Psychosis in Late Life

Understanding the Underlying Cause and How to Treat It

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What is Psychosis?

loss of contact with reality, including hallucinations, delusions and disorganized thinking

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Psychosis is a SYMPTOM

In PALTC, the most common underlying causes are:

- Dementia
- Delirium
- Substance Intoxication or Withdrawal
- Schizophrenia
- Schizoaffective disorder
- Major Depressive Disorder
- TBI
- Combinations of the above!

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Primary Psychotic Disorders

Types

- First Episode
- Schizophreniform
- Schizophrenia
- Schizoaffective
- Brief Psychotic Disorder

Common presenting symptoms

- Delusions
  - Persecutory
- Hallucinations
  - Auditory, can be command
- Disordered thinking
  - Different from general "confusion"

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Schizophrenia

DEFINITION

Represents a heterogeneous syndrome of disorganized and bizarre thoughts, delusions, hallucinations, inappropriate affect and impaired psychosocial functioning.

EPIDEMIOLOGY

- Life time prevalence ranges from 0.6-1.9 %
- Worldwide prevalence is remarkable among all cultures
- Most commonly, onset is in late adolescence or early adulthood.
- Prevalence is equal in male and female
- Onset earlier in males
- Males- first episode – early 20s
- Females – late 20s to early 30s.

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Major Mental Illness (MMI) often requires long-term psychotropics!

CONTEXT, CONTEXT, CONTEXT

MDD, schizophrenia, schizoaffective disorder, bipolar disorder

You are not required to do a GDR if resident is stable on the lowest effective dose and without new/concerning side effects – DOCUMENT.

Schizophrenia (and most MMI) does not develop in late life.

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Example risk v. benefit statement for Schizophrenia

"Mr. Garcia has a Level II classification for schizophrenia, which is a lifelong condition for which he resides in a NH. Zyprexa 20 mg daily is the dose that helped reduce his command hallucinations and as such is the least effective maintenance dose. A reduction would be unsafe. He is not sedated, nor experiencing side effects that would outweigh benefits."

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Provider role for people with Primary Psychotic Disorders (how to be a good team player with facility)

History	Documentation	Lowest dose	Match PASRR
Get good history and confirm that you agree with diagnoses.	Be responsive to pharmacist and psych pharm committee to write "risk vs. benefit" statements, also known as "contraindication to reduce."	Try to achieve the "least effective dose" of all psychotropics.	Make sure the indication for psychotropic medications is the same as the PASRR diagnoses (surveyors want these to match).

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Primary psychotic disorders and dementia

People with primary psychotic disorders can get dementia.

People with dementia DO NOT develop primary psychotic disorders.

For those with both, they may need less psychotropic medication over time as their brain becomes more vulnerable *but not always.

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Diagnostic clarity matters

- Schizophrenia does not develop in late life, nor after dementia onset.
- Using a primary psychotic disorder diagnosis in someone with dementia to justify use of an antipsychotic is fraud and the NH can be penalized.
- If someone with dementia has a justified need for an antipsychotic (*distressing psychosis and/or unprovoked aggression causing a safety concern), *it is ok to use one*; DOCUMENT well and revisit need every quarter.

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Example risk v. benefit - primary dementia on antipsychotic

"Mr. Kaplan was placed on risperidone 1mg qhs 3 months ago after an escalating pattern of paranoia that resulted in him assaulting a peer he believed to be an intruder. Since that time he has expressed little to no paranoid thoughts, has improved food intake and is more easily engaged in activities. His family is relieved and in agreement with continuing the medication. He is tolerating the medication without issue. We plan to revisit his behaviors and consider a GDR at the 6-month mark, but currently feel the benefits outweigh the risks."

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Rule out Substances or Medical Causes

- If NEW SX even in KNOWN dementia
- If NEW SX even in KNOWN primary psychotic disorder
- NEW psychotic symptoms often = DELIRIUM

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Substances and medications with capacity to induce psychosis

