



Culture of Safety Center 2022 Summit

Antipsychotic Use and Gradual Dose Reduction Strategies in the Long-Term Care Setting



www.Qsource.org



Jonathon Pouliot, MS, PharmD, BCPS | Consultant Pharmacist

Martin Serene, MSN, FNP-BC | Behavioral Health Nurse Practitioner
Aug. 24, 2022



Objectives

- Review antipsychotic medications and their use in practice
- Examine the role of antipsychotics in the long-term care setting
- Analyze the risks associated with antipsychotic use in long-term care
- Understand the concept of gradual dose reduction (GDR) and its use to manage antipsychotics
- Apply concepts of appropriate antipsychotic use and GDR strategies to patient case scenarios

Indications for Antipsychotic Medications

- Psychosis is a symptom of mental illness characterized by a distorted sense of reality
- Antipsychotic medications are commonly used in practice
- Primarily used for labeled or FDA-approved indications
 - Schizophrenia/schizoaffective disorders
 - Bipolar Disorders
 - Agitation
 - Major Depressive Disorders (adjunctive)
- Also used off-label, typically in the inpatient setting
- Associated with risks and benefits that providers and care-givers must understand

Reus VI. Overview of Psychiatric Disorders. In: Jameson J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. eds. *Harrison's Principles of Internal Medicine*, 20e. McGraw Hill; 2018

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

On-Label vs. Off-Label Uses

'Label' refers to the FDA-approved package insert of the medication of interest. FDA-approved indications are 'on-label' and other uses are deemed 'off-label'

- On-Label (FDA-approved)
 - FDA carefully evaluated benefits and risks for that specific use
 - Use of the medication is supported by strong data
 - Approved labeling for safe and effective use of the medication for that indication
- Off-Label
 - Use of a medication for an indication that is not specifically FDA-approved
 - Provider judges medical appropriateness of use (risk/benefits)
 - Data on use may exist but hasn't been evaluated by FDA

On-Label vs. Off-Label Uses

- Examples
 - A medication given in a different form than that which is FDA-approved
 - A medication given with different dosing than that which is FDA-approved
 - A medication that pre-dates the FDA approval process
 - A medication in the same class as other medications FDA-approved for use in an indication is used (assumed mechanism of action or class effect)
 - Antimicrobials
 - Oncology agents
 - Antipsychotics

Antipsychotic Medications

- General class of medications with activity in patients with various forms of psychosis
 - Most act on dopamine and serotonin pathways with other hypothetical effects
- Differ from other agents used in psychosis treatment
 - Sedatives, mood stabilizers, anti-depressants, etc
- Further defined as:
 - First-generation (or typical) antipsychotics
 - Second-generation (or atypical) antipsychotics

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Crismon M, Smith T, Buckley PF. Schizophrenia. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: <http://online.lexi.com>.

Antipsychotic Medications

First-Generation (Typical) Antipsychotics

Chlorpromazine (Thorazine)
Droperidol (Inapsine)
Fluphenazine (Prolixin)
Haloperidol (Haldol)
Perphenazine (Trilafon)
Thioridazine (Mellaril)
Thiothixene (Navane)

Second-Generation (Atypical) Antipsychotics

Aripiprazole (Abilify)
Asenapine (Saphris)
Brexpiprazole (Rexulti)
Cariprazine (Vraylar)
Clozapine (Clozaril)
Iloperidone (Fanapt)

Lurasidone (Latuda)
Olanzapine (Zyprexa)
Paliperidone (Invega)
Quetiapine (Seroquel)
Risperidone (Risperdal)
Ziprasidone (Geodon)

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Crismon M, Smith T, Buckley PF. Schizophrenia. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: <http://online.lexi.com>.

