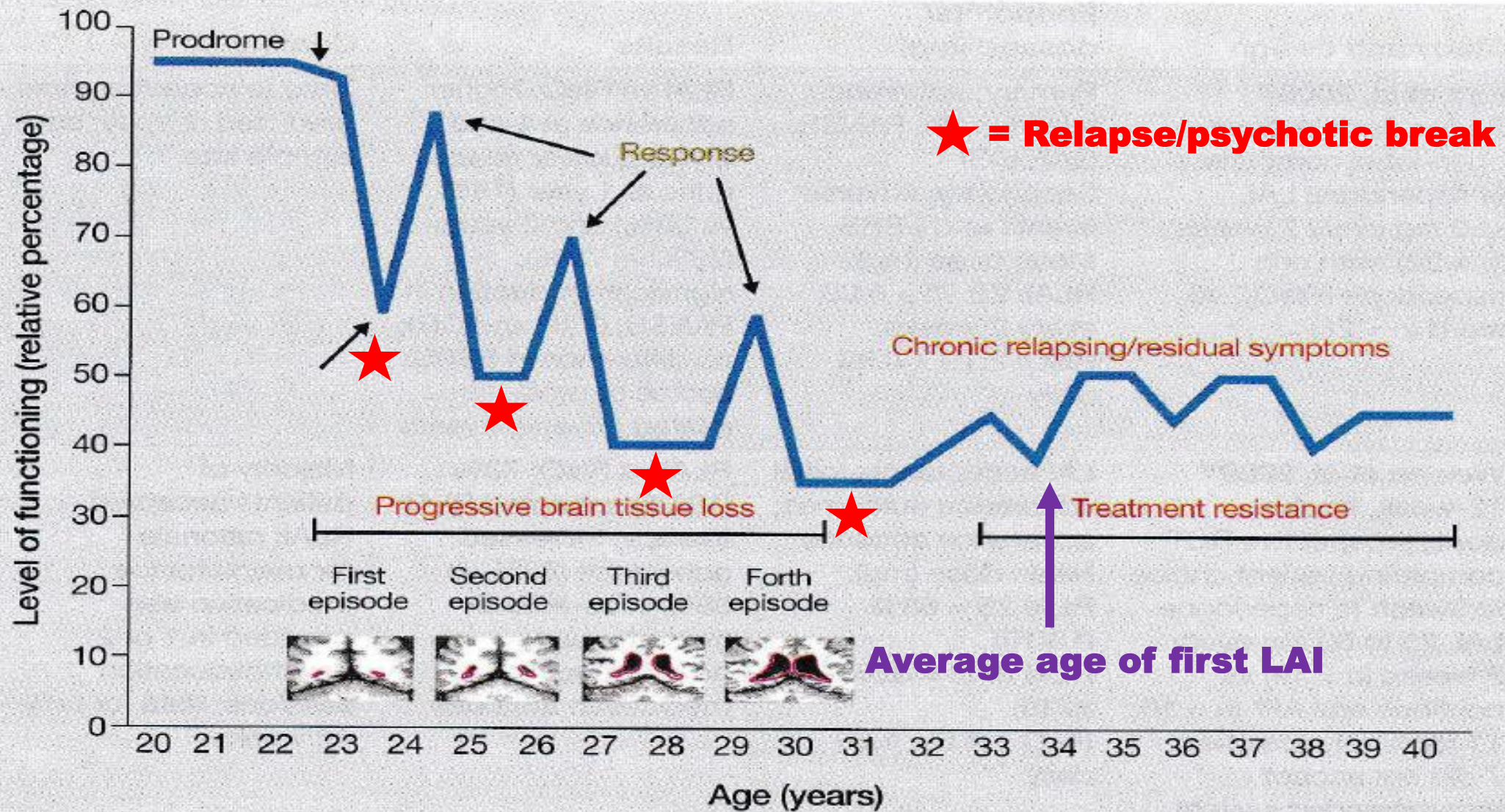
The Impact of Schizophrenia on Overall Functioning



Scope of the Issue

- **1% of population**
- **Life expectancy is 10 years less from medical illness, accidents, violence, up to 10% die by suicide**
- **90% use tobacco products**
- **High frequency of Substance Use**
- **Homeless (14% according to NIH, 2002)**
- **6.5% of incarcerated people - 2015 NIMH study**
- **long-term care beds second only to cardiac disease**
- **Estimated 2002 cost in US \$62.7 billion** Analysis Group, Inc.

