



UW PACC

Psychiatry and Addictions Case Conference

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MANAGEMENT OF PSYCHOSIS IN PRIMARY CARE

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SPEAKER DISCLOSURES

None

Planner disclosures

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

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OBJECTIVES

By the end of this session, participants will

1. Understand how to assess a person with possible psychosis, including consideration of underlying or concurrent conditions
2. Know the recommended first-line medications for treatment of psychosis
3. Identify two changes they can make in current practice to mitigate risks among their patients who are treated with antipsychotic medications

WHAT IS PSYCHOSIS?

- Psychosis refers to a condition of the mind involving a "loss of contact with reality."
- People experiencing psychosis may exhibit some personality changes and thought disorder (hallucinations, delusions, odd speech).
- May be accompanied by unusual or bizarre behavior, as well as difficulty with social interaction and impairment in daily life activities.
- Occurs in 3/100 people at some point in their lifetime

The screenshot shows the homepage of the Psychosis 101 website. At the top left, there is a green logo with the text "PSYCHOSIS 101". To its right, the text "Symptoms, myths and treatment of psychosis." is displayed. Below the logo, there is a large image of a smiling man with a beard wearing a cap. To the right of this image, the text "IT IS TREATABLE: The earlier you get treatment, the better." is shown, followed by a button labeled "GETTING HELP". At the bottom of the page, there are three sections: "REAL STORIES" with a small image of a woman, "PSYCHOSIS IS TREATABLE, THE EARLIER THE BETTER!" with a sun icon and a "GET HELP NOW: Talk to someone in your area." button, and "RESOURCES FOR FRIENDS AND FAMILY" with a group photo of people.

<http://www.psychosis101.ca>

EARLY IDENTIFICATION IS KEY

- Approximately 100,000 youth and young adults experience an episode of psychosis each year—or 274 young people each day.
- 3X as many young people who have experienced psychosis will drop out of school compared to their peers.
- Treatment works. 77% of those experiencing first episode psychosis will have a remission of symptoms with medication
- The average duration of untreated psychosis in the US is more than 2 years.



WHO IS TREATING PSYCHOSIS?