1st Generation Antipsychotic Medications

- Historically the standard of care for management of psychosis disorders
- Generally, higher side effect profile compared to atypical antipsychotics
 - More cardiac conduction effects → QT prolongation
 - More extra-pyramidal effects (EPS) → diskinesias, involuntary movements, etc
 - More anti-cholinergic effects
 - More sedation and disassociation
- Current use is mostly acute symptom control, adjunctive, or historically effective
 - Must assess risks/benefits and drug interactions with other medications

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Crismon M, Smith T, Buckley PF. Schizophrenia. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: <http://online.lexi.com>.

1st Generation Antipsychotic Medications

- Chlorpromazine (Thorazine)
 - Typically dosed at 50-150mg daily to start with titration up to 300-1000mg daily in divided doses
 - Characteristic side effects for 1st generations (sedation, EPS, anti-cholinergic effects)
 - Causes weight gain and metabolic effects
 - Used off-label for nausea/vomiting and severe hiccups.
- Haloperidol (Haldol)
 - Variety of dosing options including a long-acting depot injections
 - Characteristic side effects for 1st generations
 - More sedation and dissociation, especially with cumulative dosing
 - High risk of cardiac conduction effects
 - Used in acute agitation/mania/delirium
 - Also in patients not carrying a formal diagnosis

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Crismon M, Smith T, Buckley PF. Schizophrenia. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: <http://online.lexi.com>.

2nd Generation Antipsychotic Medications

- Mainstays of therapy for psychosis-related disorders
- Side effect profile is lower than 1st-generation antipsychotics
 - Less cardiac conduction effects although still a concern
 - Less EPS effects
 - Less anti-cholinergic effects
 - Less sedation and disassociation
- Higher incidence of metabolic effects (weigh gain and diabetes)
 - Some within the class may have lower incidence
- Commonly used for chronic management of established disease states
- Off-label use (especially in hospitalized and long-term care) increasing

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Crismon M, Smith T, Buckley PF. Schizophrenia. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: <http://online.lexi.com>.

2nd Generation Antipsychotic Medications

- Aripiprazole (Abilify)
 - Commonly used agent
 - Once daily dosing
 - Low risk of metabolic effects comparatively
 - Lower incidence of sedation and EPS effects
- Clozapine (Clozaril)
 - Used for refractory schizophrenia/mania
 - Risk Evaluation and Mitigation Strategy (REMS) program required by FDA due to hematologic side effects
 - High risk of metabolic effects comparatively
 - Uncommonly used

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Crismon M, Smith T, Buckley PF. Schizophrenia. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: <http://online.lexi.com>.

2nd Generation Antipsychotic Medications

- Olanzapine (Zyprexa)
 - Various dose forms including oral disintegrating, parenteral, and long-acting depot
 - High risk of metabolic and anticholinergic effects comparatively
 - Commonly used in practice for labeled and off-label use
- Quetiapine (Seroquel)
 - Only available as an oral agent
 - High risk of metabolic effects at high doses comparatively
 - More sedation and hypotension than other atypical agents
 - Lower incidence of movement side effects (EPS, akathisias)

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Crismon M, Smith T, Buckley PF. Schizophrenia. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: <http://online.lexi.com>.

2nd Generation Antipsychotic Medications

- **Risperidone (Risperdal)**
 - Available for oral administration or long-acting intramuscular depot
 - Especially effective for mania and bipolar, adjunctive for major depressive disorder
 - Relatively less sedation and hypotension
 - Moderate metabolic effects
- **Ziprasidone (Geodon)**
 - Available as oral or short-acting intramuscular administration
 - Once daily dosing (food aids absorption)
 - Lower metabolic effects comparatively
 - Effective for acute mania and acute agitation

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Crismon M, Smith T, Buckley PF. Schizophrenia. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: <http://online.lexi.com>.

2nd Generation Antipsychotic Medications

- Honorable Mentions
 - Asenapine (Saphris) → can only be given sublingually
 - Brexpiprazole (Rexulti) → specific benefits as adjunct for depression
 - Cariprazine (Vraylar) → benefits in bipolar I; low side effects comparative to class
 - Lurasidone (Latuda) → Very low side effect profile (anticholinergic, sedation, metabolic, hypotension)



Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Crismon M, Smith T, Buckley PF. Schizophrenia. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: <http://online.lexi.com>.