Deteriorating course, brain tissue loss, and treatment resistance with repetitive relapses after the first episode in schizophrenia

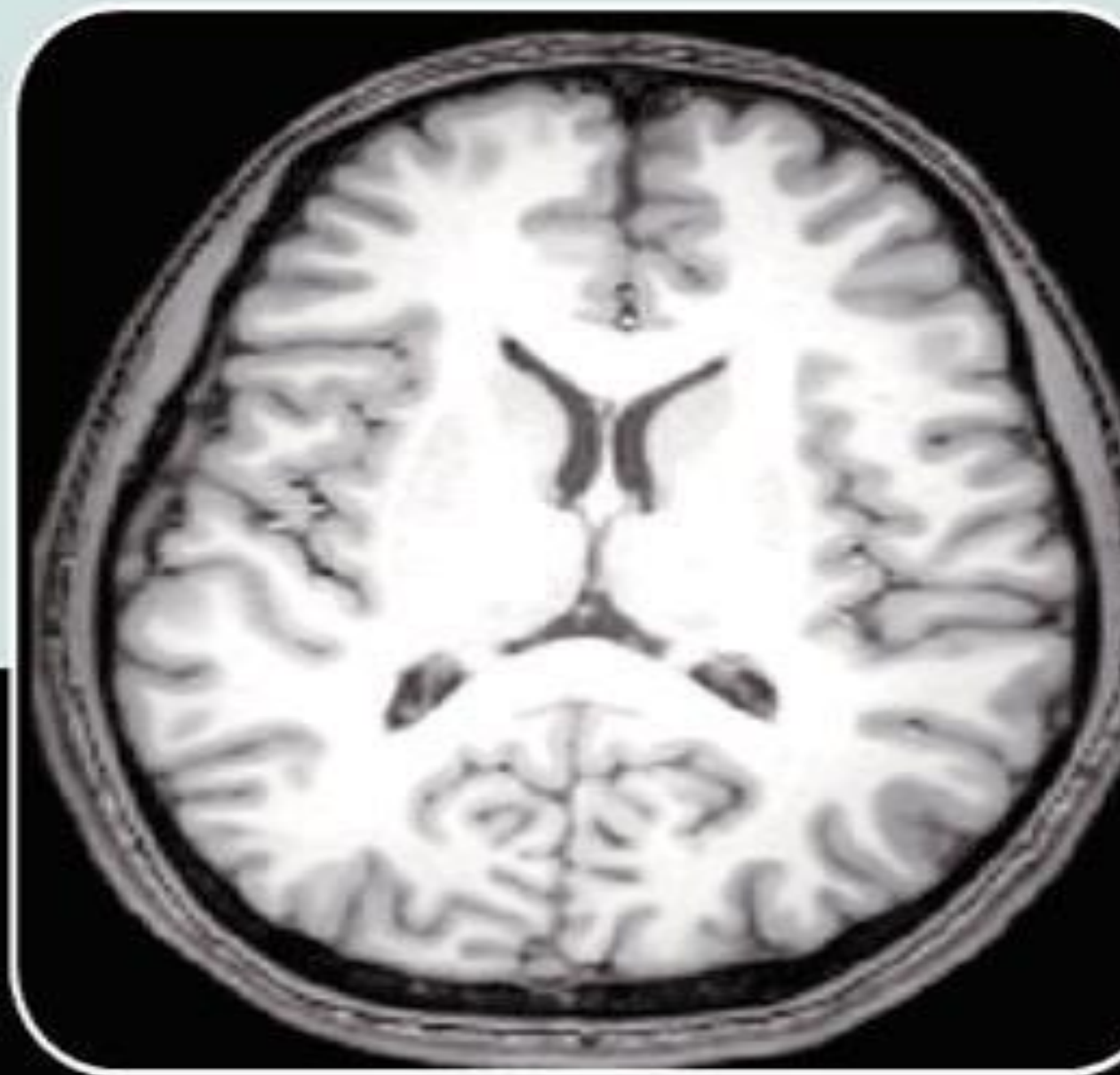


Source: Reference 27

Schizophrenia Brain



Healthy Brain



Most Common Causes of Relapse in People Who Suffer from Schizophrenia and Bipolar Disorder

- **Non adherence to oral medications**
- **Substance Use**
- **Stress**