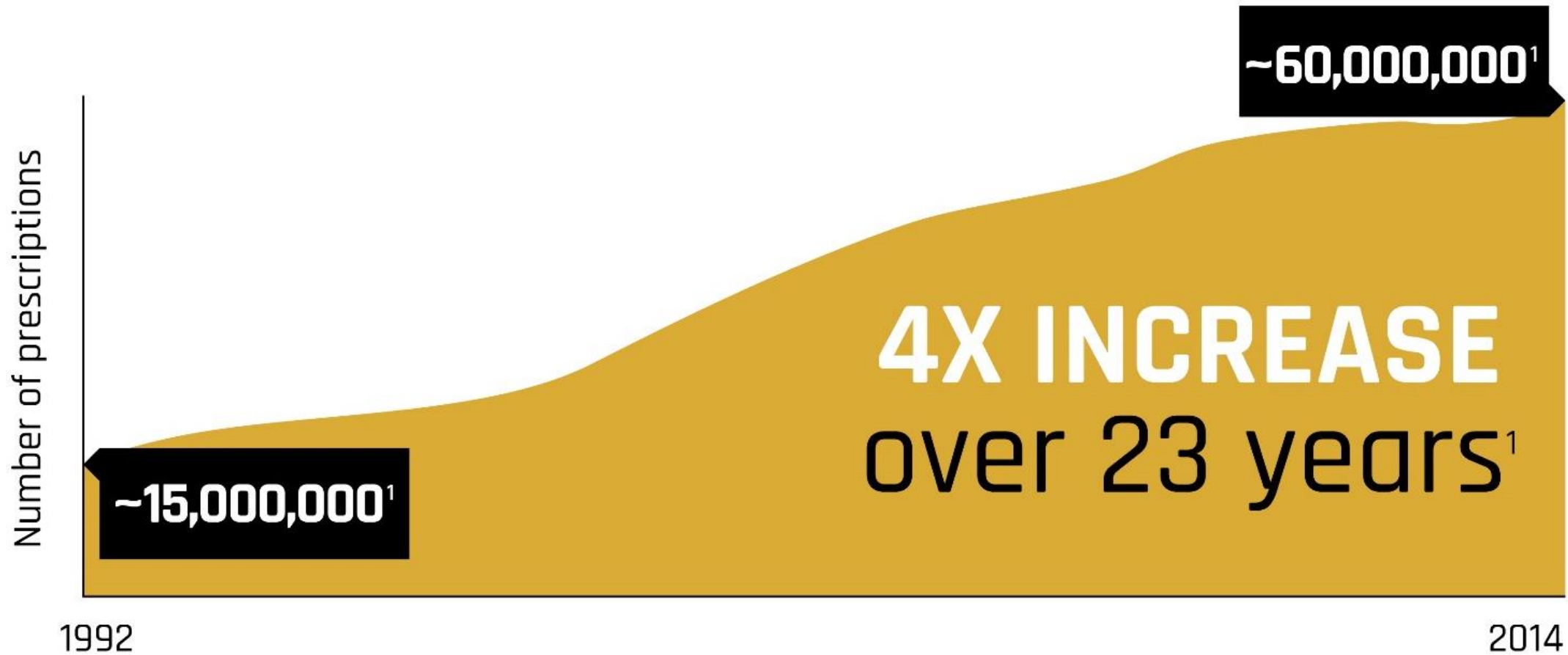


- 1.6% of US adults received prescription for antipsychotic medication in 2013-2018;¹
- 3.1 million people; \$18 B
- More than 30% were by nonpsychiatric prescribers²

¹Dennis JA, *BMC Psychiatry* 2020; 20:483;

²Olfson M et al, *J Clin Psychiatry*. 2015; Oct;76(10):1346-53

How much has antipsychotic use increased?



Source: 1. IMS Institute for Healthcare Informatics. Report to Neurocrine Biosciences, Inc. 1992-2014.

©2017 Neurocrine Biosciences, Inc. All Rights Reserved. CP-TD-US-0114 04/17

ASSESSMENT OF PSYCHOSIS

1. Identify symptoms of psychosis: history and mental status exam
2. Rule out substance use or medical cause (e.g., alcohol or delirium due to acute medical conditions) that require treatment
3. Ask about previous episodes and treatment and family history



PSYCHOSIS: KNOW THE SIGNS

F	Functioning	Functional decline
A	Atypical	Atypical perceptual experiences
C	Cognition	Cognitive difficulties
T	Thoughts	Thought disturbance or unusual beliefs
S	Speech	Speech or behavior that is disorganized

<https://www.psychosisscreening.org/>

HOW TO ASK....

Symptoms	Person	Family
Hallucinations	e.g. Do you hear voices or see things that no one else can?	e.g. Do you see the person talking to someone else when alone? As if the person is talking to someone?
Delusions	e.g. Do you believe that someone is planning to hurt you? Do you feel that you are under surveillance?	e.g. Did the person share any ideas that you found strange and unlikely to be true?

Remember the Mental Status Exam: appearance and speech

ALWAYS ASSESS SUICIDE RISK

- 20-40% of people with psychosis will attempt suicide in their lifetime and 8-10% will die by suicide
- You must always assess patients with psychosis for suicide.
- Imminent risk:
 - Current thoughts and/or plan to commit suicide or self-harm
 - History of thoughts or plan of self-harm in the past year in a person who is now extremely agitated, violent, distressed or uncommunicative



INITIAL (MEDICAL) EVALUATION



- Physical exam, emphasis on neuro
- History: travel, occupational exposure
- Urine drug screen
- Labs: ESR, ANA, TSH, Vitamin B12, Ceruloplasmin
 - HIV, FTA-ABS
- MRI if neuro exam abnormal

PSYCHOEDUCATION

- Recommend avoiding alcohol, cannabis or other nonprescription drugs.
- Advise on maintaining a healthy lifestyle.
- Encourage the person to resume social activities.
- Explain that symptoms can recur or worsen and the importance of visiting the health facility as soon as possible should this happen.
- Coordinate with available health and social resources to meet the family's physical, social, and mental health needs

STRESS REDUCTION

STRESS **MANAGEMENT** IN YOUR LIFE

The infographic consists of seven circular icons arranged in two rows. Each icon contains a white silhouette or symbol representing a stress management technique. The top row includes: 1. A person in a meditative pose (Meditation) with 'DEEP BREATHS' below. 2. A person running with musical notes (Exercise) with 'GET MOVING' below. 3. A sun with rays (Time in Nature) with 'RELAXATION' below. 4. A clock face with 'Zzz' (Sleep Well) with 'RECHARGE' below. The bottom row includes: 5. A group of people with speech bubbles (Connect Socially) with 'JOIN A CLUB' below. 6. A glass of water and an apple (Eat Well) with 'REDUCE CAFFEINE' below. 7. A checklist with a pencil (Make Lists) with 'PRIORITIZE TASKS' below.

