Antipsychotic Potpourri

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Disclosures

- No financially relevant disclosures.
- All antipsychotics are considered "off-label" use for patients with dementia.

Objectives

- Explain the difference between the old F329 and the new F757 and F758
- Give 3 reasons why psychoactive misuse occurs
- Describe the basic steps of a deprescribing algorithm for antipsychotics
- Summarize the 2016 APA guidelines on antipsychotic use

Old vs New F Tags on Unnecessary Meds

- "Old" F329 – All unnecessary medications
  - In excessive dose (including duplicate drug therapy); or
  - For excessive duration; or
  - Without adequate monitoring; or
  - Without adequate indications for its use; or
  - In the presence of adverse consequences which indicate the dose should be reduced or discontinued; or
  - Any combinations of the reasons above
- "New" F757 – Unnecessary medications (excluding psychoactives)
- "New" F758 – Unnecessary **psychotropic** medications/PRN use

F 758

- Residents who have not used psychotropic drugs are not given these drugs unless med is *necessary* to treat a *specific* condition as diagnosed and *documented* in the clinical record;
- Residents who use psychotropic drugs receive GDRs, and behavioral interventions, unless clinically contraindicated, in an effort to discontinue.

F 758 cont.

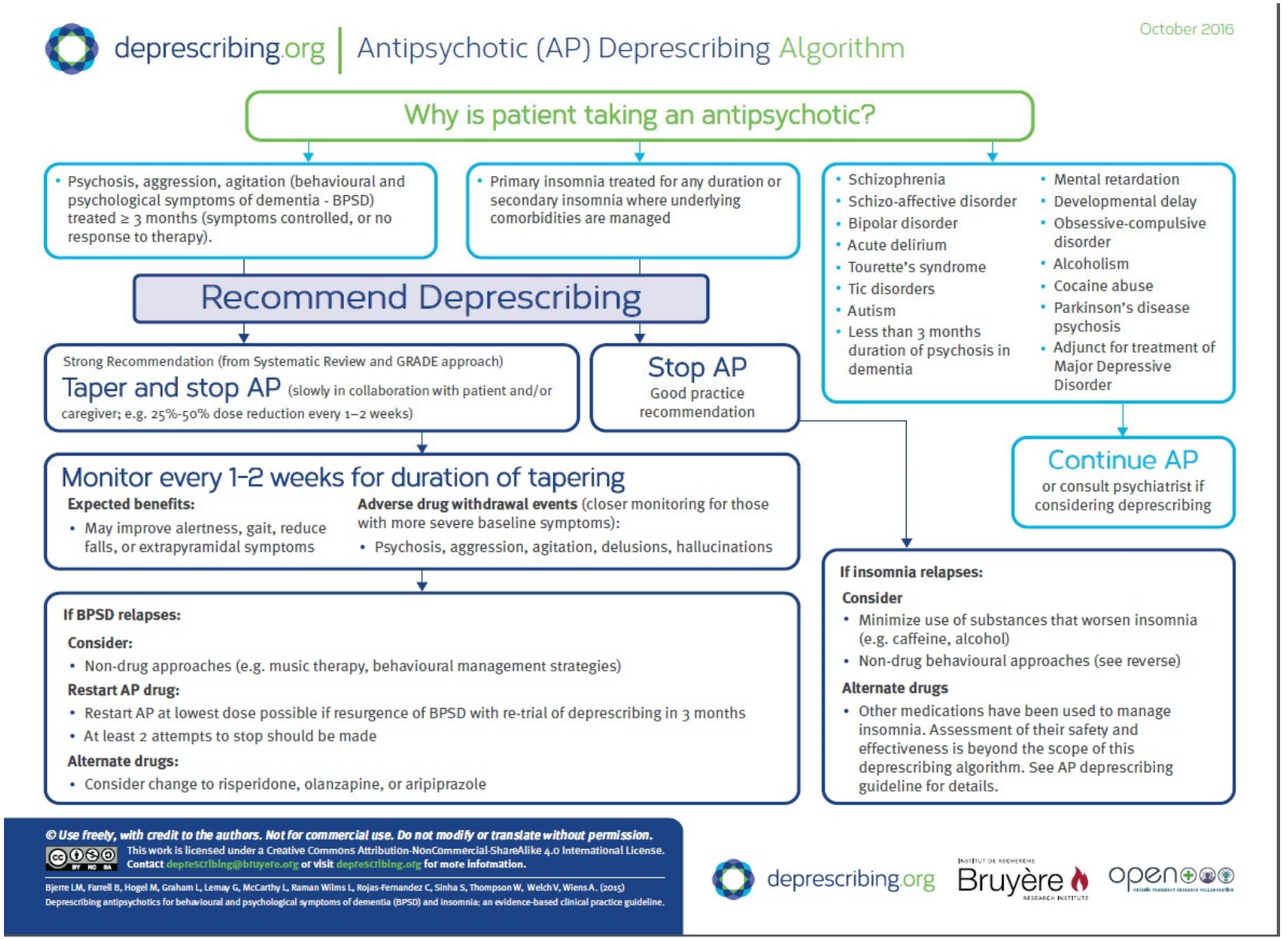
- Residents do not receive PRN psychotropic drugs unless med is *necessary* to treat a diagnosed *specific condition* that is *documented* in the clinical record
- PRN orders for psychotropic drugs are limited to 14 days. If order needs to be extended, physician should document their rationale in the medical record and indicate the duration
- PRN orders for antipsychotic drugs are limited to 14 days. Orders cannot be renewed unless physician evaluates the resident for continued appropriateness of med

