

# SCHIZOPHRENIA TREATMENT OVERVIEW

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# Learning Objectives

1. Recognize first versus second generation antipsychotics
2. Understand the link between schizophrenia and increased morbidity and mortality
3. Describe antipsychotic agents' place in therapy when treating thought disorders (i.e. Which symptoms clusters do they target? Which agents/formulations are the most effective?)
4. Understand factors that impact antipsychotic selection for an individual patient
5. Discuss acute and long-term goals of therapy when treating schizophrenia

# Antipsychotic Clinical Uses

## FDA Approved

- Schizophrenia
- Bipolar Disorder
- Refractory depression
- Autistic Disorder
- Tourette's
- Parkinson disease psychosis
- Agitation\*

\*related to schizophrenia or BPD

\*\*related to dementia or delirium

## Non-FDA Approved (Off Label)

- Agitation\*\*
- Anxiety disorders
- Depression with psychotic features
- Disruptive behavior disorders
- Insomnia

# Antipsychotics

## First Generation (Typical)

- High D2 antagonism, low 5HT-2a antagonism

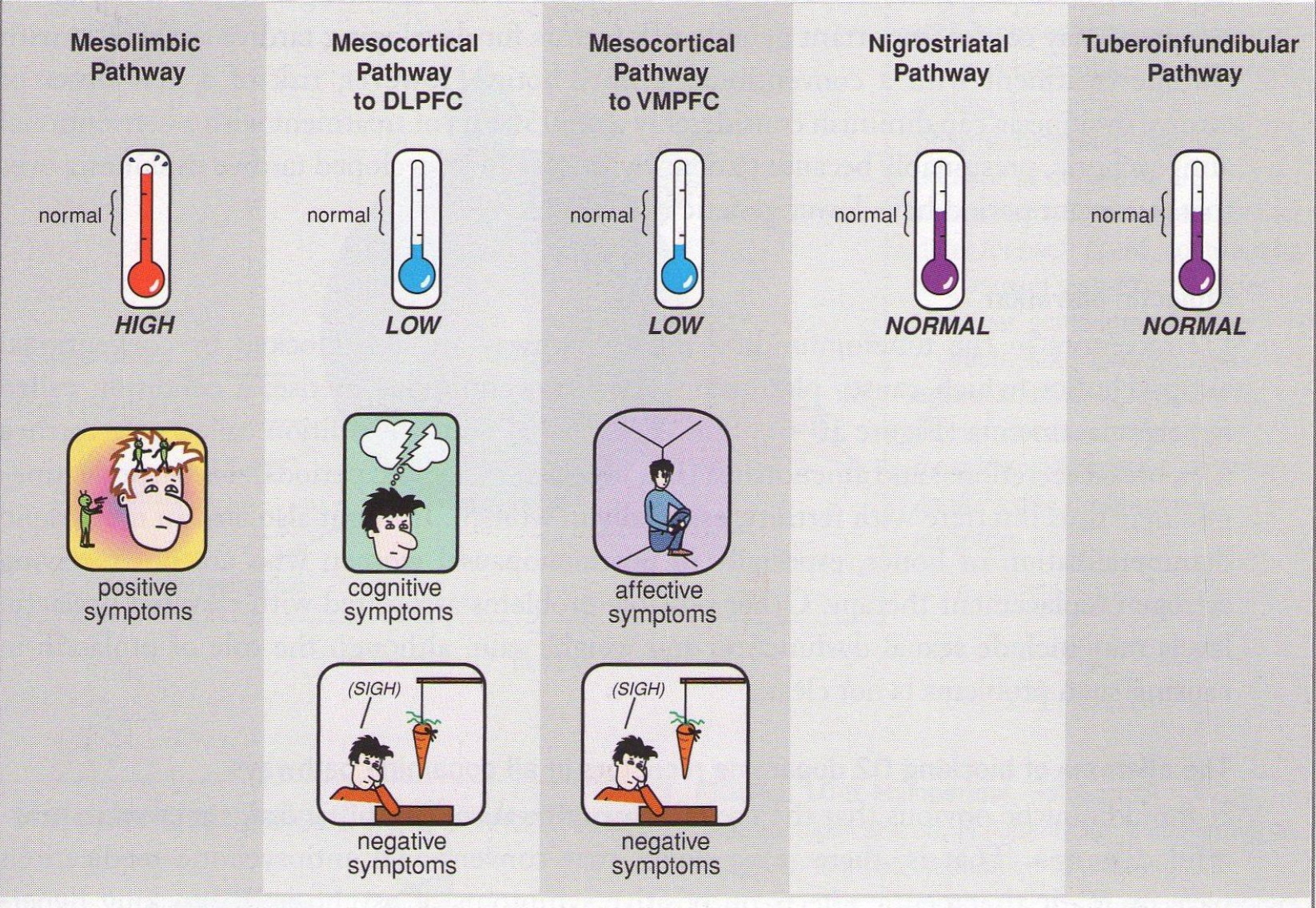
## Second Generation (Atypical)