- MEDITATION
DEEP BREATHS
- EXERCISE
GET MOVING
- TIME IN NATURE
RELAXATION
- SLEEP WELL
RECHARGE
- CONNECT SOCIALLY
JOIN A CLUB
- EAT WELL
REDUCE CAFFEINE
- MAKE LISTS
PRIORITIZE TASKS

CHECKPOINT



Think about the last prescription you wrote for an antipsychotic medication...

- What was the indication for the medication you selected?
- Is the patient part of a population that is at increased risk from antipsychotic medications?
- What did you do to monitor the treatment?

SELECTING AN ANTIPSYCHOTIC MEDICATION



- First episode (antipsychotic naïve)
- Pregnancy
- Age
 - Elderly
 - Pediatric
- Concerns about side effects (weight gain, motor)
- Cost
- Patient preferences

<https://www.ahrq.gov/health-literacy/professional-training/shared-decision/tools/factsheet.html>

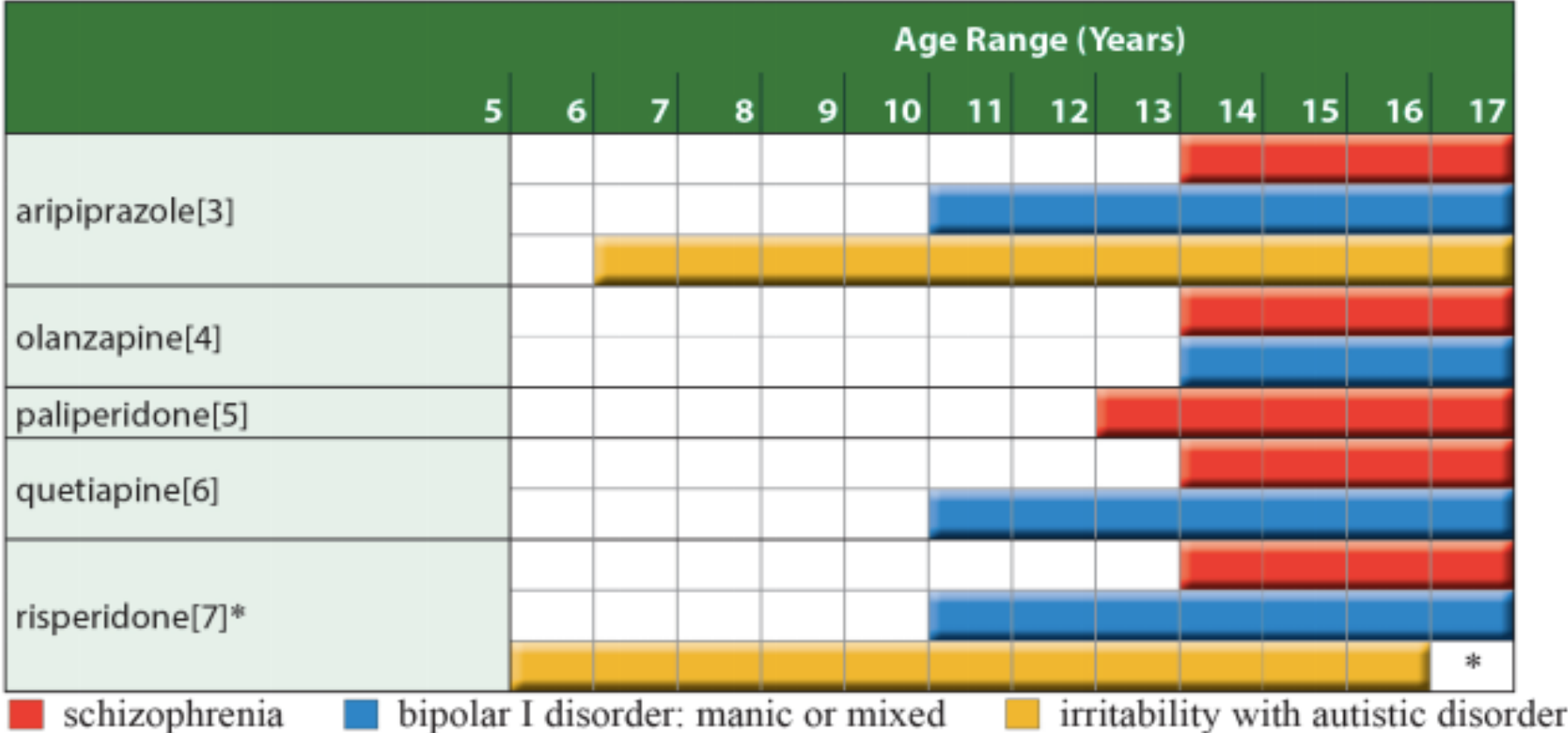
Indication	Age	Medications
Schizophrenia, acute	Adults	ARI, ASE, BRE, CAR, ILO, LUR, OLZ, PAL, QUE, RIS, ZIP
Schizophrenia, maintenance	13-17	ARI, ASE, BRE ILO, OLZ, PAL, QUE, RIS, ZIP
Schizoaffective	Adults	PAL
Treatment-resistant schizophrenia	Adults	CLZ
Reduce suicide in schizophrenia	Adults	CLZ
Bipolar disorder	Adults	ARI, ASE, ILO, OLZ, QUE, RIS, ZIP
Bipolar disorder	13-17	ILO, OLZ (10-17: ARI, QUE, RIS)
Bipolar depression	Adults	LUR, QUE
Treatment-resistant depression	Adults	OLZ
Adjunctive MDD	Adults	ARI, BRE, QUE
Irritability in autism	6-17	ARI, RIS

