SCHIZOPHRENIA TREATMENT OVERVIEW

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Learning Objectives

- 1. Recognize first versus second generation antipsychotics
- 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?)
- 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*

Non-FDA Approved (Off Label)

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

^{*}related to schizophrenia or BPD

^{**}related to dementia or delirium

Antipsychotics

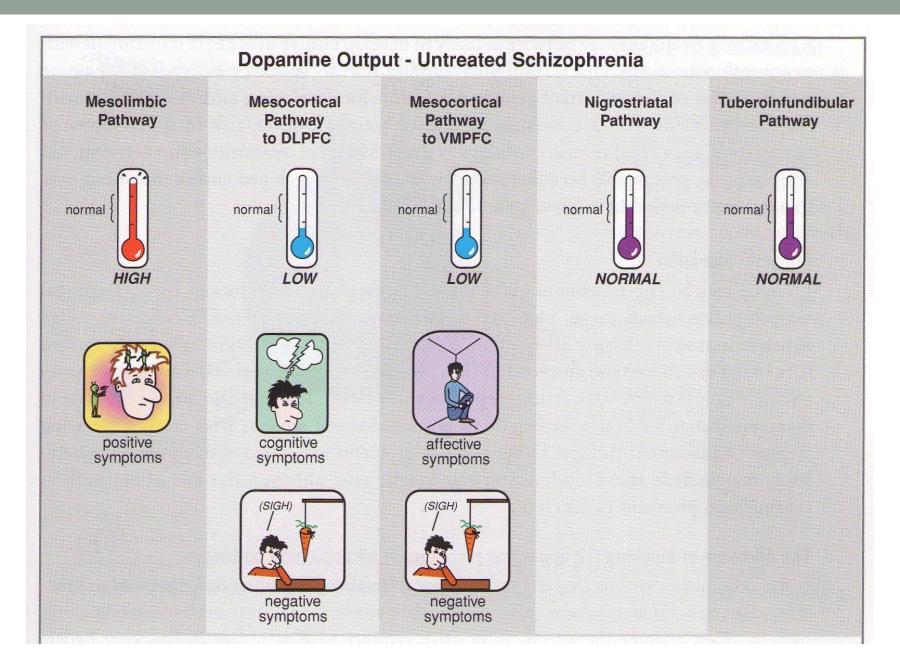
First Generation (Typical)

High D2 antagonism, low 5HT-2a antagonism

Second Generation (Atypical)

 5HT-2a antagonism > D2 antagonism

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



Stahl SM, Essential Psychopharmacology, 2008

Available Antipsychotic Agents

First-generation (typical)	Second-generation (atypical)	
chlorpromazine haloperidol fluphenazine loxapine perphenazine pimozide thioridazine thiothixene trifluoperazine	clozapine (Clozaril®) risperidone (Risperdal®) paliperidone (Invega®) olanzapine (Zyprexa®) quetiapine (Seroquel®) ziprasidone (Geodon®) aripiprazole (Abilify®)	asenapine (Saphris®) iloperidone (Fanapt®) lurasidone (Latuda®) brexpiprazole (Rexulti™) cariprazine (Vraylar™) pimavanserin (Nuplazid®) lumateperone (Caplyta™)

Available Antipsychotic Formulations

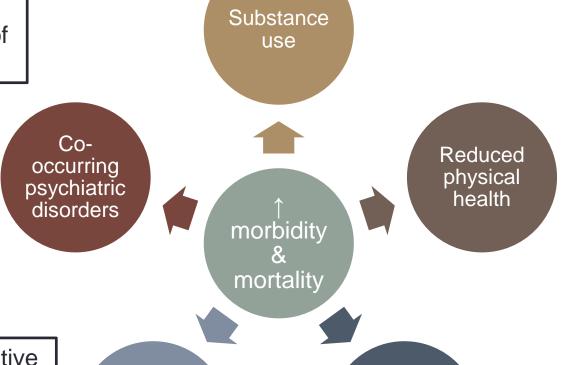
Intravenous	chlorpromazine, haloperidol
Intramuscular – immediate release	chlorpromazine, haloperidol, fluphenazine, olanzapine, ziprasidone
Inhalation	loxapine
Intramuscular – long-acting injectable antipsychotics (LAIA)	fluphenazine, haloperidol, aripiprazole, olanzapine, paliperidone, risperidone
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
- tengagement in health maintenance (diet, exercise)
- Antipsychotic ADEs

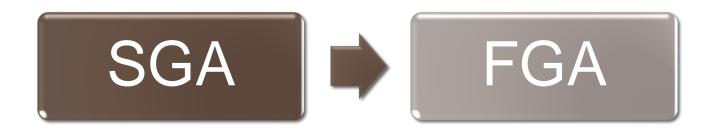
- Lack of access to preventative care, treatment of physical conditions, mental health care
- † incidence of poverty
- ↑ incidence of homelessness