10 Reasons why Psychoactive Drug Misuse occurs in LTC (from Sherman 1988)

- 1. Desire to help residents.
- 2. Belief in psychoactive drug efficacy.
- 3. Underestimation of drug toxicity.
- 4. Behavioral disturbance: problem or symptom?
- 5. Patient demand.

10 Reasons, cont.

- 6. Environmental control - ironically, a sedated resident requires more, not less care.
- 7. Family concerns - "must do something," "roommate is annoying," guilt assuagement.
- 8. Nursing staff stress.
- 9. Inadequate training regarding emotional, occupational and behavioral needs of patients.
- 10. Influence of some drug manufacturers.


deprescribing.org | Antipsychotic (AP) Deprescribing Algorithm
October 2016
Why is patient taking an antipsychotic?
• Psychosis, aggression, agitation (behavioural and psychological symptoms of dementia - BPSD) treated ≥ 3 months (symptoms controlled, or no response to therapy).
• Primary insomnia treated for any duration or secondary insomnia where underlying comorbidities are managed
• Schizophrenia
• Schizo-affective disorder
• Bipolar disorder
• Acute delirium
• Tourette's syndrome
• Tic disorders
• Autism
• Less than 3 months duration of psychosis in dementia
• Mental retardation
• Developmental delay
• Obsessive-compulsive disorder
• Alcoholism
• Cocaine abuse
• Parkinson's disease psychosis
• Adjunct for treatment of Major Depressive Disorder
Recommend Deprescribing
Strong Recommendation (from Systematic Review and GRADE approach)
Taper and stop AP (slowly in collaboration with patient and/or caregiver; e.g. 25%-50% dose reduction every 1–2 weeks)
Stop AP
Good practice recommendation
Continue AP
or consult psychiatrist if considering deprescribing
Monitor every 1-2 weeks for duration of tapering
Expected benefits:
• May improve alertness, gait, reduce falls, or extrapyramidal symptoms
Adverse drug withdrawal events (closer monitoring for those with more severe baseline symptoms):
• Psychosis, aggression, agitation, delusions, hallucinations
If BPSD relapses:
Consider:
• Non-drug approaches (e.g. music therapy, behavioural management strategies)
Restart AP drug:
• Restart AP at lowest dose possible if resurgence of BPSD with re-trial of deprescribing in 3 months
• At least 2 attempts to stop should be made
Alternate drugs:
• Consider change to risperidone, olanzapine, or aripiprazole
If insomnia relapses:
Consider
• Minimize use of substances that worsen insomnia (e.g. caffeine, alcohol)
• Non-drug behavioural approaches (see reverse)
Alternate drugs
• Other medications have been used to manage insomnia. Assessment of their safety and effectiveness is beyond the scope of this deprescribing algorithm. See AP deprescribing guideline for details.
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This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License.
Contact deprescribing@bruyere.org or visit deprescribing.org for more information.
Bjerre LM, Farrell B, Hogel M, Graham L, Lemay G, McCarthy L, Raman Wilms L, Rojas-Fernandez C, Sinha S, Thompson W, Welch V, Wiens A. (2015) Deprescribing antipsychotics for behavioural and psychological symptoms of dementia (BPSD) and insomnia: an evidence-based clinical practice guideline.
deprescribing.org
Bruyère Research Institute