Antipsychotic Use in Practice

- Agents of choice for:
 - Schizophrenia/schizoaffective disorders
 - Bipolar Disorders
 - Acute agitation/mania
 - Other psychosis-related conditions
- Adjunctive agents for:
 - Major Depressive Disorders
 - Depression
 - Some Major Neurocognitive Disorders



Reus VI. Overview of Psychiatric Disorders. In: Jameson J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. eds. *Harrison's Principles of Internal Medicine*, 20e. McGraw Hill; 2018

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Antipsychotic Use in Practice – Off-Label Uses

- Selected Off-Label Indications
 - Anxiety
 - Attention-deficit hyperactivity disorder (ADHD)
 - Dementia
 - Depression
 - Eating Disorders
 - Insomnia
 - Obsessive-compulsive disorder (OCD)
 - Personality disorder
 - Post-traumatic Stress Disorder (PTSD)
 - Substance abuse
 - Tourette's Syndrome

TABLE 3 Efficacy of Atypical Antipsychotics by Condition and Strength of Evidence

	Aripiprazole	Olanzapine	Quetiapine	Risperidone	Ziprasidone
Anxiety					
Generalized anxiety disorder	○	-	++	-	-
Social phobia	○	+	-	○	○
Attention-deficit hyperactivity disorder					
No co-occurring disorders	○	○	○	+	○
Bipolar children	-	○	○	○	○
Mentally retarded children	○	○	○	+	○
Dementia					
Overall	++	+	+	++	○
Psychosis	+	+-	+-	++	○
Agitation	+	++	+-	++	○
Depression					
MDD augmentation of SSRI/SNRI	++ ^a	+- ^a	++ ^a	++	+
MDD monotherapy	○	-	++	○	○
Eating disorders	○	--	-	○	○
Insomnia	○	○	-	○	○
Obsessive-compulsive disorder					
Augmentation of SSRI	○	+	--	++	-
Augmentation of citalopram	○	○	+	+	○
Personality disorder					
Borderline	+	+-	+	○	-
Schizotypal	○	○	○	+-	○
Post-traumatic stress disorder	○	+-	+	++	○
Substance abuse					
Alcohol	--	-	-	○	○
Cocaine	○	-	○	-	○
Methamphetamine	-	○	○	○	○
Methadone clients	○	○	○	-	○
Tourette's syndrome	○	○	○	+	-

Antipsychotic Use in Practice – Off-Label Uses

- Inpatient Delirium Prevention/Treatment
 - Historically antipsychotics were thought to be beneficial
 - Still some use in practice
 - A systematic review and meta analysis by Neufeld et al provided evidence that antipsychotics should **not** be used routinely
 - The Prevention and Management of Pain, Agitation/Sedation, Delirium Guidelines recommend **against** routine use of antipsychotics for prevention/treatment of delirium
- Insomnia
 - Insufficient evidence to support antipsychotic use for insomnia
 - Utilizing side-effect of sedation to help with sleep
 - Sedation **does not** promote sleep quality!
- Acute agitation
 - Some evidence for efficacy
 - Should not be continued without a formal evaluation/diagnosis

Neufeld KJ, Yue J, Robinson TN, et al. *J Am Geriatr Soc*. 2016;64:705-714.
Devlin JW, Skrobik Y, Gelinas C, et al. *Crit Care Med*. 2018;46(9):e825-e873

Initiating Antipsychotic Therapy

- Indication for use
 - FDA-approved indication
 - Off-label data for use
- Patient-specific factors
 - Side effect profile and patient risk
 - Comparative efficacy based on patient symptoms
- Some level of trial and error in order to individualize patient care



Antipsychotic Use in Long-Term Care

- Differentiating patients with documented psychiatric conditions
 - Ensuring correct documentation for use
 - FDA-approved indication vs. Off-label use
- Individualized benefit and risk assessment
 - Re-assessment at set intervals
- Assessment of transitions of care
 - Medications added in the hospital that should be stopped
 - Medications not continued in the hospital that should be continued
- Polypharmacy assessment
- Adverse Drug Effects