Health disparities Suicide

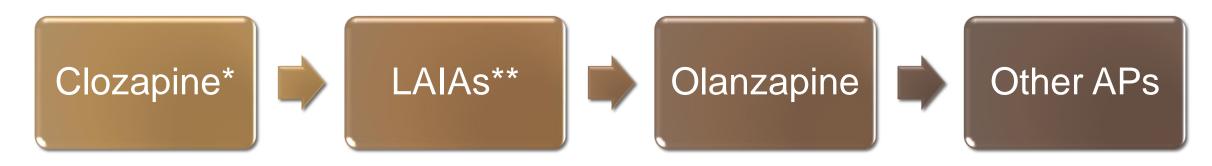
 4-10% of individuals with schizophrenia die by suicide

Treatment Phase	Goals of Treatment	Course of Treatment
Prodromal / Acute	Prevent hospitalization, ↓ severity of psychotic thoughts and behaviors (reduce to manageable/functional level), minimize adverse effects of treatment	 Most rapid improvement in first 2 weeks, may continue to improve weeks to months 2 – 6 week efficacy trial ~33% of patients do not respond following 2 antipsychotic trials (treatment resistance) Poor response predictors: early intolerable ADEs, minimal improvement within first 2 weeks, longer duration of symptoms/illness
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	 Patients whose symptoms have improved with an antipsychotic medication should continue to be treated with the same antipsychotic Utilize lowest effective dose Suboptimal adherence is common Risk of relapse is highest in 3 mo following abrupt discontinuation If discontinued, slow titration off with close monitoring recommended

Efficacy in Schizophrenia



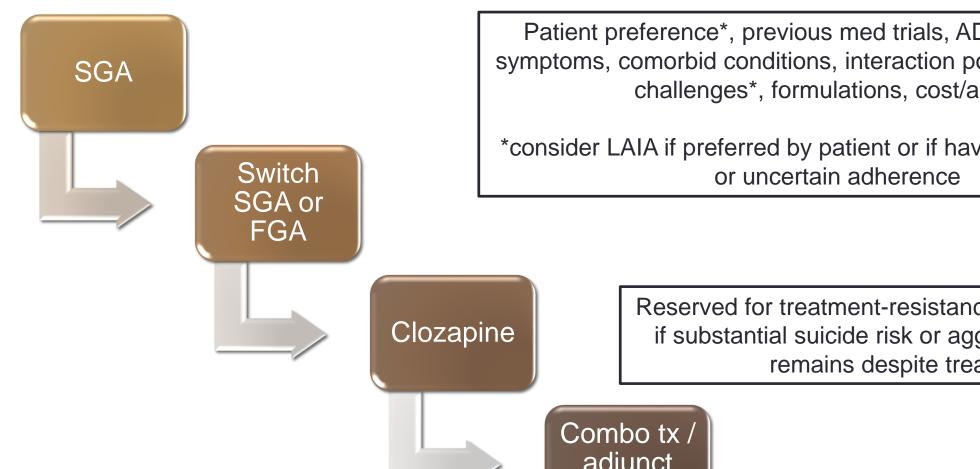
Reduction in negative, cognitive and mood symptoms



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

Tihonen J, Mittendorfer-Rutz E, Majak M, et al. Real-world effectiveness of antipsychotic treatments in a nationwide cohort of 29,823 patients with schizophrenia. JAMA Psychiatry. 2017;74(7):686-693. Fusar-Poli P, Papanastasiou E, Stahl D, et al. Treatments of Negative Symptoms in Schizophrenia: Meta-Analysis of 168 Randomized Placebo-Controlled Trials. Schizophr Bull. 2015;41:892-899. Kane JM, Schooler NR, Marcy P, et al. Effect of long-acting injectable antipsychotics vs usual care on time to first hospitalization in early-phase schizophrenia. JAMA Psychiatry. 2020 Jul 15;e202076.

Guideline Recommended Approach to Medication



Patient preference*, previous med trials, ADE profile, target symptoms, comorbid conditions, interaction potential, adherence challenges*, formulations, cost/access

*consider LAIA if preferred by patient or if have a history of poor

Reserved for treatment-resistance: Consider earlier if substantial suicide risk or aggressive behavior remains despite treatment

adjunct therapies

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

Medication

Coordinated care program

CBT for psychosis

Psychoeducation

Supported employment services

Assertive community treatment

Family interventions

Selfmanagement skill training

Cognitive remediation

Social skills training

Supportive psychotherapy

Questions??

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