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Challenges and Solutions for Psychopharmacology Management in the Geriatric Patient

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Disclosure

I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation (within the last 12 months).

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Presentation Objectives

Objectives for Pharmacists:

1. Identify common drug-related problems in the geriatric patient struggling with mental health issues.
2. Recommend evidence-based treatment options to manage the common mental health disorders encountered in the geriatric population.
3. Recognize opportunities for deprescribing and non-pharmacological interventions in the geriatric population.

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Presentation Objectives

Objectives for Pharmacy Technicians :

1. Identify common drug-related problems in the geriatric patient struggling with mental health issues.
2. Describe treatment options to manage the common mental health disorders encountered in the geriatric population.
3. Recognize opportunities for deprescribing and non-pharmacological interventions in the geriatric population.

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COMMON DRUG-RELATED PROBLEMS IN THE GERIATRIC PATIENT WITH MENTAL HEALTH ISSUES

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The Original Eight Drug-Related Problems (or Medication-Related Issues)

- Untreated Indication
- Improper Drug Selection
- Subtherapeutic Dose
- Supratherapeutic Dose / Overdosage
- Adverse Drug Reaction
- Drug-Drug Interaction
- Drug Use Without An Indication
- Failure to Receive Drugs

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Common Drug-Related Problems in Geriatric Persons with Mental Illness

- Untreated Indication
  - –Many persons go undiagnosed and untreated even if diagnosed
- Improper Drug Selection
  - –Not considering PK issues, PD issues, Evidence-based practice
- Subtherapeutic Dose
  - –Start Low, and Go Slow, but get to an individualized Treatment Dose
- Supratherapeutic Dose / Overdosage
  - –Easy to do if using Adult Dosing and not Considering PK changes and PD sensitivities, or P-genomics

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Common Drug-Related Problems in Geriatric Persons with Mental Illness

- Adverse Drug Reaction
  - –Anticholinergic, Sedation, Orthostasis,
- Drug-Drug (or Drug-Disease or Drug-Food) Interactions
  - –Older we get, more diseases, more drugs to potentially interact
- Drug Use Without An Indication
  - –Many share medications, taking spouses pain medication, sleeping medication, etc.
- Failure to Receive Drugs
  - –Adherence, Unable to Purchase Drugs, Forgetfullness/Dementia, Active vs Passive Non-Adherence issues

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TREATMENT OPTIONS FOR COMMON PSYCHIATRIC DISORDERS

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Mental Health Disorders in Geriatric Patients

- **Depression**
- Anxiety Disorders
  - –Obsessive-Compulsive Disorder
    - Hoarding
  - –Panic Disorder
  - –Social Anxiety Disorder
  - –Generalized Anxiety Disorder (GAD)
- Post-traumatic Stress Disorder (PTSD)
- Substance Use Disorders
- Chronic Pain Syndromes
- Bipolar Disorder
- **Schizophrenia**
- **Insomnia**
- **Disturbed Behaviors & Psychosis related to Alzheimer's Disease**

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Are we treating…… Target Symptoms or Diagnoses ?

- Multiple disease states may have similar, or even the same symptoms
- The practice of using side-effects of the psychotropic for symptom management.
  - –***Examples:*** _____ _____ _____
- **'Cure' vs 'Disease Management'**

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Depression

- **Epidemiology of Depression**
  - –10-20% lifetime prevalence
- **Common Ages / Facts**
  - –25-45 years old is highest risk in general population
  - –Lower in ambulatory / outpatient setting elderly
  - –**Higher in Nursing Homes (20-35%)**
  - –**Less than 50% of cases are recognized / diagnosed**
  - –Women 2x > Men
  - –**Elderly White Male** is at highest risk for successful suicide

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Differential Diagnosis

- Medical Problems associated with Depression or Depressive Symptoms
- Other Psychiatric Disorders associated with Depression or Depressive Symptoms
- Drug-Induced Depression
- Pseudo-Dementia

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Diagnosis of Depression

S = ***Sleep disturbance***
I = Loss of Interests
G = Guilt
Every Day for ≥2 weeks
E = ***Low Energy***

C = ***Poor Concentration / Memory***
A = ***Change in Appetite***
P = ***Psychomotor Agitation / Retardation***
S = Suicidal Ideation