Substance or medication	Examples
Alcohol and sedatives/hypnotics	Alcohol (intoxication or withdrawal), barbiturates, and benzodiazepines (particularly withdrawal)
Anabolic steroids	Testosterone, methyltestosterone
Analgesics	Meperidine, pentazocine, indomethacin
Anticholinergics	Atropine, scopolamine
Antidepressants	Bupropion, others if triggering a manic switch
Antiseizure medications	Zonisamide, other antiseizure medications at high doses
Antimalarial	Mefloquine, chloroquine
Antiparkinsonian	Levodopa, selegiline, amantadine, pramipexole, bromocriptine
Antivirals	Abacavir, efavirenz, nevirapine, acyclovir
Cannabinoids	Marijuana, synthetic cannabinoids (ie, "spice"), dronabinol
Cardiovascular	Digoxin, disopyramide, propafenone, quinidine
Corticosteroids	Prednisone, dexamethasone, etc
Hallucinogens	LSD (lysergic acid diethylamide), PCP (phencyclidine), ketamine, psilocybin-containing mushrooms, mescaline, synthetic "designer drugs" (eg, 2-CB, "N-Bomb" [25I-NBOMe]), salvia divinorum
Inhalants	Toluene, butane, gasoline
Interferons	Interferon alfa-2a/2b
Over-the-counter	Dextromethorphan, diphenhydramine, some decongestants
Stimulants	Cocaine, amphetamine/methamphetamine, methylphenidate, certain diet pills, "bath salts" (MDPV [methylenedioxypyrovalerone], mephedrone), MDMA (3,4-methylenedioxymethamphetamine)/ecstasy
Toxins	Carbon monoxide, organophosphates, heavy metals (eg, arsenic, manganese, mercury, thallium)

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Types of Hallucinations give Clues

Auditory classic for Primary Psychotic Disorders

- Always ask about command AH to harm self or others – safety assessment

Visual common for Parkinsonian disorders and medical/substances delirium

Tactile common for DT's and for delusional parasitosis

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Rule Out Delirium

Sharon Inouye MD has published more than 140 papers on delirium and is a leading researcher on this topic - her definition:

"an acute, temporary change in cognition characterized by relatively rapid onset and variable symptoms, including difficulty maintaining attention"

Studies show the prevalence of psychotic symptoms is ~ 40-50%

Of those – 1/3 have visual hallucinations, 1/5 have auditory hallucinations, and ¼ have delusions. The presence of visual hallucinations is significantly associated with more active medical diagnoses and multiple etiologies causing the delirium.

Learn how to spell it! D-E-L-I-R-I-U-M (one E, two I's… I know, right??)

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Agar MR, Lawlor PG, Quinn S, et al. Efficacy of Oral Risperidone, Haloperidol, or Placebo for Symptoms of Delirium Among Patients in Palliative Care: A Randomized Clinical Trial. *JAMA Intern Med*. 2017;177(1):34–42.

Neufeld, K. J., Yue, J., Robinson, T. N., Inouye, S. K., & Needham, D. M. (2016). Antipsychotic Medication for Prevention and Treatment of Delirium in Hospitalized Adults: A Systematic Review and Meta-Analysis. *Journal of the American Geriatrics Society*, *64*(4), 705–714. https://doi.org/10.1111/jgs.14076

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Treatment for Primary Psychotic Disorders

- "What gets you well keeps you well"
- Choose 2nd gen over 1st AP's when you can
- Consider long-acting injectables early
- Clozapine is superior for refractory psychosis and SI
  - Must allow blood draws, and be medically stable
- Make choice based on patient preference, side effect profile, availability, and insurance
  - Start with Risperidone or Olanzapine if AP-naïve

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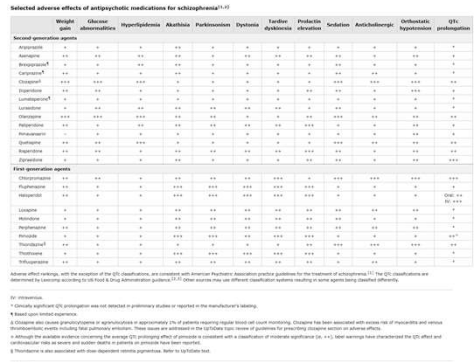

Selected adverse effects of antipsychotic medications for schizophrenia[1,2]