FIRST-LINE TREATMENT FOR EARLY PSYCHOSIS

- Risperidone (Risperdal) 3-4 mg (max 8 mg)
- Aripiprazole (Abilify) 10-30 mg (max 30 mg)
- Ziprasidone (Geodon) 80-120 mg (max 160 mg)

ANTIPSYCHOTIC MEDICATIONS IN CHILDREN

Figure 1. FDA-Approved Pediatric Age Ranges and Indications for Atypical Antipsychotics



*Risperidone should not be used by patients older than age 16 who have been diagnosed with irritability with autistic disorder.

AP MEDICATION MANAGEMENT IN ELDERLY

- Increased mortality among elderly with dementia

Medication	Schizophrenia
Aripiprazole	15-30 mg
Clozapine	50-150 mg
Olanzapine	10-20 mg
Paliperidone	3-12 mg
Quetiapine	200-300 mg
Risperidone	2-3 mg

APA practice guidelines

<https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9780890426807>

MEDICATION USE DURING PREGNANCY



- 1.3% of pregnancies exposed to AP meds
- Quetiapine and aripiprazole most prescribed
- Discontinuation: 53% increased risk of relapse (compared to 16%)
- Low reproductive risk
- Gestational diabetes RR = 1.28
- Breastfeeding not contraindicated (CLZ?)

Betcher HK et al. Curr Treat Options Psychiatry. 2019 Mar; 6(1): 17–31.

WHAT ABOUT LAI?

- Benefits
 - Reduce relapse (5% vs 33%)
 - Reduce hospitalizations
 - Reduce mortality?
- Factors to consider
 - Patient preference
 - Tolerability
 - Individualized risk (of relapse)
 - Level of support



Kishimoto T, et al. Lancet Psychiatry 2021; 8(5): 387-404; Pacchiarotti, I et al Eur Neuropsychopharmacol. 2019 Apr;29(4):457-470.

LAI: WHICH?

Aripiprazole (Maintena)	400 mg once a month
Aripiprazole (Aristada)	441-882 monthly; 882 mg q 6wks
Olanzapine (Zyprexa Relprevv)	150-300 mg q 2 w; 300-405 q m
Paliperidone (Invega Sustenna)	39-117 mg once monthly
Paliperidone (Invega Trinza)	410 mg q 3 months (273-819 mg)
Risperidone (Consta)	25-50 mg q 2 weeks

Problem	Are you experiencing this problem?		Questions for your psychiatrist
	Yes	No	
Daytime sedation/drowsiness/sleeping too much			
Problems with memory or concentration			
Changes in appetite or weight			
Muscles being too tense or stiff, or muscles trembling or shaking			
Feeling restless, jittery, or the need to move around and pace			
Blurry vision, dry mouth, constipation, or urinary retention or hesitancy			
Changes in sexual function			
[In women only], menstrual or breast problems			
Feeling unlike my usual self			
Other concerns			
	Yes	No	Questions for your Psychiatrist
I think the pros of using medication outweigh the cons of using medication			

WHAT IS TARDIVE DYSKINESIA (TD)?