- 5HT-2a antagonism > D2 antagonism

Variable blocking of  
muscarinic, histaminergic,  
and alpha-1 receptors



# Dopamine Output - Untreated Schizophrenia





# Available Antipsychotic Agents

## First-generation (typical)

chlorpromazine  
haloperidol  
fluphenazine  
loxapine  
perphenazine  
pimozide  
thioridazine  
thiothixene  
trifluoperazine

## Second-generation (atypical)

clozapine (Clozaril®)	asenapine (Saphris®)
risperidone (Risperdal®)	iloperidone (Fanapt®)
paliperidone (Invega®)	lurasidone (Latuda®)
olanzapine (Zyprexa®)	brexpiprazole (Rexulti™)
quetiapine (Seroquel®)	cariprazine (Vraylar™)
ziprasidone (Geodon®)	pimavanserin (Nuplazid®)
aripiprazole (Abilify®)	lumateperone (Caplyta™)

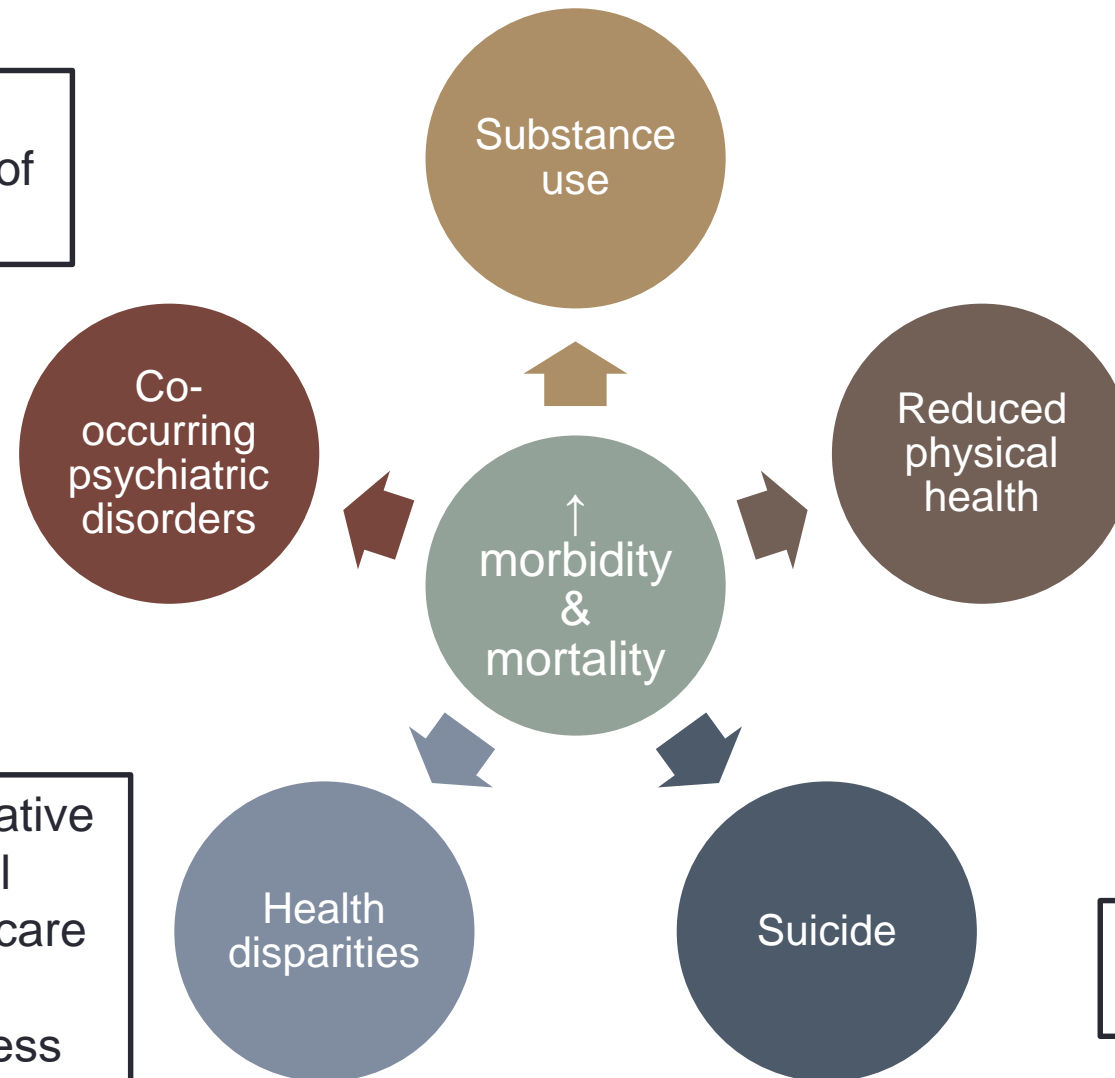
# Available Antipsychotic Formulations

Intravenous	chlorpromazine, haloperidol
Intramuscular – immediate release	chlorpromazine, haloperidol, fluphenazine, olanzapine, ziprasidone
Inhalation	loxapine
<b>Intramuscular – long-acting injectable antipsychotics (LAIA)</b>	<b>fluphenazine, haloperidol, aripiprazole, olanzapine, paliperidone, risperidone</b>
Oral disintegrating	aripiprazole, clozapine, olanzapine, risperidone
Sublingual	asenapine
Transdermal	asenapine
Oral solution	clozapine
Extended-release oral	quetiapine

\*\*All have immediate release oral tablet/capsule formulation

# Schizophrenia and Health Outcomes

- Shortened life expectancy
- Mortality ratios 2-4x those of general population



- ↑ incidence of obesity, diabetes, hyperlipidemia, CVD, smoking
- ↓ engagement in health maintenance (diet, exercise)
- Antipsychotic ADEs