Antipsychotic Risks in Long-Term Care



- General Medication Risk Factors:
 - Often geriatric
 - Multiple comorbidities
 - Increased risk for polypharmacy
 - Limitations to independent activities of daily living
 - Increased risk for falls, depression, etc
 - Limitations to real-time multidisciplinary care
 - In comparison to other healthcare settings
 - Limited resources for care
 - Issues with transitions of care

Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Meyer JM. Pharmacotherapy of Psychosis and Mania. In: Brunton LL, Hilal-Dandan R, Knollmann BC. eds. *Goodman & Gilman's: The Pharmacological Basis of Therapeutics*, 13e. McGraw Hill; 2017.

Polypharmacy and Antipsychotics

- Polypharmacy
 - Using/prescribing more medications than clinically indicated (typically defined as 5 or more)
 - Created/worsened by:
 - Multiple comorbidities
 - Multiple providers and pharmacies
 - Transitions of care
 - Cascading of medication additions
 - Increases risk of ADE and drug interactions
 - Vicious cycle



Polypharmacy and Antipsychotics

- Antipsychotic polypharmacy (multiple agents) may be beneficial in some patient scenarios
- Focus should be on minimizing drug interactions with other medications
- Are we treating side effects of medications with more medications?

WELL, THE **WHITE PILL** LOWERS MY BLOOD PRESSURE BUT MAKES MY LEGS SWELL, THE **YELLOW PILL** LOWERS THE SWELLING BUT **CAUSES ME TO PEE**, THE **BLUE PILL** STOPS ME FROM PEEING BUT **MAKES ME CONFUSED**, THE **TAN PILL** IMPROVES MY MEMORY BUT **MAKES MY NOSE RUN**, THE **PINK PILL** STOPS MY NOSE FROM RUNNING BUT **MAKES ME SLEEPY**, THE **ORANGE PILL** WAKES ME UP BUT **INCREASES MY BLOOD PRESSURE**, SO THE **WHITE PILL** LOWERS MY BLOOD PRESSURE BUT...