TARDIVE DYSKINESIA (TD)

is a condition characterized by uncontrollable, abnormal and repetitive movements of the trunk, extremities and/or face.^{1,2}

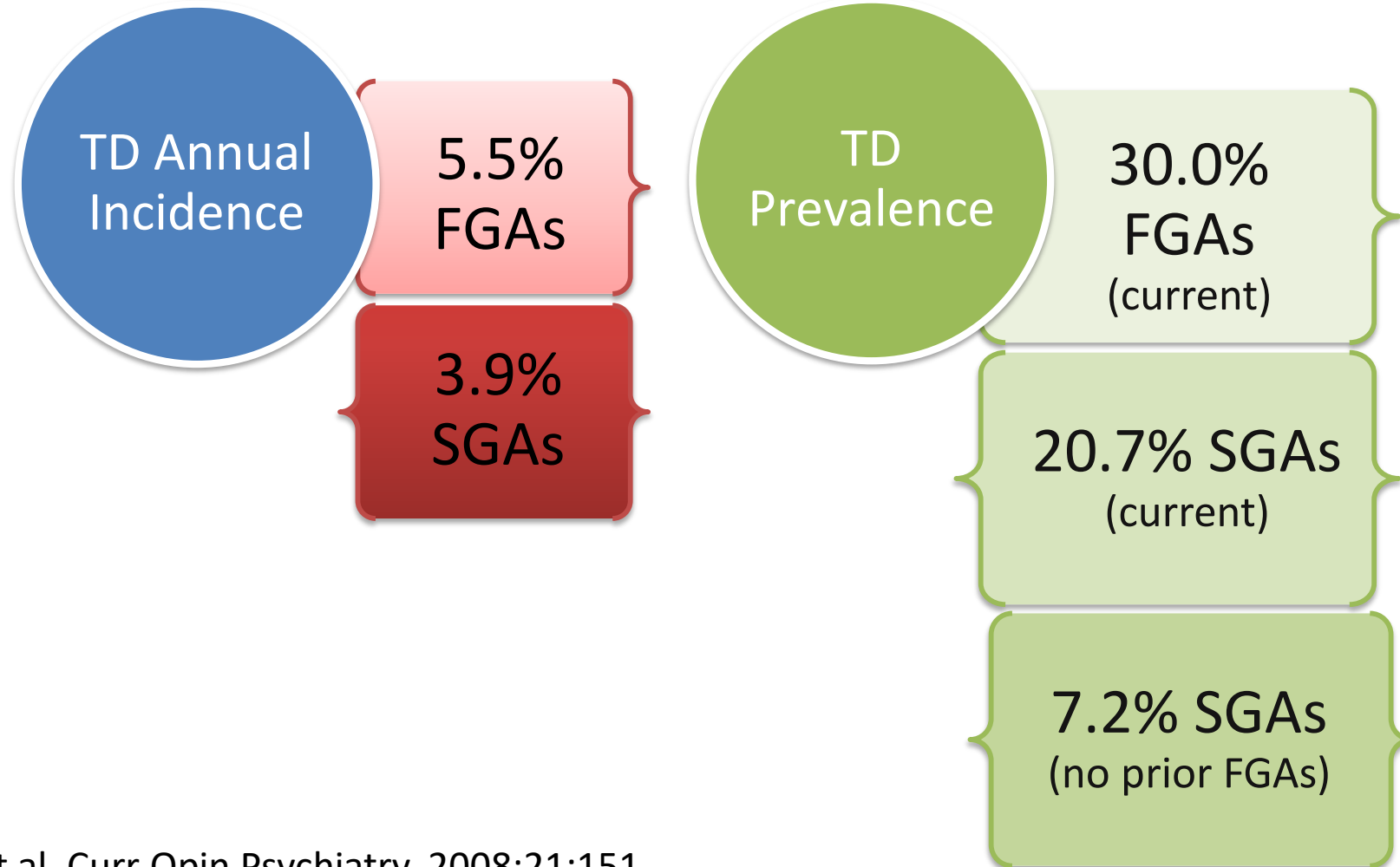
TALK

- Associated with the use of a dopamine receptor blocking agent (DRBA) for 3 or more months
- Regions affected: generally the tongue, lower face and jaw, and extremities