- **The Most Common Response is to change the person's oral medication**

CATIE Trial:

Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia

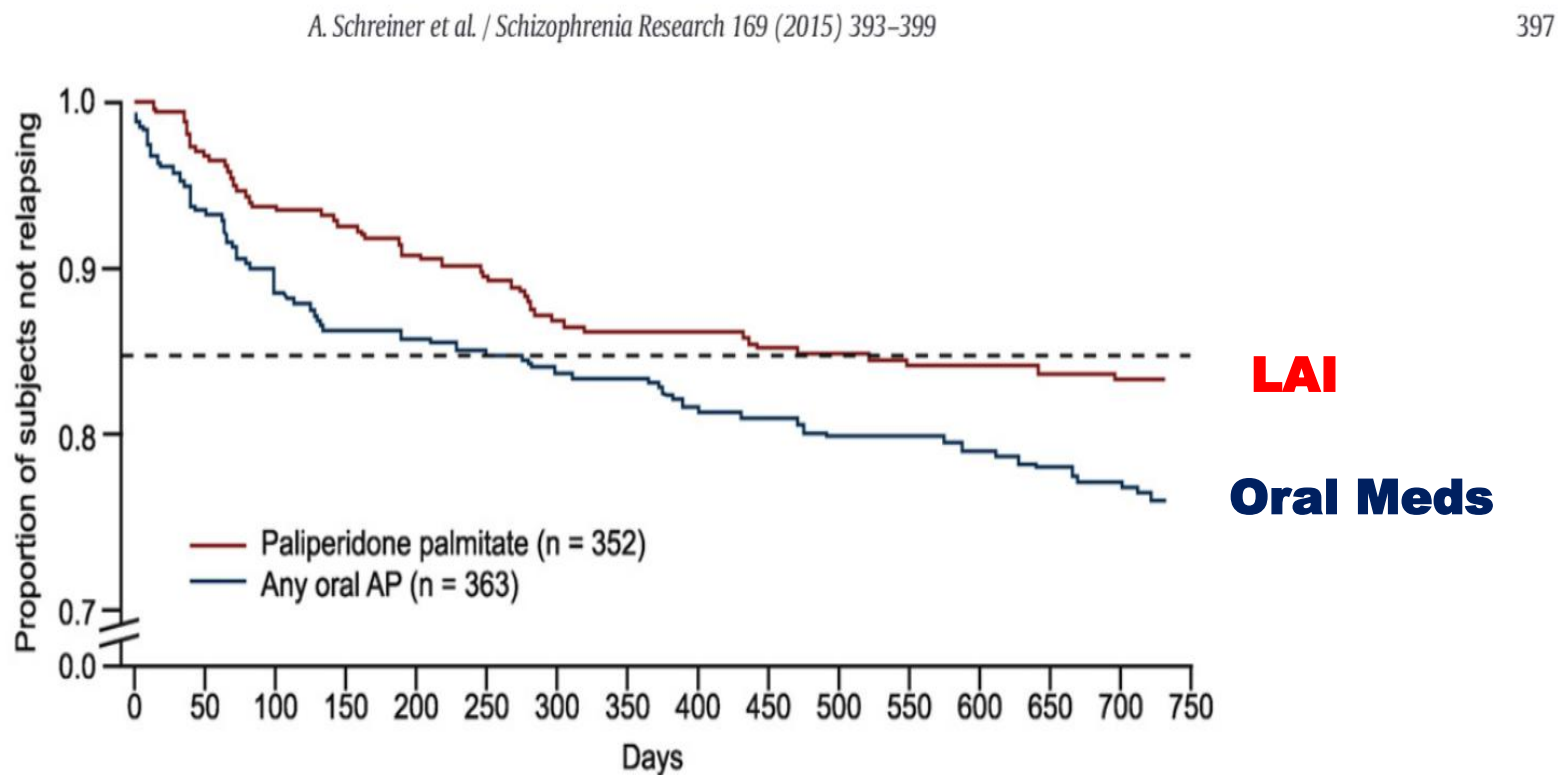
- **1460 chronic, moderately ill, people with schizophrenia - NIMH sponsored**
- **18 month, 3 phase trial, dosing set in 1999, other meds allowed, $\frac{3}{4}$ males, average age 41**
- **Primary end point = discontinuation for any reason**
- **NEJM Sep 2005, J. A. Lieberman, et al.**