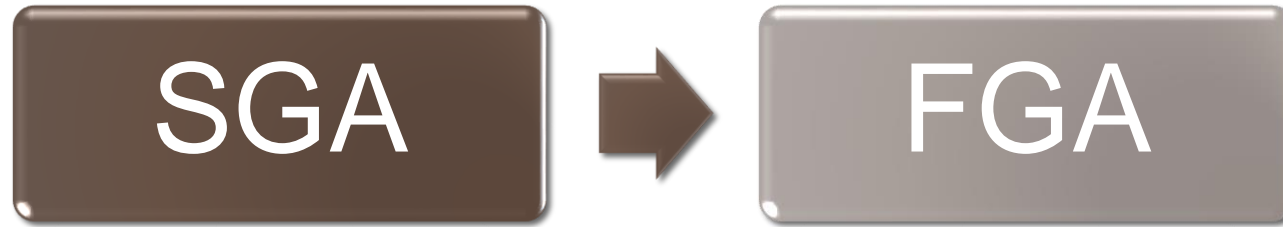
- Lack of access to preventative care, treatment of physical conditions, mental health care
- ↑ incidence of poverty
- ↑ incidence of homelessness

- 4-10% of individuals with schizophrenia die by suicide

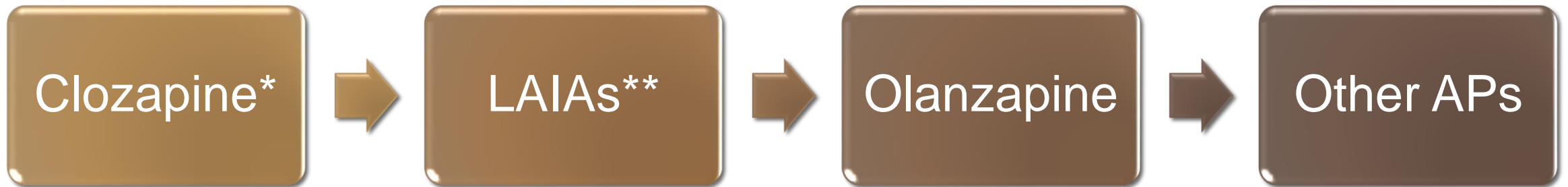


Treatment Phase	Goals of Treatment	Course of Treatment
Prodromal / Acute	Prevent hospitalization, ↓ severity of psychotic thoughts and behaviors (reduce to manageable/functional level), <b>minimize adverse effects of treatment</b>	<ul style="list-style-type: none"> <li>▪ Most rapid improvement in first 2 weeks, may continue to improve weeks to months</li> <li>▪ 2 – 6 week efficacy trial</li> <li>▪ ~33% of patients do not respond following 2 antipsychotic trials (treatment resistance)</li> <li>▪ Poor response predictors: early intolerable ADEs, minimal improvement within first 2 weeks, longer duration of symptoms/illness</li> </ul>
Maintenance	Minimize schizophrenia symptoms and related functional impairments, promote recovery (optimize functioning and QOL), prevent relapses, reduce significant psychosocial and health consequences, prevent mortality and morbidity	<ul style="list-style-type: none"> <li>▪ Patients whose symptoms have improved with an antipsychotic medication should continue to be treated with the same antipsychotic</li> <li>▪ Utilize lowest effective dose</li> <li>▪ Suboptimal adherence is common</li> <li>▪ Risk of relapse is highest in 3 mo following abrupt discontinuation</li> <li>▪ If discontinued, slow titration off with close monitoring recommended</li> </ul>