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Medical Problems Associated with Depression or Depressive Symptoms

- Endocrine disorders (e.g.. hypothyroidism)
- Vitamin and mineral deficiencies and excesses
- Infections (e.g.. encephalitis, hepatitis, tuberculosis, HIV)
- Neurologic disorders
  - (e.g.. CVA, Parkinson's Disease, Wilson's Disease)
- Systemic Lupus Erythematosis (SLE)
- Cardiovascular Disease
- Malignancies and Carcinomas
- Chronic Pain Syndromes

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Other Psychiatric Disorders associated with Depression or Depressive Symptoms

- Alcoholism / Other Substance Abuse Disorders
- Anxiety disorders
  - Trauma Disorders
  - Impulse Control Disorders
- Bipolar Disorder **(bipolar-depression)**
- Eating disorders
- Schizophrenia

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Drug-Induced Depression

- Alcohol / Illicit drugs
- Propranolol
- Clonidine / Guanfacine
- Steroids (glucocorticoids or anabolics)
- Levodopa / Amantadine
- Oral contraceptives
- CNS depressants / sedative-hypnotics / Benzodiazepines
- NSAIDS
- Opiate analgesics
- Finasteride ?
- Reserpine / Methyldopa / Guanethidine / Hydralazine

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The Available Antidepressants

- Amitriptyline
- Imipramine
- Doxepin
- Nortriptyline
- Desipramine
- Protriptyline
- Maprotiline
- Amoxapine
- Duloxetine
- Levomilnacipran
- Gepirone
- Fluoxetine / Sertraline
- Paroxetine / Fluvoxamine*
- Citalopram / Escitalopram
- Trazodone / Nefazodone
- Bupropion / Mirtazepine
- Venlafaxine / Desvenlafaxine
- Selegiline / Phenelzine
- Tranycypromine
- Vilazodone / Vortioxetine
- ***Dextromethorphan+Bupropion***
- Zuranolone / Esketamine

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Antidepressant Selection Criteria

Primary Criteria:
- Patient's history of response
- Family history of response
- Patient's medical status / Age
- Side effect profile
- Patient's clinical presentation

- ***Other Secondary Criteria***

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Antidepressant Selection Criteria

Secondary Criteria:
- Patient's concomitant medications
  - –Drug-Drug/ Drug-Food Interactions
- Cost
- Compliance / Adherence issues
- Dosing Regimen / Formulations
- Stigma

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Black Box Warnings- SUICIDAL THOUGHTS AND BEHAVIORS

- Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies.
  - –Not seen in patients over age 24.
  - –*There was a trend toward reduced risk with antidepressant use in patients aged 65 and older.*
- In patients of all ages who are started on antidepressant therapy, monitor closely for worsening, and for emergence of suicidal thoughts and behaviors.
- Advise families and caregivers of the need for close observation and communication with the prescriber.

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TCAs / Heterocyclics

• Tertiary Amines:	
–Amitriptyline (Elavil)	25-300 mg/d
–Imipramine (Tofranil)	25-300 mg/d
–Doxepin (Sinequan)	25-300 mg/d
–Trimipramine (Surmontil)	25-300 mg/d
• Secondary Amines:	
–Nortriptyline (Pamelor)	25-200 mg/d
–Desipramine (Norpramin)	25-300 mg/d
–Protriptyline (Vivactil)	15-60 mg/d
• Heterocyclics:	
–Amoxapine (Asendin)	50-600 mg/d
–Maprotiline (Ludiomil)	50-225 mg/d

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TCAs Adverse Effects

- CNS adverse effects / Sedation / Activation
- Anticholinergic effects
- Decrease seizure threshold / Autonomic effects
- Orthostatic hypotension
- Arrhythmias
- Others: weight gain, sexual dysfunction
- Risk for Falls
- *On the **Beers Criteria** List*

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Monoamine Oxidase Inhibitors

- **Phenelzine (Nardil)**
  - –15-90 mg/d, divided TID
- **Tranylcypromine (Parnate)**
  - –10-60 mg/d, divided BID
- **Selegiline (EMSAM)**
  - –6-12 mg/d, transdermal once per day – rotating sites
- Class Adverse Effects:
  - –Orthostatic hypotension, CNS effects
  - –Anticholinergic (less than TCAs)
  - –Hepatic complications, Sexual dysfunction
  - –Hypertensive crisis
    - Tyramine-free diet recommended*