CATIE Trial

- **Discontinued for any reason: 74%!**
- **Patient's decision – 30%**
- **Effectiveness – 24%**
- **Tolerability – 15%**
- **67% substance use**
 - **37% substance dependent (worst outcomes)**
- **Poor adherence to oral medications and comorbid substance use suggest early use of LAI antipsychotics and aggressive SU screening have the best chance for relapse prevention**

Paliperidone palmitate Long-Acting Injectable antipsychotic in people with schizophrenia compared to oral antipsychotics: 15% relapse rate vs 21%,
a 29% reduced risk of relapse over 2 years

Better



Subjects in treatment phase																
PP	352	326	306	292	278	272	260	256	252	244	237	233	230	225	221	0
Oral AP	363	323	297	280	265	258	246	242	230	227	216	212	207	201	198	0

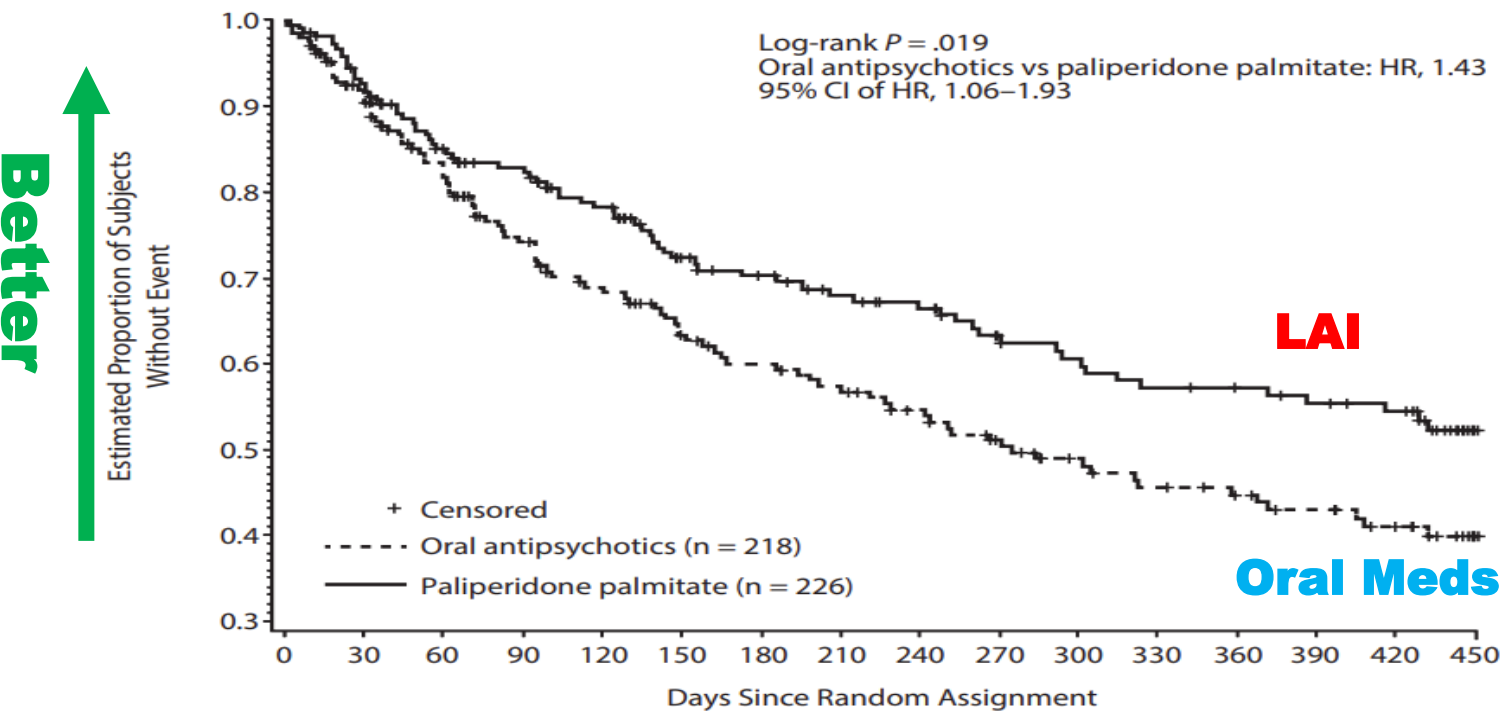
The average time to relapse was 7 months longer in the group who received LAI vs oral antipsychotics

Paliperidone Palmitate LAI compared to oral anti-psychotics in people with schizophrenia who were incarcerated twice within the last 2 years and potentially using drugs/alcohol and/or homeless.

LAI delayed the time until rehospitalization or reincarceration by over 176 days or almost six months; the relapse rate was 40% vs 54%

Paliperidone Palmitate vs Oral Antipsychotic Therapy