deprescribing.org | Antipsychotic (AP) Deprescribing Notes

October 2016

Commonly Prescribed Antipsychotics

Antipsychotic	Form	Strength
Chlorpromazine	T IM, IV	25, 50, 100 mg l25 mg/mL
Haloperidol (Haldol®)	T L IR, IM, IV LA IM	0.5, 1, 2, 5, 10, 20 mg 2 mg/mL 5 mg/mL 50, 100 mg/mL
Loxapine (Xylac®, Loxapac®)	T L IM	2.5, 5, 10, 25, 50 mg 25 mg/L 25, 50 mg/mL
Aripiprazole (Abilify®)	T IM	2, 5, 10, 15, 20, 30 mg 300, 400 mg
Clozapine (Clozaril®)	T	25, 100 mg
Olanzapine (Zyprexa®)	T D IM	2.5, 5, 7.5, 10, 15, 20 mg 5, 10, 15, 20 mg 10mg per vial
Paliperidone (Invega®)	ER T PR IM	3, 6, 9 mg 50mg/0.5mL, 75mg/0.75mL, 100mg/1mL, 150mg/1.5mL
Quetiapine (Seroquel®)	IR T ER T	25, 100, 200, 300 mg 50, 150, 200, 300, 400 mg
Risperidone (Risperdal®)	T S D PR IM	0.25, 0.5, 1, 2, 3, 4 mg 1 mg/mL 0.5, 1, 2, 3, 4 mg 12.5, 25, 37.5, 50 mg

IM = intramuscular, IV = intravenous, L = liquid, S = suppository, SL = sublingual, T = tablet, D = disintegrating tablet, ER = extended release, IR = immediate release, LA = long-acting, PR = prolonged release

Antipsychotic side effects

- **APs associated with increased risk of**:
  - Metabolic disturbances, weight gain, dry mouth, dizziness
  - Somnolence, drowsiness, injury or falls, hip fractures, EPS, abnormal gait, urinary tract infections, cardiovascular adverse events, death
- **Risk factors**: higher dose, older age, Parkinsons', Lewy Body Dementia

Engaging patients and caregivers

Patients and caregivers should understand:

- The rationale for deprescribing (risk of side effects of continued AP use)
- Withdrawal symptoms, including BPSD symptom relapse, may occur
- They are part of the tapering plan, and can control tapering rate and duration

Tapering doses

- No evidence that one tapering approach is better than another
- Consider:
  - Reduce to 75%, 50%, 25% of original dose on a weekly or bi-weekly basis and then stop; **or**
- Consider slower tapering and frequent monitoring in those with severe baseline BPSD
- Tapering may not be needed if low dose for insomnia only

Sleep management

Primary care:

1. Go to bed only when sleepy
2. Do not use your bed or bedroom for anything but sleep (or intimacy)
3. If you do not fall asleep within about 20-30 min at the beginning of the night or after an awakening, exit the bedroom
4. If you do not fall asleep within 20-30 min on returning to bed, repeat #3
5. Use your alarm to awaken at the same time every morning
6. Do not nap
7. Avoid caffeine after noon
8. Avoid exercise, nicotine, alcohol, and big meals within 2 hrs of bedtime

Institutional care:

1. Pull up curtains during the day to obtain bright light exposure
2. Keep alarm noises to a minimum
3. Increase daytime activity and discourage daytime sleeping
4. Reduce number of naps (no more than 30 mins and no naps after 2pm)
5. Offer warm decaf drink, warm milk at night
6. Restrict food, caffeine, smoking before bedtime
7. Have the resident toilet before going to bed
8. Encourage regular bedtime and rising times
9. Avoid waking at night to provide direct care
10. Offer backrub, gentle massage

BPSD management

- Consider interventions such as: relaxation, social contact, sensory (music or aroma-therapy), structured activities and behavioural therapy
- Address physical and other disease factors: e.g. pain, infection, constipation, depression
- Consider environment: e.g. light, noise
- Review medications that might be worsening symptoms

Bjerre LM, Farrell B, Hogel M, Graham L, Lemay G, McCarthy L, Raman Wilms L, Rojas-Fernandez C, Sinha S, Thompson W, Welch V, Wiens A. (2015) Deprescribing antipsychotics for behavioural and psychological symptoms of dementia (BPSD) and insomnia: an evidence-based clinical practice guideline.

deprescribing.org | Institut de recherche Bruyère Research Institute | open

Case

- 70 y/o female admitted from out of state nursing home
- 3 months prior fell and broke hip
- Previously living with family and ambulatory without device
- Stage 4 pressure ulcer on sacrum with wound vac
- Heart failure, COPD, legally blind, h/o PE

Psychoactive Medications

- Ziprasidone 40mg BID
- Haloperidol 5mg 4x's daily
- Alprazolam 1mg q8 hrs. PRN
- Donepezil 10mg HS
- Mirtazapine 7.5mg qHS

Behaviors

- Presumed Alzheimer's dementia
- Constantly trying to walk
- Pulling wound vac off
- Requesting pain medication

Why is she taking 2 antipsychotics?