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Selegiline

- **Brand: EMSAM**
  - **MAO-I**
- **Pharmacokinetics:**
- **Dosing**
  - Initial: 6mg/24 hrs QD topical patch
  - Dosage Range: 6-12 mg/24 hrs QD
- **Adverse effects**
  - HA, dry mouth, insomnia, dizziness, low sexual dysfunction
  - BP changes
- **Drug & Food interactions**

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Selective Serotonin Reuptake Inhibitors (SSRIs)

• Fluoxetine (Prozac)	10-80 mg/day
• Sertraline (Zoloft)	25-200 mg/day
• Paroxetine (Paxil)	10-50 mg/day
• Fluvoxamine (Luvox)	50-300 mg/day
• Citalopram (Celexa)	20-60 mg/day
• Escitalopram (Lexapro)	10-40 mg/day

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SSRIs Adverse Effects

- **Similarities >> Differences**
- **Class profile:**
  - Nausea / GI Disturbances
  - Headache
  - Sexual dysfunction
  - **Insomnia** / somnolence
  - Activation / Anxiety
  - **Rare: Hyponatremia / EPS**
- **All are less toxic (*better tolerated?)* than TCAs**

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Other Antidepressants

- **Bupropion (Wellbutrin)**
- **Trazodone (Desyrel)**
- Nefazodone
- Venlafaxine (Effexor)
- Desvenlafaxine (Pristiq)
- **Mirtazapine (Remeron)**
- Duloxetine (Cymbalta)
- Vilazodone (Viibryd)
- Vortioxetine (Trintellix)
- Gepirone (Exxua)
- **Dextromethorphan+Bupropion (Auvelity)**
- Esketamine (Spravato)

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Mirtazapine

- **Brand:** REMERON
- **Pharmacokinetics** (*Clearance reduced 40% in elderly*)
- **Dosing**
  - Initial: 7.5-15 mg/HS (available as the SolTab)
  - Therapeutic Range: 7.5-45 mg/HS
- **Adverse effects**
  - somnolence (54%), ↑ appetite/wt. gain (17%), dizziness
  - ↑ cholesterol by ≥20% (15%), ↑ LFTs (2%)
- **Drug interactions**
  - P450-2D6, 1A2, and 3A4 substrate

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Duloxetine

- **Brand:** CYMBALTA
- **Pharmacokinetics:** Half-life=12 hrs, >90% Protein bound
- **Dosing**
  - Initial: 20mg BID
  - Therapeutic Range: 40mg - 60mg/day
    - QD or divided BID; Max dose: 120mg
- **Adverse effects**
  - Nausea, dry mouth, constipation, ↓ appetite, tremor, insomnia, etc. Hepatotoxicity, ↑ LFTs, ↑ BP, discontinuation syndrome
- **Drug interactions**
  - P450: CYP2D6, and CYP1A2 substrate
  - Moderate inhibitor of CYP2D6 (caution with 2D6 substrates)

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Vortioxetine

- **Brand:** TRINTELLIX (name change)
  - Serotonin Reuptake Inhibitor
  - 5HT-1a agonist; 5HT-3 antagonist; 5HT-7 antagonist; 5HT-1d antagonist
- **Pharmacokinetics:**
  - Half-life = 66 hrs. 98% PPB; Metabolites: Inactive
  - P450-2D6 substrate: reduce dose in poor metabolizers
- **Dosing:**
  - 10 mg QD x 7 days, 20 mg QD for treatment, (5, 10, 15, 20 mg IR tablets)
- **Adverse effects:**
  - Nausea/vomiting, Constipation, Dizziness, Dry mouth, Hyponatremia
  - Discontinuation Syndrome and Serotonin Syndrome
- **Drug Interactions:**
  - P450-2D6 substrate and therefore, sensitive to inducers or inhibitors

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Options for the Treatment of the Severe or Refractory Patient

- **Combination of Antidepressants:**
  - Use agents having two (2) or more mechanism of actions
  - Use two different and selective acting antidepressants
- **Adjunctive therapy:**
  - ***Atypical Antipsychotic Agents***
  - Mood Stabilizers?
    - could it actually be a type of bipolar disorder?
  - Thyroid augmentation
  - Buspirone, Pindolol, Psychostimulants