 Alphas, J Clin Psych; May 2015

Figure 3. Kaplan-Meier Estimate of Time to First Psychiatric Hospitalization or Arrest/Incarceration^a



No. of subjects at risk	0	30	60	90	120	150	180	210	240	270	300	330	360	390	420	450
Oral antipsychotics	218	187	151	127	114	101	92	86	78	69	61	56	52	47	41	29
Paliperidone palmitate	226	192	163	148	128	108	100	92	87	75	70	66	64	61	58	33

Table 2. Summary of Treatment-Emergent Adverse Events (TEAEs) in $\geq 5\%$ of Subjects by Preferred Term^{a,b}

TEAE, n (%)	Paliperidone Palmitate (n = 226)	Oral Antipsychotics (n = 218)
Any	194 (85.8)	174 (79.8)
Injection site pain	42 (18.6)	0
Insomnia	38 (16.8)	25 (11.5)
Weight increased	27 (11.9)	13 (6.0)
Akathisia	25 (11.1)	15 (6.9)
Anxiety	24 (10.6)	16 (7.3)
Depression	17 (7.5)	14 (6.4)
Fatigue	17 (7.5)	6 (2.8)
Erectile dysfunction	17 (7.5)	0
Sedation	15 (6.6)	16 (7.3)
Dry mouth	15 (6.6)	18 (8.3)
Increased appetite	15 (6.6)	8 (3.7)
Nasopharyngitis	15 (6.6)	12 (5.5)
Headache	14 (6.2)	18 (8.3)
Libido decreased	13 (5.8)	3 (1.4)
Upper respiratory tract infection	13 (5.8)	10 (4.6)
Back pain	13 (5.8)	8 (3.7)
Schizophrenia	10 (4.4)	15 (6.9)
Somnolence	10 (4.4)	15 (6.9)
Toothache	10 (4.4)	12 (5.5)
Dizziness	5 (2.2)	11 (5.0)
Suicidal ideation	8 (3.5)	13 (6.0)