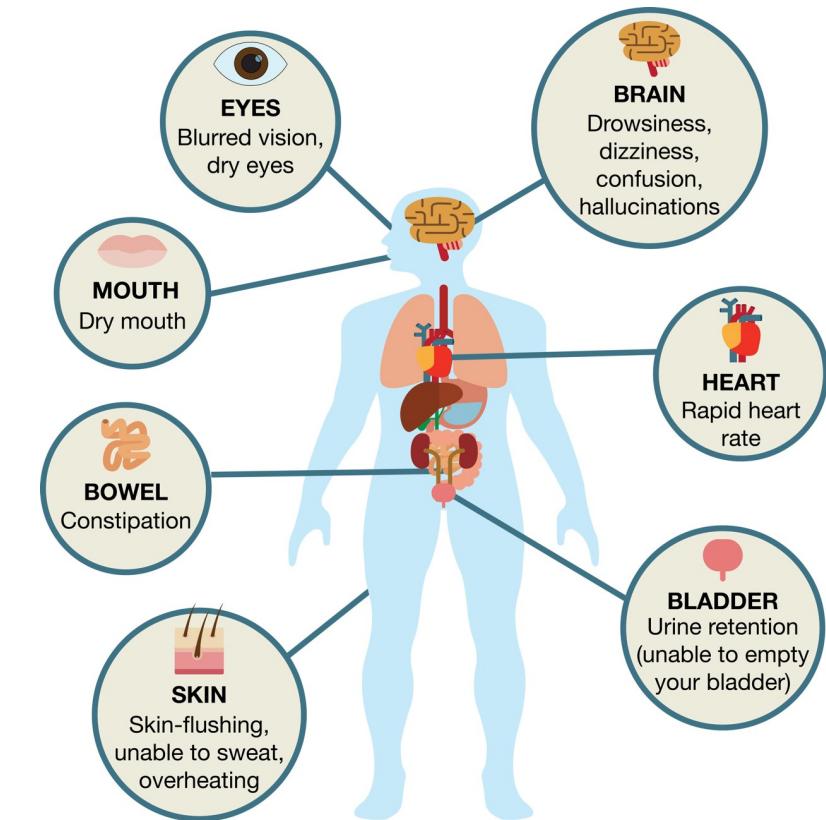


By Edwin Tan (c) 2015
www.facebook.com/edsrant

Hoel RW, Giddings RM, Takahashi PY. *May Clin Proc*. 2021;96(1):242-56.
Lahteenluoma M, Tiihonen J. *Drugs*. 2021;81:1273-84
Gnjic et al. *J Clin Epidemiol*. 2012;65(9):989-95.

Antipsychotic Risks in Long-Term Care

- Adverse Drug Event Risk is Elevated in Long-Term Care Patients
 - Falls risk → sedation, hypotension, anticholinergic effects
 - Poor sleep → sedation, anticholinergic effects
 - Depression → sedation
 - Cardiovascular disease → worsening of metabolic syndrome and weight gain

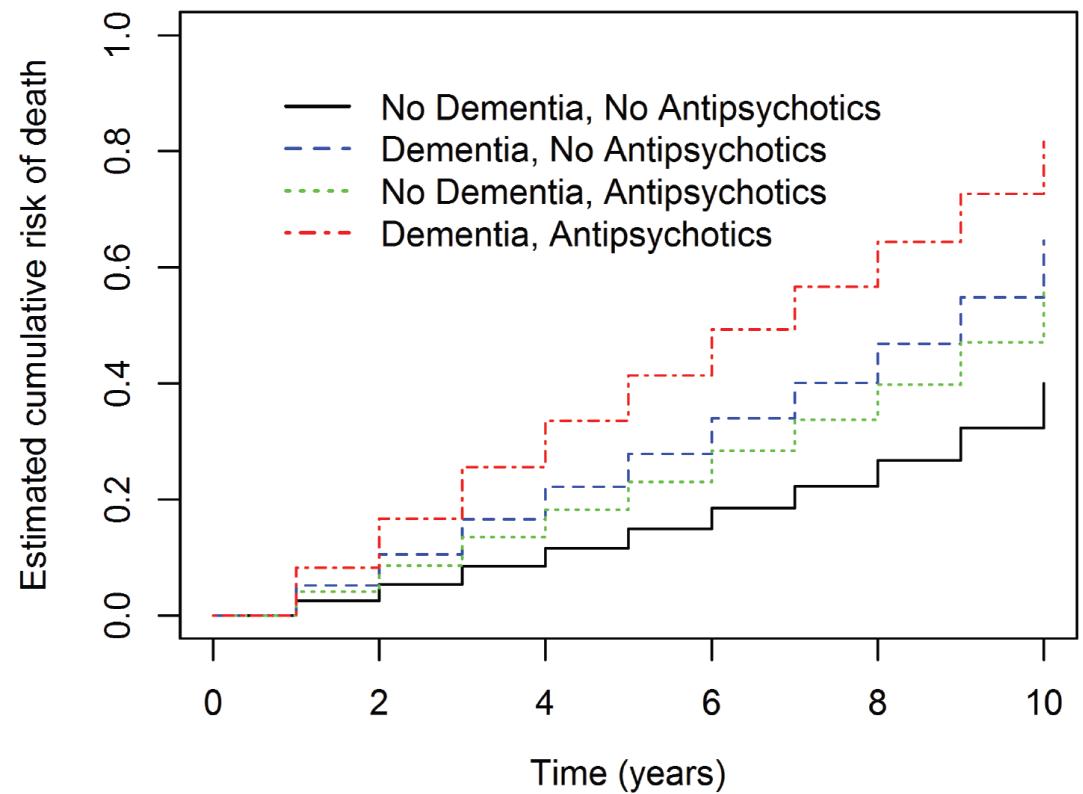


Schneiderhan ME, Nelson L, Bishop JR, Bauer S. Evaluation of Psychiatric Disorders. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 11e. McGraw Hill; 2020.