# Efficacy in Schizophrenia

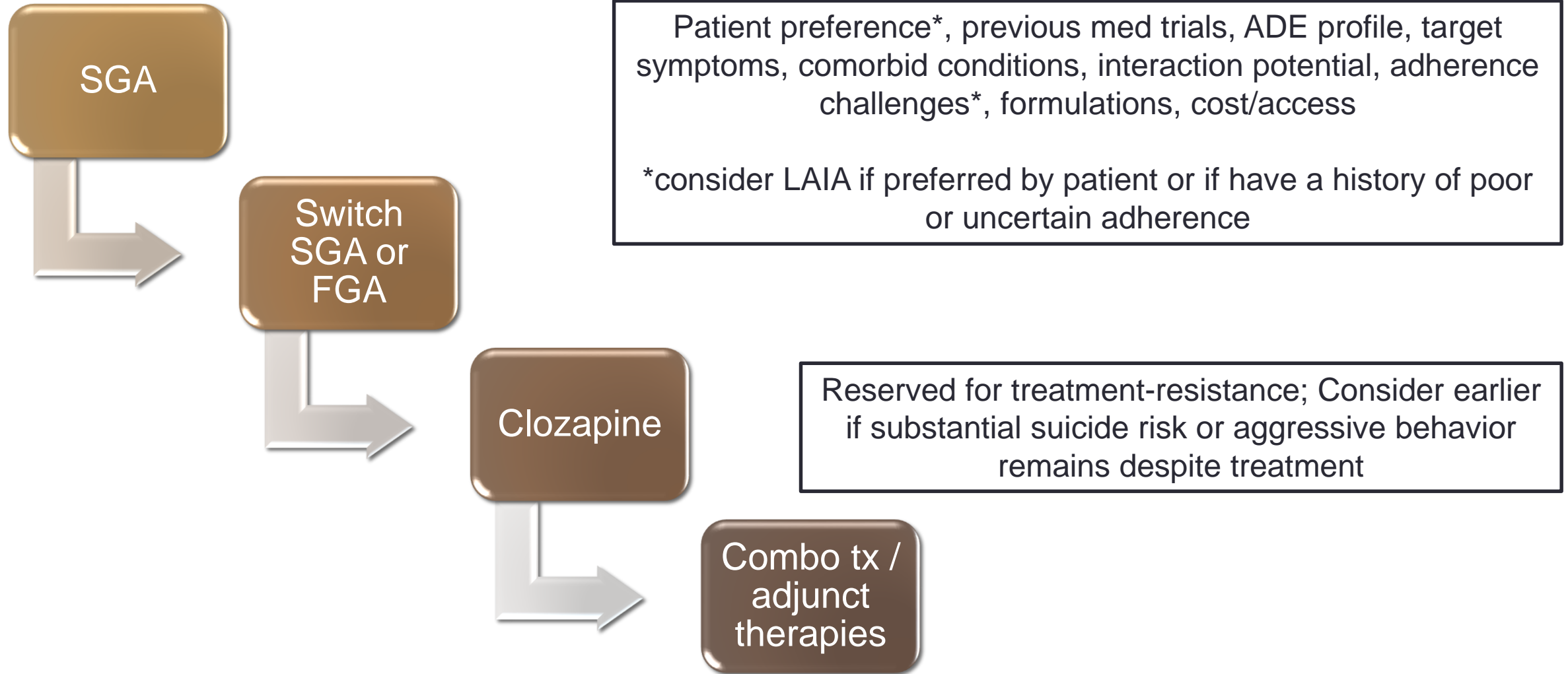


Reduction in negative, cognitive and mood symptoms



Reduction in re-hospitalizations, treatment failure, suicide attempts\*, time to first hospitalization\*\*

# Guideline Recommended Approach to Medication



# Holistic Treatment Approach

American Psychiatric Association Practice Guideline for the Treatment of Schizophrenia, Third Edition. 2019. Available at: <https://psychiatryonline.org/doi/book/10.1176/appi.books.9780890424841>





# Questions??

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