B. Reason for First Treatment Failure

Alphs, J Clin Psych; May 2015

Reason	Paliperidone Palmitate (n = 226), n (%)	Oral Antipsychotics (n = 218), n (%)
Any 23% less on LAI	90 (39.8)	117 (53.7)
Arrest/incarceration 28% less on LAI	48 (21.2)	64 (29.4)
Psychiatric hospitalization 31 % less on LAI	18 (8.0)	26 (11.9)
Discontinuation of antipsychotic treatment due to safety or tolerability	15 (6.6)	8 (3.7)
Treatment supplementation with another antipsychotic due to inadequate efficacy	5 (2.2)	6 (2.8)
Discontinuation of antipsychotic treatment due to inadequate efficacy	1 (0.4)	9 (4.1)
Increase in level of psychiatric services to prevent imminent psychiatric hospitalization	3 (1.3)	4 (1.8)
Suicide	0	0

^aData from randomization until end of randomly assigned treatment (28 days after last injection of paliperidone palmitate or 1 day after last dose of oral antipsychotic).

Abbreviation: LAI, long-acting injection.

Which Person with Schizophrenia or Bipolar Disorder is a candidate for LAI?

- **poor insight into illness and need for treatment, homeless or unstable housing situation, poor support system, history of multiple (>2) hospitalizations for psychotic relapses, history of violence to others, living alone, history of a suicide attempt, substance use disorder, prominent psychotic symptoms, young adult (age 18–25 years), and cognitive impairment.**
- **LAIs Very Underused (13%) of treated schizophrenics, (over 50% in Europe)**
- **The average time of LAIs use in patients after a decade or more of illness and multiple pill failures**
- **Patient choice is the most common reason for not using LAIs = “I asked and he said no.”**

The Barriers to Using LAIs exist in Clients, Prescribers, Health Care Systems and Payor Systems

How LAI Therapy Is Offered Will Affect Patient Acceptance

- **67% were favorable or neutral to various styles of offering LAIs**
 - **36% were favorable**
 - **12% concerned but willing**
 - **18% were neutral**
- **After a positive offer, 96% of patients (27 of 28) were willing to try an LAI¹**

Potential Advantages of LAIs

- **Continued improvement and symptom reduction**
- **Improved client function, self esteem and confidence**
- **Reduces risk of relapse and reincarceration**
- **Potentially, shorter inpatient stays for substance use induced relapse**
- **Reassurance to families and caregiver**
- **Reduced household conflict over medications**
- **Reduction of dose and polypharmacy**
- **Smaller day to day changes in serum levels**
- **Avoid first pass metabolism**
- **Improved adherence monitoring and intervention**
- **Water-based – less painful**
- **Can be started with injections only within the first day or week, or first injection can be started with pills for the first few weeks**
- **One, two and three month options**
- **6 month formulation (2 injections per year complete monotherapy for treatment of schizophrenia)**

What Would Help

- **Integrated approach**
- **State sponsored subscriber/treatment team education**
 - **Presentations, Pamphlet, online, etc.**
- **State sponsored education for patients and families**
- **Injection team specialists/consultant/POC**
- **Inpatient discharge checklist item – “was patient offered LAI by multiple treatment team members”**
- **Medicaid/Medicare reminder letters with trigger thresholds**
- **Pharmacy program pop-ups**
- **Lower prior authorization barriers**
- **Setting a state wide goal to double LAI usage by 2025: “25% by 2025”**