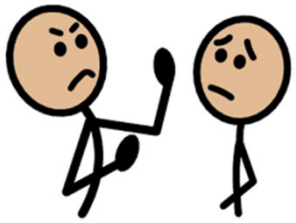
- No known mental health history
- No known developmental delay
- Memory impairment was "mild" prior to surgery per family
- History of opiate misuse but not alcohol
- No history of insomnia per family

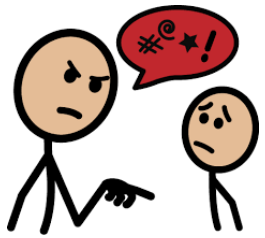
Deprescribing

- Ziprasidone decreased to 20mg BID
  - Cognition improved
- Ziprasidone decreased to 20mg daily
  - Cognition improved
- Ziprasidone discontinued
  - Cognition improved

Thoughts

- Gradual deprescribing
- Requires nurse and family buy-in
- Likely delirium from surgery in setting of mild dementia





AMERICAN PSYCHIATRIC ASSOCIATION

- AMERICAN PSYCHIATRIC ASSOCIATION PRACTICE GUIDELINE on the use of Antipsychotics to Treat Agitation or Psychosis in Patients with Dementia
- May 2016

Background

- Overwhelming majority of older adults with dementia will develop psychosis or agitation during the course of their illness.
- Symptoms are often persistent, occur with increasing frequency as cognition worsens, and are more prevalent among NH residents or inpatient facilities compared to community settings

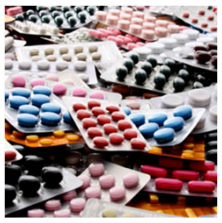
Caveats

- Applies to individuals with dementia in *all settings of care* as well as to care delivered by generalist and specialist clinicians
- Not intended to apply to individuals who are receiving antipsychotic medication for another indication (e.g., chronic psychotic illness) or individuals who are receiving an antipsychotic medication in an urgent context.

More Caveats

- For most behavioral interventions there have not been a sufficient number of large-scale, well-controlled studies from which to draw conclusions about efficacy or safety in treating agitation or psychosis
- None of the available studies have reported direct harm to patients from behavioral interventions
- Placebo-controlled trials of non-antipsychotic medications have not been reviewed in this practice guideline, and, thus, no recommendations are made about the appropriateness or sequence of their use based on their benefits and harms.
- No conclusions can be drawn from head-to-head comparisons *between non-antipsychotic drugs* (e.g., antidepressants, cholinesterase inhibitors, memantine*) and antipsychotic drugs* because of insufficient evidence

Positive™ Approach to Care



Caveats, cont.

- Patients with dementia who are enrolled in clinical trials are not likely to be representative of the full range of individuals for whom clinical use of an antipsychotic medication might be considered.
- Significant physical illness (e.g., cardiopulmonary or renal impairments, cancer), use of certain medications (e.g., anticoagulants), or severe aggression requiring emergent intervention are typical exclusions.
- Other psychiatric disorders, including substance use disorders, are also common exclusion criteria.

Recommendation Evidence

- A "recommendation" (denoted by the numeral 1 after the guideline statement) indicates confidence that the benefits of the intervention clearly outweigh the harms.
- "Strength of supporting research evidence." Three ratings are used:
  - A - high
  - B - moderate
  - C - and low
- (Agency for Healthcare Research and Quality 2014; Balshem et al. 2011; Guyatt et al. 2006)

Assessment of Behavioral/Psychological Symptoms of Dementia

- **Statement 1.** Patients should be assessed for the type, frequency, severity, pattern, and timing of symptoms. **(1C)**
- **Statement 2.** Patients should be assessed for pain and other potentially modifiable contributors to symptoms as well as for factors, such as the subtype of dementia, that may influence choices of treatment. **(1C)**
- **Statement 3.** In patients with dementia with agitation or psychosis, response to treatment be assessed with a quantitative measure. **(1C)**
  - Neuropsychiatric Inventory Questionnaire (NPI-Q)
  - Cohen-Mansfield Agitation Inventory (CMAI)