	Weight gain	Glucose abnormalities	Hyperlipidemia	Akathisia	Parkinsonism	Dystonia	Tardive dyskinesia	Prolactin elevation	Sedation	Anticholinergic	Orthostatic hypotension	QTc prolongation
Second-generation agents												
Aripiprazole	+	+	+	++	+	+	+	+	+	+	+	+
Asenapine	++	++	++	++	+	++	++	++	++	+	++	+
Brexpiprazole[¶]	+	+	++	++	+	+	+	+	++	+	+	+
Cariprazine[¶]	++	+	+	++	+	+	+	+	++	++	+	+
Clozapine[‡]	+++	+++	+++	+	+	+	+	+	+++	+++	+++	++
Iloperidone	++	++	+	+	+	+	+	++	++	+	+++	+
Lumateperone[¶]	+	+	+	+	+	+	+	+	+	+	+	+
Lurasidone	+	++	++	++	++	++	++	+	++	+	+	+
Olanzapine	+++	+++	+++	++	++	+	+	++	+++	++	++	++
Paliperidone	++	+	++	++	++	++	++	+++	+	+	++	+
Pimavanserin	-	+	+	+	+	+	+	+	+	+	++	+
Quetiapine	++	++	+++	+	+	+	+	+++	+++	++	++	++
Risperidone	++	++	+	++	++	++	++	+++	++	+	++	++
Ziprasidone	+	+	+	++	+	+	+	++	++	+	++	+++
First-generation agents												
Chlorpromazine	++	++	+	++	++	++	+++	+	+++	+++	+++	+++
Fluphenazine	++	+	+	+++	+++	+++	+++	+++	+	+	+	+
Haloperidol	++	+	+	+++	+++	+++	+++	+++	+	+	+	Oral: ++ IV: +++
Loxapine	+	+	+	++	++	++	++	++	++	++	++	+
Molindone	+	+	+	++	++	++	++	++	++	+	+	+
Perphenazine	++	+	+	++	++	++	++	++	++	++	++	+
Pimozide	+	+	+	+++	+++	++	+++	+++	+	+	+	+++*
Thioridazine[‡]	++	+	+	+	+	+	++	+++	+++	+++	+++	++
Thiothixene	+	+	+	+++	+++	+++	+++	+++	+	+	+	+
Trifluoperazine	++	+	+	++	++	++	++	++	+	++	+	+

Adverse effect rankings, with the exception of the QTc classifications, are consistent with American Psychiatric Association practice guidelines for the treatment of schizophrenia.[1] The QTc classifications are determined by Lexicomp according to US Food & Drug Administration guidance.[3-5] Other sources may use different classification systems resulting in some agents being classified differently.

IV: intravenous.

* Clinically significant QTc prolongation was not detected in preliminary studies or reported in the manufacturer's labeling.

¶ Based upon limited experience.

‡ Clozapine also causes granulocytopenia or agranulocytosis in approximately 1% of patients requiring regular blood cell count monitoring. Clozapine has been associated with excess risk of myocarditis and venous thromboembolic events including fatal pulmonary embolism. These issues are addressed in the U.S. Food and Drug Administration's topic review of guidelines for prescribing clozapine section on adverse effects.

+ Although the available evidence concerning the average QTc prolonging effect of pimozide is consistent with a classification of moderate significance (ie, ++), label warnings have characterized the QTc effect and cardiovascular risks as severe and sudden deaths in patients on pimozide have been reported.

§ Thioridazine is also associated with dose-dependent retinitis pigmentosa. Refer to UpToDate text.

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Clozapine

- Superior treatment for resistant psychotic disorders and serious SI
- Serious potential side effects: neutropenia, seizures, cardiomyopathy
- Common side effects: drooling, weight gain, sedation; less likely to cause EPS
- Requires pretreatment EKG, CBC with ANC and weekly/monthly monitoring for ANC; must enroll in REMS registry
- Slow titration: 25mg qd 1 week, then 50 mg qd 1 week, etc ;target dose 300 mg/d – maintenance dose 300-600 , with average 400 mg/d
- Check levels at 300 mg before proceeding; goal = 250 to 350 ng/mL

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Extra Pyramidal Side Effects (worse for FGA's)

Akathisia is suggested by a sensation of restlessness, frequent pacing, a compelling urge to move, or an inability to sit still.

Parkinsonism is suggested by finding of masked facies, bradykinesia, tremor, or rigidity.

Dystonia is a tonic contraction of a muscle or muscle group that is typically disturbing to the patient and obvious to the examiner.