Risk factors

- Duration of exposure to AP Med
- Higher potency medication
- Age 50 +
- Post-menopausal
- Diagnosed with mood disorder
- History of drug or alcohol use disorder

ALL PATIENTS ON ANTIPSYCHOTICS ARE AT RISK OF DEVELOPING TD



¹Correll et al. Curr Opin Psychiatry. 2008;21:151.

²Carbon et al. J Clin Psychiatry. 2017;78:e264.

IDENTIFYING TD

Look for movements throughout the body

- Orofacial movements
- Neck and trunk movements
- Arm and leg movements

Observation for involuntary movements

- In the waiting room
- Walking to the consultation room
- During the visit

If TD is suspected, perform a more thorough evaluation

- Observe (“look, not listen”)
- Activation maneuvers
- AIMS

AIMS IS STANDARD STRUCTURED EXAM TO ASSESS TD

	Movement Ratings	Score				
Facial and Oral Movements	1. Muscles of facial expression	0	1	2	3	4
	2. Lips and perioral area	0	1	2	3	4
	3. Jaw	0	1	2	3	4
	4. Tongue	0	1	2	3	4
Extremity Movements	5. Upper (arms, wrists, hands, fingers)	0	1	2	3	4
	6. Lower (legs, knees, ankles, toes)	0	1	2	3	4
Trunk Movements	7. Neck, shoulders, hips	0	1	2	3	4
	8. Severity of abnormal movements overall	0	1	2	3	4
Global Judgments	9. Incapacitation due to abnormal movements	0	1	2	3	4
	10. Patient awareness of abnormal movements	0	1	2	3	4
Dental Status	11. Current problems with teeth/dentures?	No				Yes
	12. Are dentures usually worn?	No				Yes

Scoring

- Total score is calculated using items 1-7 for a total (max) score of 28

0 = None
1 = Minimal
2 = Mild
3 = Moderate
4 = Severe

- Item 8 score is based on the highest single score in any of the items 1-7

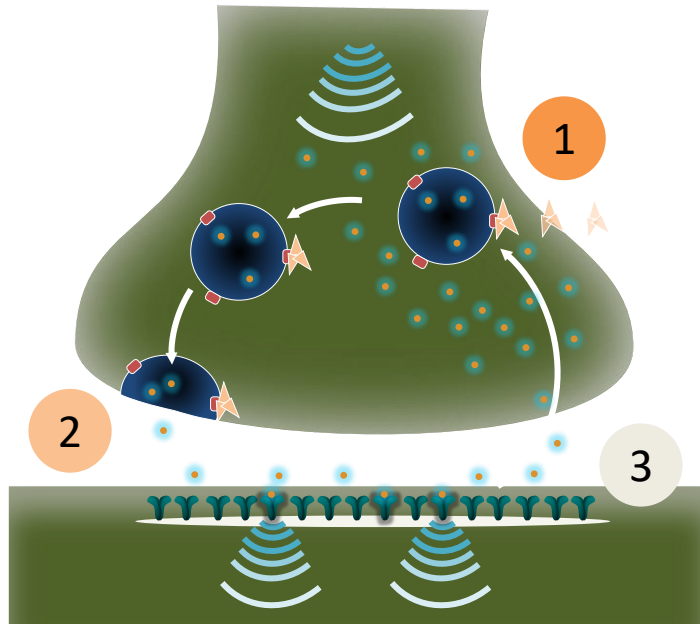
TD TREATMENT CONSIDERATIONS

- Minimize the use of anticholinergics (eg, benztropine), which can aggravate TD symptoms