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Adjunctive Treatments for Resistant or Partial Responders to Antidepressants for Unipolar Major Depression

The medications that are FDA-approved:

- _____
- _____
- _____
- _____
- _____
- _____* (for TRD)

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Bipolar-Depression

The medications that are FDA-approved:

- _____
- _____
- _____
- _____
- _____

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Co-Morbid Psychiatric Diagnoses with Pain Syndromes

- **Depression**
  - ***Especially with Chronic Pain***
- Bipolar Disorder
- Anxiety Disorders
  - ***Generalized Anxiety Disorder***
  - Panic Disorder
  - Others (OCD, SAD, PTSD)
- ***Chronic Insomnia***
- ***Current Substance Use Disorder***

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FDA-Approved Treatments for Insomnia

Benzodiazepines
Temazepam (Restoril)
Flurazepam (Dalmane)
Triazolam (Halcion)
Quazepam (Doral)
Estazolam (Prosom)

Melatonin-Receptor agonists
Ramelteon (Rozerem)
Tasimelteon (Hetlioz)
Melatonin*

- **BZD_1-Receptor agonists**
  - Zolpidem (Ambien)
  - Zaleplon (Sonata)
  - Eszopiclone (Lunesta)
- **Histamine antagonists**
  - Doxepin (Silenor)
  - Diphenhydramine
- **Dual Orexin Receptor Antagonists (DORAs)**
  - Suvorexant (Belsomra)
  - Lemborexant (Dayvigo)
  - Daridorexant (Quiviviq)

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'Two Birds with One Stone' Approach to Pharmacotherapy

- **Psychiatric Disorders**
  - –Anxiety, ***Depression***, Bipolar Disorder, Insomnia
- **Pain Syndromes**
  - –Neuropathic Pain, Headaches, Back Pain
- ***Can we treat both issues (Co-morbid Diagnoses) with one medication?***

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***Two Birds* with One Stone**

- Pain Syndrome
  - –Diabetic Neuropathic Pain
- Psychiatric Disorder
  - –**Depression**
- ***Can we treat these issues with one medication?***

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***Two Birds* with One Stone**

- Pain Syndrome
  - –Chronic Low Back Pain
- Psychiatric Disorder
  - –Generalized Anxiety (with Insomnia)
  - –Decreased quality of life……secondary **Depression**
- ***Can we treat these issues with one medication?***

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***Three Birds* with One Stone**

- Fibromyalgia (over sedation from opioids)
- **Depression (fatigue)**
- Generalized Anxiety Disorder
  - –leading to alcohol dependence d/t self medicating
- ***Can we treat these issues with one medication?***

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***Four Birds* with One Stone**

- Neuropathic Pain
- **Depression**
- Generalized Anxiety Disorder
- Smoking Cessation
- ***Can we treat these issues with one medication?***

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Clinical Pearls of Practice

- Is it depression, or something else?
  - –'All the Fluoxetine (Prozac) in the world won't treat……'
- The current Antidepressants take time to work, so don't switch treatments quickly.
- Did you give an adequate dose for adequate period of time?
- If 2 or 3 trials of antidepressants haven't worked, re-think your diagnosis.

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OPPORTUNITIES FOR DEPRESCRIBING PSYCHOTROPICS

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Opportunities for Deprescribing Psychotropics

Initiating the Deprescribing Process

Managing Adverse Effects and Safety Monitoring

Pharmacokinetic, Pharmacodynamic, and Pharmacogenomic Considerations

Treatment Adherence Considerations

The Psychological Context of Deprescribing and the Role of Psychotherapy

Deprescribing Decisions During Pregnancy and Lactation

Deprescribing Decisions in Older Adults and the Medically Ill

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5-step Deprescribing Process:

(1) Ascertain all drugs the patient is currently taking and reasons for each;

(2) Consider overall risk of drug-induced harm in individual patients;

(3) Assess each drug in regard to its current or future benefit potential compared with current or future harm or burden potential;

4. Prioritize drugs for discontinuation that have the lowest benefit-harm ratio and lowest likelihood of adverse withdrawal reactions or disease rebound syndromes;

5. Implement a discontinuation regimen and monitor patients closely for improvement or worsening.

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Opportunities for Deprescribing Psychotropics