Development of a Comprehensive Treatment Plan

- **Statement 4.** Patients should have a documented comprehensive treatment plan that includes appropriate person-centered nonpharmacological and pharmacological interventions, as indicated. **(1C)**
  - Must be reassessed over time, with modifications made to address changes in the patient's cognitive status, symptom evolution, and treatment response

Assessment of Benefits and Risks of Antipsychotic Treatment for the Patient

- **Statement 5.** Non-emergency antipsychotic medication should only be used in patients with dementia when agitation and psychosis symptoms are severe, are dangerous and/or cause significant distress to the patient. **(1B)**
- **Statement 6.** Response to non-drug interventions should be reviewed prior to use of antipsychotic medication.**(1C)**
- **Statement 7.** Before non-emergency treatment with an antipsychotic, the potential risks and benefits should be assessed by the physician and discussed with the patient and the patient's surrogate decision maker, with input from the family. **(1C)**

Dosing, Duration, and Monitoring of Antipsychotic Treatment

- **Statement 8.** Treatment should be initiated at a low dose and titrated to the minimum effective dose.**(1B)**
- **Statement 9.** If the patient experiences significant side effects, the risks and benefits should be reviewed to determine if the antipsychotic should be discontinued.**(1C)**
- **Statement 10.** If there is no significant response after a 4-week time period, the medication should be tapered and withdrawn. **(1B)**

Dosing, Duration, Monitoring, cont.

- **Statement 11.** In a patient who has shown a positive response to treatment, decision making about possible tapering of antipsychotic medication should be accompanied by a discussion with the patient (if clinically feasible), surrogate decision maker/family (if relevant) and caregivers. **(1C)**
- **Statement 12.** In patients who show adequate response to the medication, an attempt to taper and withdraw the antipsychotic should be made within four months of starting. **(1C)**
- **Statement 13.** In patients whose antipsychotic medications are being tapered, symptoms should be assessed at least every month during tapering and for at least four months after the medication is discontinued.**(1C)**

Use of Specific Antipsychotic Medications, Depending on Clinical Context

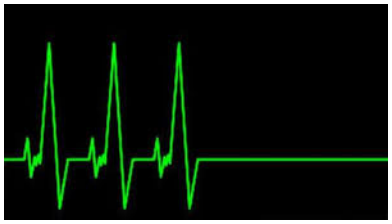
- **Statement 14**. If non-emergency antipsychotic medication treatment is to be used, haloperidol should not be used first.(1B)
- **Statement 15**. A long-acting injectable antipsychotic should NOT be used unless it is administered for a co-occurring chronic psychotic disorder.(1B)

Long-acting injectables

- No studies have examined the use of long-acting injectable antipsychotic medications in individuals with dementia.
- Longer duration of action of these medications suggests that they would be associated with an increased risk of harm relative to oral formulations or short-acting parenteral formulations of antipsychotic medications, particularly in frail elders.

Risks

- In addition to mortality, other serious adverse events of antipsychotic medications in individuals with dementia have been reported, including stroke, acute cardiovascular events, metabolic effects, and pulmonary effects



Cost

- No known studies on the cost-effectiveness of antipsychotic treatment for individuals with dementia in inpatient or nursing facilities or for severely agitated or aggressive individuals who require constant supervision.

Limitations

- Small number of head-to-head trials *comparing different pharmacological and nonpharmacological treatments* for agitation or psychosis in dementia and an even fewer number of trials with parallel placebo or sham treatment arms.
- Trials often fail to examine *quality of life* or other outcomes that patients and families view as most important.
- Studies also have not assessed the *optimal time at which an attempted tapering* of antipsychotic medication is indicated.
- There is insufficient evidence to determine whether individuals with *more severe* dementia, psychosis, or agitation will have a greater *risk of relapse* with antipsychotic discontinuation.

Limitations, cont.

- Studies have not examined optimal timing of assessment *during* antipsychotic treatment *or after* an attempt at tapering antipsychotic treatment
- The optimal frequency of laboratory and physical assessments to detect metabolic or other side effects of treatment is unknown.
- Unclear whether laboratory data or other findings could predict which patients are at the highest risk of stroke or mortality or whether other interventions could reduce such risks.

Quality Measures

- Choosing Wisely recommendations from APA
  - "Don't prescribe antipsychotic medications to patients for any indication without appropriate initial evaluation and appropriate ongoing monitoring"
  - "Don't routinely use antipsychotics as first choice to treat behavioral and psychological symptoms of dementia."

References, cont.

- Sherman DS. Psychoactive Drug Misuse in Long-Term Care: Some Contributing Factors. *J. J. Pharm Prac* 1988: 189-194