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Abnormal involuntary movement scale

Copyright apply

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Meds for Akathisia

- Propranolol 10 mg bid up to 60 mg bid
- Benztropine 1mg bid up to 3 mg bid (remember, highly anti-cholinergic)
- Clonazepam 0.5 mg tid up to 3mg

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Psychosis and Parkinsonism

- Discern whether PD, LBD or primary medication side effect and assess that symptoms cause *subjective* distress or *safety* concern
- In PD, must weigh balance of movement v. psychosis
- Best intervention is to reduce +DA meds if possible
  - Sinemet, amantadine, pramipexole, ropinirole
- FDA approved for PD Psychosis: Pimavanserin (Nuplazid) but data are concerning for study design, increased mortality, limited efficacy and approval process*
- Clozapine least likely to cause EPS, but rarely worth risk
- Seroquel best bet for minimizing EPS; dose 12.5 bid/tid and increase as tolerated; sedation/falls main risk (half life ~5h – so not good just at night)

*Schubmehl S, Sussman J. Perspective on Pimavanserin and the SAPS-PD: Novel Scale Development as a Means to FDA Approval. Am J Geriatr Psychiatry. 2018 Oct;26(10):1007-1011. doi: 10.1016/j.jagp.2018.06.001. Epub 2018 Jun 14. PMID: 30072306.

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Tardive Dyskinesia

- TD develops from chronic antipsychotic use, worse from 1st generation exposure, characterized by the following features:

- Sucking, smacking of lips
- Choreoathetoid movements of the tongue
- Facial grimacing
- Lateral jaw movements
- Choreiform or athetoid movements of the extremities and/or truncal areas

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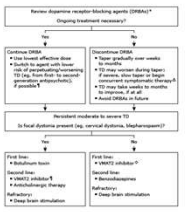
Management of new-onset tardive dyskinesia (TD)



The most common manifestations of TD involve spontaneous movements of the mouth and tongue; the arms, legs, trunk, and respiratory muscles can also be affected. Less commonly, the prominent feature is dystonia involving a focal area of the body such as the neck. TD can be irreversible and lifelong, with major negative impacts on psychologic health and quality of life. TD is important to recognize, since early discontinuation of the offending drug offers the best chance of recovery. In patients who require ongoing antipsychotic drug therapy for management of psychiatric disorders, symptomatic therapies for TD can help lessen movements.

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FDA approved meds for TD

Vesicular Monoamine Transporter Type 2 Inhibitors (VMAT2) reduce dopamine release presynaptically

- Valbenazine (Ingrezza) 1st choice
  - 30-40% reduction in AIMS scores sustained at 48 weeks
  - Start 40 mg q week x 1 week up to 80 mg q week
  - Serious reactions: QT prolongation, Parkinsonism
  - Common reactions: somnolence, anticholinergic, balance probs, HA, akathisia
  - GoodRX cost ~$7000.00/mo.
- Deutetrabenazine (Austedo)
  - Harder to dose: start 6 mg /d up to 48 mg /d but max 18 mg/dose
  - Black box for SI in HD
  - GoodRX cost ~$4000.00-$6000.00/mo

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Worst SGA for weight gain:

Clozapine
Olanzapine

Recommendations for metabolic risk factor monitoring in patients with severe mental illness or on antipsychotic medication

Risk factor	Timing of assessment					
	First year of antipsychotic				Ongoing monitoring*	
	Baseline	6 weeks	3 months	12 months	Quarterly¶	Annually¶
Personal and family history of diabetes, hypertension, or cardiovascular disease	X					X
Smoking status, physical activity, diet◊	X	X	X		X	
Weight, body mass index◊	X	X	X		X	
Blood pressure◊	X	X	X		X	
Fasting glucose or HbA1c◊	X	X§	X	X		X
Lipid profile (fasting or nonfasting)	X		X	X		X

* In subsequent years of antipsychotic and in patients with severe mental illness.

¶ Ongoing quarterly and annual monitoring is appropriate when health indicators are within the normal range. More frequent monitoring is indicated when health indicators are out of range.

Δ Assess regularly as part of general health maintenance.

◊ HbA1c is usually more practical to obtain than fasting glucose but either can be used.

§ Fasting glucose at 6 weeks is only recommended by European guidelines, but given evidence for rapid-onset hyperglycemia in some individuals starting antipsychotics, this represents prudent monitoring, especially for clozapine and olanzapine.

Adapted from: De Hert M, Detraux J, van Winkel R, et al. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. Nature Rev Endocrinol 2011; 8:114.

UpToDate

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Practical summary

Psychosis is a symptom, not a disorder.

Primary psychotic disorders require maintenance treatment, and monitoring.

For delirium and dementia, risks typically outweigh benefits (and evidence) for antipsychotic use, unless very *short-term* for safety or subjective distress.

Antipsychotic use must be well documented in a "risk v. benefit" statement by regulation.

Misusing diagnoses to justify antipsychotic use is fraud.

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