As patients who are on a **benzodiazepine** become older adults, risk-benefit considerations should be carefully reviewed again to determine whether or not the benzodiazepine should be deprescribed

The medication list of older adults should be routinely evaluated for the cumulative (total) **anticholinergic burden**. If the anticholinergic burden is found to be significant, collaborative efforts should be made to discontinue or reduce medications with substantial anticholinergic activity. If needed, these patients may be switched to alternative medications with lower anticholinergic activity

The medication list of patients (especially older adults) who either have or are at significant risk for **orthostatic hypotension** should be evaluated to identify medications that may contribute to orthostatic hypotension. A systematic effort should be made in these patients to discontinue these medications or, at least, minimize their doses

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Opportunities for Deprescribing Psychotropics

In patients (especially older adults and those with respiratory disease) who need to be on an **opioid medication**, if clinically feasible, attempts should usually be made to discontinue benzodiazepines or, at least, minimize their doses

In older adults who have had a fall (or are at an **increased risk of falling**), we should routinely check orthostatic vital signs and conduct a thorough clinical evaluation that may include use of a standardized assessment such as the STOPP Fall tool to identify fall-risk-increasing drugs (FRIDs) and deprescribe them where possible, using its guidelines

Before deprescribing a psychotropic medication—particularly in older adults or the medically ill, who may be especially likely also to be taking nonpsychiatric medications—clinicians should comprehensively **check for drug-drug interactions** (such as relevant cytochrome p450 substrates) that might be affected by the elimination of a particular psychotropic drug

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NON-PHARMACOLOGICAL INTERVENTIONS

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Treatment Options for Mental Illness

Psychotherapy
Cognitive Behavior Therapy for Insomnia (CBTI)
Virtual Reality Interventions
Exercise and Strength Training
Physical Therapy
Occupational Therapy / Interventions for Safety and ADLs
Don't Retire
Increase Social Interactions
PDTs

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What are PDTs?

- *The Personal Data Transmitter, also known as a PDT, was a form of personal locator and monitoring device surgically implanted into the bodies of extrasolar colonists by both the Weyland-Yutani Corporation and the Colonial Marines…*

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Digital Therapeutics

- Digital Therapeutics (DTx) are evidence-based therapeutic interventions driven by software to prevent, manage, or treat a medical disorder or disease.
- In other words, DTx are patient-facing software applications that help patients treat, prevent, or manage a disease and that have a proven clinical benefit.

- What are Prescription Digital Therapeutics (PDTs)?

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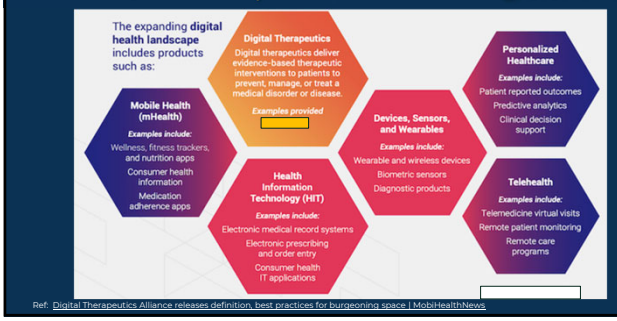

Ref: Digital Therapeutics Alliance releases definition, best practices for burgeoning space | MobiHealthNews

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Psychosis / Agitation / Mood Disorders

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Expert Consensus Panel for Using Antipsychotics in Older Patients (2004)

- Agitated dementia +/- delusions: AP (risp 1st)
- Late-life schizophrenia: AP (risp 1st)
- Psychotic major depression: AP + AD
- Severe non-psychotic mania: AP + MS
- Psychotic mania: AP + MS
- Parkinson's disease w/psychosis: AP (quet 1st)

J Clinical Psychiatry. Feb. 2004.

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Black Box Warnings

- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.