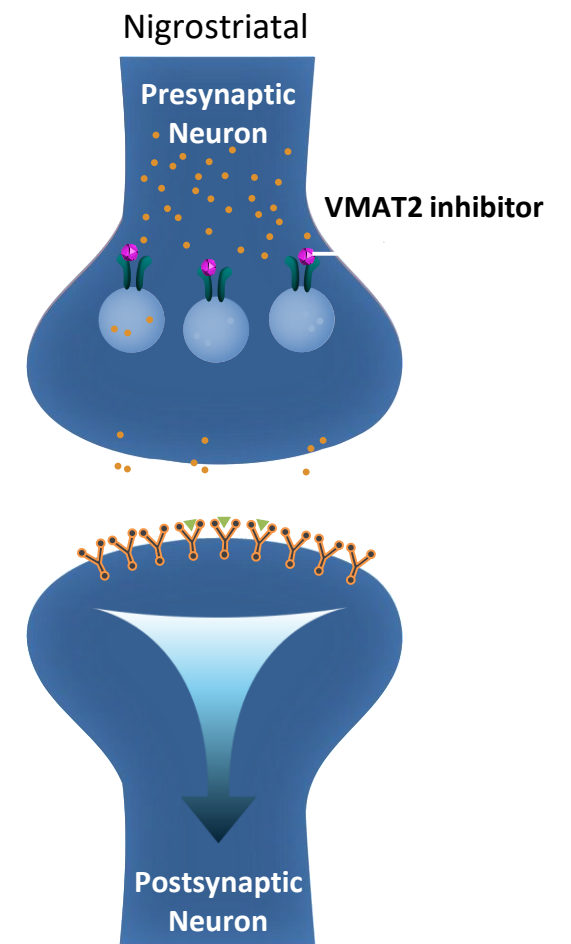
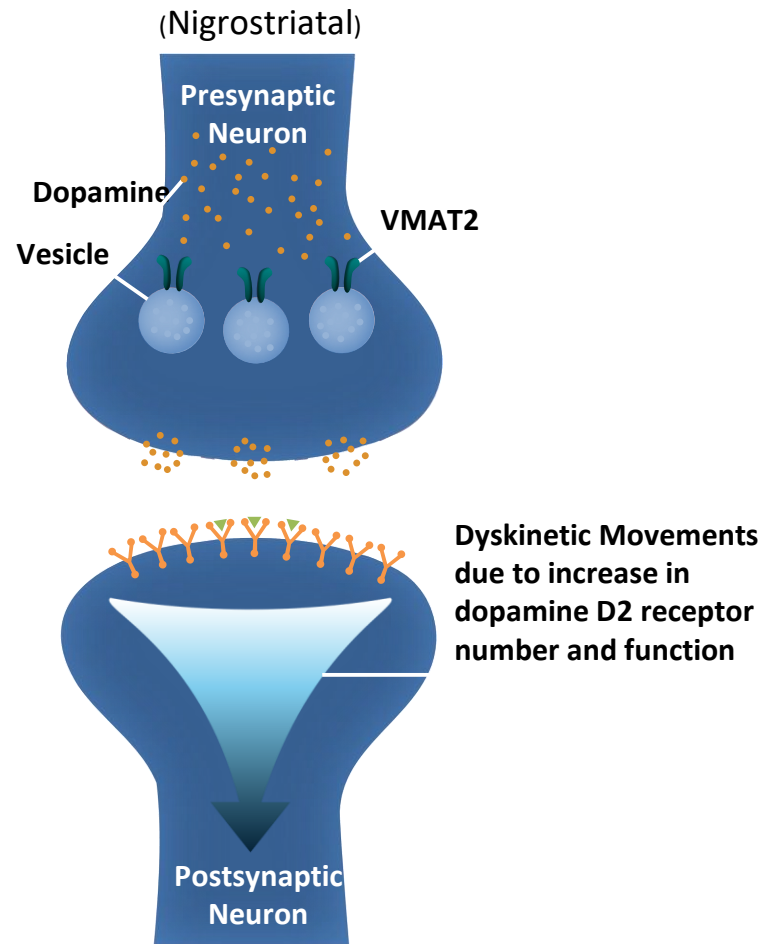
- Dose reduction or discontinuation may not be feasible when the antipsychotic has already been optimized to improve mental health
- Reducing antipsychotic dose increases TD symptoms in the short term and may not improve TD symptoms in the long term
- TD may be irreversible, even upon antipsychotic discontinuation

- TD symptoms that have an impact on the patient, regardless of movement severity, should be managed first line with VMAT2 inhibitor

MECHANISM OF ACTION: VMAT2 INHIBITION



- VMAT2 is a transporter protein found in presynaptic neurons of the CNS
- VMAT2 packages monoamines (including dopamine) for release into the synaptic cleft