Meyer JM. Pharmacotherapy of Psychosis and Mania. In: Brunton LL, Hilal-Dandan R, Knollmann BC. eds. *Goodman & Gilman's: The Pharmacological Basis of Therapeutics*, 13e. McGraw Hill; 2017.

Antipsychotic Risks in Long-Term Care

- Antipsychotic use in dementia patient is associated with an increased risk of mortality
- Association appears to be dose-related
 - Higher doses → increased mortality
- One study showed relative mortality based on agent
 - haloperidol > risperidone > olanzapine > quetiapine



Antipsychotic Risks in Long-Term Care

- Inadequate control of psychosis-related symptoms also a risk for long-term care patients
 - Typically hypo-active or depression-related symptoms
- Transitions of care concern for missed medications/inaccurate dosing
- Other medications masking symptoms
 - Opiates, benzodiazepines, hypnotics
- Consider extra attention to these patients

Medication Management Strategies

- Medication Reconciliation
- Identification of medication appropriateness
- Evaluation for deprescribing and under-prescribing opportunities
 - Engage gradual dose reduction strategies if appropriate
- Evaluation for drug interactions and dosing appropriateness

Medication Management Strategies

- Medication Reconciliation

- 'The process of comparing a patient's medication orders to all of the medications that the patient is taking.' – Joint Commission
- Sources of information
 - Pharmacy fill history
 - Medication list from physician's office/hospital
 - Patient interview
 - Other sources
- Goal → identify the most accurate list of medications the patient is actually taking

- Medication Appropriateness

Questions to ask about each individual medication:

- 1. Is there an indication for the medication?
- 2. Is the medication effective for the condition?
- 3. Is the dosage correct?
- 4. Are the directions correct?
- 5. Are the directions practical?
- 6. Are there clinically significant drug–drug interactions?
- 7. Are there clinically significant drug–disease/condition interactions?
- 8. Is there unnecessary duplication with other medication(s)?
- 9. Is the duration of therapy acceptable?
- 10. Is this medication the least expensive alternative compared to others of equal utility?

Gradual Dose Reduction Strategies

- Gradual Dose Reduction (GDR) is a strategy for slowly but methodically lowering medication doses to optimize medication use
- Goals
 - Remove a medication completely
 - Find a dose that optimizes efficacy and minimizes side effects
- Individualized to patient and medication



**THE ART OF
THE GRADUAL
DOSE
REDUCTION**

LTCPHARM.D.COM

Gradual Dose Reduction Strategies

- Tjia et al. provided a literature search and identified that while discontinuation strategies are important, they are ‘unstandardized’ and ‘not validated’
- They recommend a pharmacology-based gradual reduction strategy

Generic/Brand	$t_{1/2}$	Adjusted $t_{1/2}$ for Increased Age (65–89 Yr: $1.5 \times t_{1/2}$)	Calculated Time to Steady-State (5–7 Half-Lives to Reach Steady State)	Time to Next Gradual Dose Reduction (Leave at Steady State for ~ 7 Days)	Clinically Recommended Time Between Gradual Dose Reduction	Estimated Time to Discontinuation
Aripiprazole/ Abilify	Parent: 75 hrs Active metabolite: 94 hrs	Parent: 83 hrs Active metabolite: 141 hrs	41 days (based on active metabolite)	48 days	2 months	4 months
Olanzapine/ Zyprexa	Parent: 21–54 hrs	Parent: 32–81 hrs	9–24 days	16–31 days	2–4 weeks	4–8 weeks
Quetiapine/ Seroquel	Parent: IR: 6 hrs ER: 7 hrs	Parent: IR: 9 hrs ER: 11 hrs	Parent: IR: 2.5 days ER: 3 days	Parent: IR: 9.5 days ER: 10 days	2 weeks	4 weeks
Risperidone/ Risperdal	Parent: 3–20 hrs Active metabolite: 21–30 hrs	Parent: 4–30 hrs Active metabolite: 32–45 hrs	Parent: 1–9 days Active metabolite: 9–13 days	Parent: 8–16 days Active metabolite: 16–20 days	2–3 weeks	4–6 weeks