"…..*Pick your Antipsychotic*….." is not approved for the treatment of patients with dementia - related psychosis

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Risk of Death (all cause mortality)

• Aripiprazole	1.73
• Olanzapine	1.91
• Quetiapine	1.67
• Risperidone	1.30
• **Overall**	**1.54**

Schneider L. NIMH-NCDEU Meeting. Boca Raton, FL June 6, 2005

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BBW on Antipsychotics

- **April 2005:**
- Increased mortality in elderly patients (4.5% vs 2.6% with overall RR = 1.54) with dementia related psychosis
- **CATIE-AD Trial in 2006:**
  - Quetiapine = Placebo
  - Risperidone or Olanzapine > Placebo, but ADRs negate the benefits, overall…… No difference between APs vs Placebo
- **May 2016 APA Guidelines:**
  - Risperidone for 'Psychosis'
  - Risperidone, Olanzapine, Aripiprazole for 'Agitation'

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Brexpiprazole (Rexulti)

- May 11th, 2023 **First Medication** to receive FDA-approval for treating Agitation related to Dementia of the Alzheimer's type (no other type of dementia-related agitation)
- Dose:
  - 2-3 mg/day
- ADRs:
- Study 7 included 345 patients with a mean age of 74 years old, and a range of 56 and 90 years old; 44% were male; 95%, 4%, and 1% were White, Black or African American, and Asian, respectively; and 31% and 69% were Latino/Hispanic and not Latino/Hispanic, respectively.
- Cohen-Mansfield Agitation Inventory total (CMAI)

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Dextromethorphan + Bupropion (Auvelity)

- **Indications:** **Agitation Associated with Dementia Due to Alzheimer's Disease**
  Major Depressive Disorder
- **MoA**: NMDA receptor antagonist; sigma 1 receptor agonist;
  (also has Serotonin Reuptake Inhibition, but they don't talk about it)
  Norepinephrine & Dopamine Reuptake Inhibitor;
  P450-2D6 Inhibition to increase DM plasma levels
- **Dosing**: 30+105 mg/tab x 7 days; then 30+105 BID x 7 days;
  then 45+105 BID (90+210 mg/day) (dosing at least 8 hours apart)
  not 'PRN'
- **ADRs**: Dizziness, headache, diarrhea, somnolence, dry mouth, sexual dysfunction, and hyperhidrosis.
- **Notes:** Claiming first "fast-acting oral antidepressant", d/t statistical & minimal clinical separation from placebo at week 1.

Clinical response measured as ≥50% reduction in MADRS score was statistically significant with 54% of Auvelity responders compared to 34% for placebo. The Remission Rates are better than expected from ADs

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- Axsome Therapeutics Announces FDA Approval of AUVELITY (dextromethorphan HBr and bupropion HCl) for the Treatment of Agitation Associated with Dementia due to Alzheimer's Disease
- **April 30, 2026**
- **First and only non-DA binding medication / antipsychotic with this indication.**

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Alternatives for Dementia-Related Agitation / Behavioral Disturbances

- **SSRI's** (best evidence*)
  - –related to central serotonin deficits
    - **Citalopram**
      - –equal to risperidone, decreased side effects
    - **Sertraline** (proven efficacy)
- Antiepileptic: (fair evidence)
  - –Valproic Acid
  - –Carbamazepine
- Anxiolytics (poor evidence)
  - –**Benzodiazepines**
  - –Buspirone
- Beta Blockers (poor evidence)
  - –Propranolol
  - –Pindolol
- ***Behavioral*****

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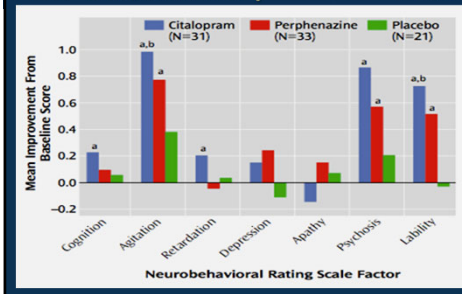

- a. Significant difference within group between baseline and termination scores (Wilcoxon signed-rank test, p<0.05).
- b. Significant difference between the citalopram and placebo groups (Kruskal-Wallis test, p<0.05).

Pollack BG, Mulsant BH, Rosen J, et al. Comparison of Citalopram, Perphenazine, and Placebo for the Acute Treatment of Psychosis and Behavioral Disturbances in Hospitalized, Demented Patients. *Am J Psychiatry*. 2002;159:460–465.