VESICULAR MONOAMINE TRANSPORTER 2 (VMT2) INHIBITORS

- FDA Approved medications
 - *Tetrabenazine*
 - Deutetrabenazine (Austedo)
 - 6 mg once daily, increase by 6 mg/ day weekly; two divided doses; max dose 48 mg /d
 - Valbenazine (Ingrezza)
 - 40 mg once daily, increase to 80 mg once daily or continue 40-60 mg daily
- Side effects (similar effectiveness and tolerability)
 - Somnolence, diarrhea, dry mouth, HA, dizziness
 - QT prolongation

VESICULAR MONOAMINE TRANSPORTER 2 (VMT2) INHIBITORS

- Expensive
- Specialists/ Specialty pharmacy
- Duration of treatment? 12-week trials. Symptoms tend to recur when medication is stopped
- Alternatives
 - Discontinue any anticholinergic medications
 - OLZ, ILO, QUE, *CLZ* have lower risk of TD
 - Vitamin E, amantadine, clonazepam

Metabolic Monitoring Guidelines

ADA-APA workgroup. Diabetes Care 2004; 27: 596-601.

	entry	4 weeks	8 weeks	12 weeks	monthly	annual
PMH / Family History	X					X
Weight (BMI)	X	X	X	X	X	
Waist Circumference	X					X
Blood Pressure	X	X	X	X	X	X
Hemoglobin A1c	X			X		X
Lipid panel	X			X		X
Smoking Status	X	X	X	X	X	X
Physical activity	X	X	X	X	X	X


SECOND GENERATION: METABOLIC RISKS

Low Risk	Moderate Risk	High Risk
Aripiprazole (Abilify)	Asenapine (Saphris)	Clozapine (Clozaril)
Brexpiprazole (Rexulti)	Iloperidone (Fanapt)	Olanzapine (Zyprexa)
Cariprazine (Vraylar)	Paliperidone (Invega)	
Lumateperone (Caplyta)	Quetiapine (Seroquel)	
Lurasidone (Latuda)	Risperidone (Risperdal)	
Ziprasidone (Geodon)		

Barton BB et al Expert Opin Drug Saf. 2020 Mar;19(3):295-314.

Corponi F et al Eur Neuropsychopharmacol. 2019 Sep;29(9):971-985.

WHEN SWITCH MEDICATIONS?



Time For Change

- Intolerable side effects
 - weight gain = 5-7% of body weight
 - Any magnitude of weight gain that leads to non-adherence with medication
 - New diagnosis of diabetes

<https://www.psychiatrictimes.com/cme/switching-antipsychotics-why-when-and-how/page/0/2>

HOW SWITCH?



Takeuchi H, et al. *Schizophr Res.* 2018 Mar;193:29-36

- Options
 - Abrupt discontinuation and immediate initiation of second medication at clinically effective dose
 - Cross-taper (reduce 25-50% every 4-5 days) with gradual initiation of new antipsychotic
 - Overlap and discontinuation: continue pre-switch med at full dose while starting and titrating new med
- No one strategy uniformly superior

AVOID POLYPHARMACY

- Meta-analysis of 147 studies
- 19.6% receive APP
- Rate increased 34% between 1980s and 2000s in North America
- APP associated with increased
 - hospitalization rates and length of stay
 - Costs
 - adverse effects, including mortality
- Augmentation of clozapine may be the exception



Gallego JA et al, Schizophr Res. 2012 Jun; 138(1): 18–28.

Choosing Wisely[®]

An initiative of the ABIM Foundation

<https://www.choosingwisely.org>

1	Don't routinely prescribe antipsychotic medications as a first-line intervention for insomnia in adults.
2	Don't routinely use antipsychotics as first choice to treat behavioral symptoms of dementia.
3	Don't routinely prescribe to treat behavioral symptoms of childhood mental disorders in the absence of approved or evidence supported indications
4	Don't routinely prescribe two or more antipsychotic medications concurrently
5	Don't prescribe antipsychotic medications for any indication without initial evaluation and ongoing monitoring.

CONCLUSIONS

- More than 1/3 of AP meds are prescribed by PCPs. Support improved care by
 - Clarifying indication, avoiding polypharmacy, recognizing special population
- Given superiority of LAI, these medications should be considered earlier. Guide to support shared decision making
- Choose Wisely. Tools are available to support monitoring