Gradual Dose Reduction Strategies

- Takeuchi et al. conducted a systematic review and meta-analysis on immediate vs. gradual dose reduction.
- No major differences in outcome measures
- Researchers found advantages to individualizing the strategy based on patients risk/benefit and medication list.
- Graff-Guerrero et al. conducted an evaluation of gradual dose reduction in stable late-life schizophrenia patients
- Showed dose-reductions were feasible and safe.
- Results showed improvements in illness severity and reduction in adverse reactions.
- Even when discontinuation is not the goal, dose reductions can be beneficial

Gradual Dose Reduction Strategies

- Dose reduction strategies should be individualized to patients
- Focus on:
 - Maintaining disease management
 - Minimizing side effects
 - Reaching an attainable goal → discontinuation or lowered dose
- Gradual dose reduction strategies have been shown to be beneficial in the literature and in practice

Case Discussion 1

- WM, 79 y/o female
- Diagnoses – Bipolar disorder, Major Depressive Disorder (MDD)
- Background
 - Long-term mental health patient
 - Assisted living patient
 - Poor family resources/support

Case Discussion 1

- Medication
 - risperidone 0.5mg BID
 - lorazepam 0.5mg BID as needed
- Baseline Function
 - Patient ambulatory with walker
 - Talks to herself
 - Inserts herself into conversations
 - Otherwise pleasant and cooperative

Case Discussion 1

- GDR was done on WM's risperidone and stopped for 60 days
- Changes in behavior:
 - Pleasant but increasingly suspicious, especially other residents she doesn't get along with
 - Slow development of visual hallucinations (worsening her suspicion of others)
 - Increasingly fearful and guarded
 - Overall the patient became more erratic, labile and accusatory

Case Discussion 1

- Change in behavior identified
- Provider restarted risperidone
 - 0.25mg daily for 1 week then slowly back to 0.5mg BID
- Patient gradually returned to a calm and cooperative state
 - Free of psychosis, hallucinations, and paranoia

Case Discussion 1 Pearls

- Important to consider patient's quality of life when attempting GDR
 - Patient had some social issues on medication but off medication her psychosis was much worse
- Reasonable and prudent to use medications to maintain patient and staff safety
- Document specific psychosis-related events to justify antipsychotic use
- Use lowest dose possible and monitor for side effects
 - AIMS testing for tardive dyskinesia and drug-induced Parkinsonism

Case Discussion 1 Pearls

- Medication considerations
 - Don't try to re-invent the wheel
 - Start with the patient, their comorbidities and psychiatric-related conditions before choosing a medication
 - Use low doses
 - Titrate to quality of life or functional effect
- In this case risperidone was chosen
 - Patient had positive experience/tolerability
 - Lower falls risk in a mobile patient
 - Less sedating relatively