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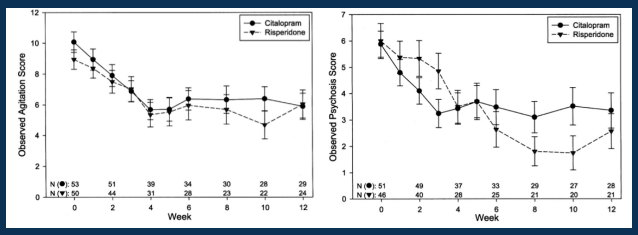
Citalopram vs Risperidone for Psychosis associated with Dementia



- Dementia patients hospitalized for psychosis or agitation had similar efficacy in reducing psychosis
- **Citalopram group experienced less side effects**

Pollock BG, Mulsant BH, Rosen J, et al. A double-blind comparison of of citalopram and risperidone for the treatment of behavioral and psychotic symptoms associated with dementia. *Am J Geriatr Psychiatry*. 2010;18(4):332-340.

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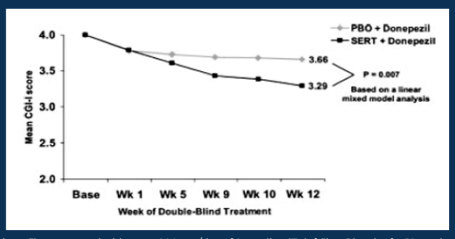
Sertraline vs. Placebo in AD Patients



- Donepezil (Aricept®) augmented with up to 200 mg/day of Sertraline (Zoloft®) or Placebo for 12 weeks
- Post hoc analyses: Sertraline significantly decreased CGI-I scale; other parameters were not significant between group

Finkel SI, Mintzer JE, Dysken M, et al. A randomized, placebo-controlled study of the efficacy and safety of sertraline in the treatment of the behavioral manifestations of Alzheimer's disease in outpatients treated with donepezil. *Int J Geriatr Psychiatry* . 2004;19:9–18.

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Benzodiazepines

- **Minimal efficacy data**
- Sedating
- **Cause falls**
- **Further inhibit learning and memory**
- **Paradoxical disinhibition**
- Commonly used
  - **lorazepam**
  - **oxazepam**

Source: Coccaro. *Am J Psychiatry*. 1990;147:1640-1645.

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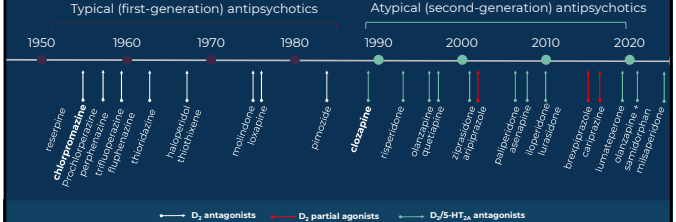
Antipsychotic Oral Treatments of Schizophrenia



2024: First non-DA binding medication for schizophrenia:, Xamomeline + Trospium

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Conventional / Older / Typical First Generation Antipsychotics (FGAs)

Chlorpromazine	Thorazine	1954*
Trifluoperazine	Stelazine	1957
Perphenazine	Trilafon	1957
Thioridazine	Mellaril	1959
Fluphenazine	Prolixin	1959
Thiothixene	Navane	1967
Haloperidol	Haldol	1967
Loxapine*	Loxitane	1973
Molindone*	Moban	1974

Tenth FGA currently on US Market, practically never used for schizophrenia, despite FDA-approval?

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Atypical Antipsychotics (SGAs / TGAs?)

Clozapine	Clozaril	Novartis	1990
Risperidone	Risperdal	Janssen	1994
Olanzapine	Zyprexa	Lilly	1995
Quetiapine	Seroquel	Zeneca	1997
Ziprasidone	Geodon	Pfizer	2001
Aripiprazole	Abilify	BMS/Otsuka	2002
Paliperidone	Invega	Janssen	2007
Illoperidone	Fanapt	Vanda	2009
Asenapine	Saphris	Merck	2009
Lurasidone	Latuda	Sunovion	2010
Brexpiprazole	Rexulti	Otsuka	2015
Cariprazine	Vraylar	Allergan	2015
Lumateperone	Caplyta	ITCI	2019
Olanzapine+Samidorphan (Lybalvi)		Alkermes	2021
Xanomeline+Trospium (Cobenfy)		BMS	2024
Milsaperidone	Bysanti	Vanda	2026

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Long-Acting Injectable Antipsychotics