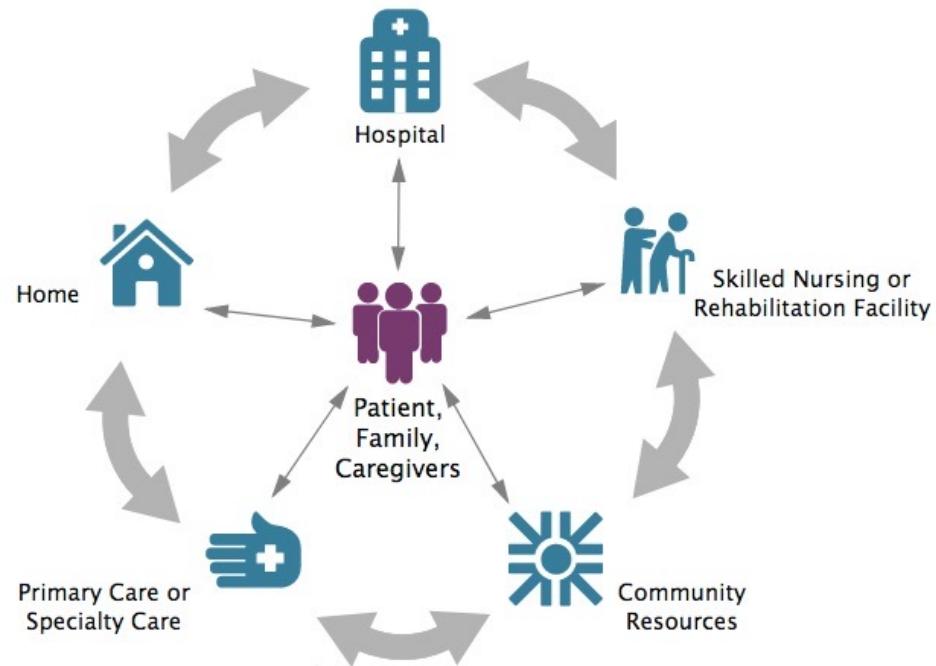


Case Discussion 2

- GS, 61 y/o female
- Diagnoses
 - Cognitive Communication Deficit
 - Schizoaffective disorder, depressive type
 - Anxiety
 - Major Depressive Disorder
 - Insomnia
- Home Medication List
 - escitalopram 20mg PO QAM
 - lorazepam 0.5mg PO Q8hr prn anxiety
 - quetiapine 300mg PO QHS
- Good baseline medication compliance and family resources/support
- Stable connection to outpatient psychiatrist

Case Discussion 2

- Background
 - Admitted to hospital then SNF secondary to a fall and femur fracture
 - Poor historian
 - Medication list in the hospital and transition to SNF did not include quetiapine
 - Patient withdrew from high-dose quetiapine in the hospital and SNF



Case Discussion 2

- Resolution
 - Psychiatric care provider assumed care 3 days into SNF stay
 - Patient had become increasing anxious, tearful, guarded, and paranoid
 - Provider contacted outpatient psychiatrist who provided medication and history information
 - Patient was restarted on quetiapine 100mg PO QHS
 - After 3 days, symptoms resolved and patient stabilized, completed recovery from her fracture and was discharged home on a lower dose

Case Discussion 2 Pearls

- Always ensure you have a complete picture of the patient's history and medication list
- Be cautious with information flow at transitions of care
 - There are places where information can be lost
- Use these situations as opportunities to ensure patient is optimally treated
 - Did she need to be on 300mg in the first place?

Case Discussion 2 Pearls

- Medication Considerations
 - Quetiapine is commonly used in practice for numerous mental health disorders
 - Can be prescribed for insomnia, especially if poorly controlled
 - In this case, quetiapine was likely chosen for its effect on schizoaffective disorder, psychosis, insomnia, and anxiety
 - Use the lowest dose possible and avoid abrupt discontinuation



Conclusion

- Antipsychotic medications are common in practice and have variable efficacy and safety considerations
- Risks and benefits to starting, continuing and discontinuing agents should be evaluated, especially in the long-term care population
- Off-label use of antipsychotic agents is common however benefits may be setting and situation-specific
- Gradual dose reduction strategies have shown benefit in patient care and should be implemented when deemed necessary
- Patient's quality of life should be a main factor in determining goals of care

Connect With Us

Jonathon Pouliot, MS, PharmD, BCPS
Consultant Pharmacist, Qsource
Email: jonathond.pouliot@gmail.com

Martin Serene, MSN, FNP-BC
Behavioral Health Nurse Practitioner
Email: mserene@cheservices.com



Facebook
www.facebook.com/QsourceLiveWell



Twitter
www.twitter.com/Qsource



LinkedIn
www.linkedin.com/in/qsource-healthcare-consultants