- Fluphenazine Decanoate
- Haloperidol Decanoate
- Risperidone Microspheres (Risperdal Consta)
- Paliperidone
  - –Invega Sustenna
  - –Invega Trinza
  - –Invega Hafyera
- Aripiprazole Monhydrate
  - –Abilify Maintena
  - –*Abilify Asimtufii*
- *Aripiprazole Lauroxil (Aristada)*
- *Risperidone SC (Uzedy)*
- Risperidone ER Suspension (generic Consta)
- Risperidone (Risvan)?
- *Paliperidone ER Suspension (Erzofri)*

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Long-Acting Injectable Antipsychotics

GENERIC	BRAND	DOSE	Relapse Rates
Fluphenazine	**Prolixin Decanoate**	25-75 mg q 2 weeks IM / SC	30%
Haloperidol	**Haldol Decanoate**	50-450 mg q 4 weeks	25-30%
Risperidone	**Risperdal Consta**	25-50 mg q 2 weeks	15-22%
Olanzapine	**Zyprexa Relprevv *****	150-300 mg q 2-4 weeks	10%
Paliperidone	**Invega Sustenna**	39-234 mg q 4 weeks	10%
Aripiprazole	**Abilify Maintena** **Abilfy Asimtufii**	400 mg q 4 weeks 960 mg q 8 weeks	10% ???
Paliperidone	**Invega Trinza** **Invega Hafyera**	273 – 819 mg q 12 weeks 1092-1560 mg q 24 weeks	4.9-7% 7.5%
Aripiprazole	**Aristada** **Aristada Initio (675 mg)**	441 – 882 mg q 4 weeks 882 mg q 6 weeks 1064 mg q 8 weeks	??
Risperidone	**Risvan ??**	75-100 mg q 4 weeks IM equivalent to 3-4 mg oral RISP	??
Risperidone	**Uzedy**	50-125 mg q 4 weeks SC 100-250 mg q 8 weeks SC	7-13% >13%?
Risperidone	**Generic Consta**	25-50 mg q 2 weeks	???

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Challenges to Treatment

- Recognition and Diagnosis of Mental Disorders
- Co-Morbid Illnesses*
  - –Matching treatments ***(2 birds….1 stone)***
- Medication Adherence
- Side Effect Profiles of Psychotropics
- Direct and Indirect Costs of Treatment
- ***Treatment Resistance / Partial Response / Refractory***

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Options for the Treatment of the Severe or Refractory Patient

- **Combination of Psychotropics (eg. ADs+APs or AD+AD or AP+AP or AP+MS)**
  - – Use agents having two (2) or more mechanism of actions
  - – Use two different and selective acting antidepressants or antipsychotics
  - – Symbyax™ (Olanzapine+Fluoxetine) is FDA-approved for ***TRD***
- **Adjunctive therapy:**
  - ***Atypical Antipsychotic Agents****
  - ***Esketamine NS (Adjunctive in 2019 or Monotherapy in 2025)***
  - Thyroid augmentation, Buspirone, Pindolol, Psychostimulants

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Combination Products in Psychiatry…….
The Trend is Back

- Triavil (Perphenazine + Amitriptyline)
- Limbitrol (Chlordiazepoxide + Amitriptyline)

- **Symbyax (Olanzapine + Fluoxetine)**
- **Lybalvi (Olanzapine + Samidorphan)**
- **Auvelity (Dextromethorphan + Bupropion)**
- **Cobenfy (Xanomeline + Trospium)**

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Summary

- **Identification of Drug-Related Problems which are common in Geriatrics**
- **Engage in Psychotropic Deprescribing when possible**
- **Utilize Non-Pharmacological Interventions for various disorders**

- **We have many pharmacological treatments to choose from…… *(but still no cures)***

- **Monotherapy is still the Gold Standard**
  - **Evidence-based medicine *rarely* supports combination tx.**
  - **Growing trend to combination of psychotropics**
  - **Evidence does support LAIs over Oral antipsychotics *(in relapse prevention)***

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Questions?

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Challenges and Solutions for Psychopharmacology Management in the Geriatric Patient

Jose A Rey, MS, PharmD, BCPP, FAAPP

Professor, Nova Southeastern University, Barry and Judy Silverman College of Pharmacy
Clinical Psychopharmacologist, South Florida State Hospital – Recovery Solutions

Thank you!

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