Debate:

Antipsychotic Use in the Elderly

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Learning Objectives

**Pharmacist**

- **Discuss** the literature that both supports and discourages the use of antipsychotics in the elderly for behavioral and psychological symptoms of dementia (BPSD)
- **Summarize** the evidence supporting the antipsychotic’s Black Box Warning and rationale behind its continued use
- **Describe** the age related changes that make the geriatric population more susceptible to psychotropic related adverse effects

**Technician**

- **List** the FDA approved indications for second generation antipsychotics
- **Identify** common adverse effects associated with antipsychotic use
- **Explain** the benefits of pharmacological and non-pharmacologic treatment for individuals with dementia
Debate Outline

Introduction

• Antipsychotics **should be used** first line for older adults for BPSD
  o Kayode Giwa

• Antipsychotics **should not be used** first line in older adults for BPSD
  o Austin De La Cruz

• Patient Case

• Q & A with audience
Debate Disclaimer

• This debate will only discuss BPSD as an indication
• The off-label use of the medications discussed during this presentation are solely for educational purposes
• Antipsychotic (AP) use in the elderly is a widely debated topic and each incident should be evaluated on a case to case basis
• Two Pharm.D.’s enter the debate arena, but only one survives ..
  o May the best man win
Introduction to the Atypical Antipsychotics
How Did We Get Here?

• Chlorpromazine (Thorazine)- FDA approved:1957

• Haloperidol (Haldol)- FDA approved:1967

• The very first atypical antipsychotic
  o Clozapine (Clozaril)- FDA approved:1989
  o Risperidone (Risperdal)- FDA approved:1993

• It took 10 years to make a product substantially better than chlorpromazine

• To make a substantially better product than haloperidol it took only 50 years!

• It’s been 24 years ... where is the “better” product?

# Table 1

## Binding affinities of antipsychotic medications at select receptors

<table>
<thead>
<tr>
<th>Drug</th>
<th>$D_2$</th>
<th>$5HT_{2A}$</th>
<th>$A_1$</th>
<th>$H_1$</th>
<th>$M_1$</th>
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</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>126</td>
<td>16</td>
<td>7</td>
<td>6</td>
<td>1</td>
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<tr>
<td>Risperidone</td>
<td>4</td>
<td>0.5</td>
<td>0.7</td>
<td>20</td>
<td>&gt;1,000</td>
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<tr>
<td>Olanzapine</td>
<td>11</td>
<td>4</td>
<td>19</td>
<td>7</td>
<td>1.9</td>
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<tr>
<td>Quetiapine</td>
<td>770</td>
<td>31</td>
<td>8.1</td>
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<td>Ziprasidone</td>
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<td>0.4</td>
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<td>50</td>
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<tr>
<td>Aripiprazole</td>
<td>0.45</td>
<td>3.4</td>
<td>47</td>
<td>61</td>
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<td>Paliperidone</td>
<td>4.6</td>
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<td>80</td>
<td>13.6</td>
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<td>Iloperidone</td>
<td>6.3</td>
<td>5.6</td>
<td>36</td>
<td>473</td>
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<td>Asenapine</td>
<td>1.3</td>
<td>0.006</td>
<td>1.2</td>
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<tr>
<td>Lurasidone</td>
<td>0.99</td>
<td>0.47</td>
<td>10.8</td>
<td>&gt;1,000</td>
<td>&gt;1,000</td>
</tr>
</tbody>
</table>

*Abbreviations: D, dopamine; 5HT, serotonin; H, histamine; M, muscarine; A, alpha*

*Data presented as Ki values*
Receptor Binding Profiles

Olanzapine  Clozapine  Haloperidol  Aripiprazole

Risperidone  Quetiapine  Ziprasidone

## Comparison of Proton Pump Inhibitors

**Table I. Pharmacokinetic properties of PPIs (oral)**

<table>
<thead>
<tr>
<th></th>
<th>Omeprazole</th>
<th>Esomeprazole</th>
<th>Lansoprazole</th>
<th>Rabeprazole</th>
<th>Pantoprazole</th>
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</thead>
<tbody>
<tr>
<td>Bioavailability (%)</td>
<td>30-40</td>
<td>50-68</td>
<td>80-85</td>
<td>52</td>
<td>77</td>
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<tr>
<td>Time to maximum plasma concentration (h)</td>
<td>0.5-3.5</td>
<td>1.0-2.0</td>
<td>1.5-2.0</td>
<td>1.0-2.0</td>
<td>1.1-3.1</td>
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<tr>
<td>Plasma elimination half-life (h)</td>
<td>0.5-1.0</td>
<td>1.3</td>
<td>1.3-1.7</td>
<td>0.7-1.5</td>
<td>1.0-1.9</td>
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<td>Plasma kinetics</td>
<td>Non-linear</td>
<td>Non-linear</td>
<td>Linear</td>
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<td>Protein binding (%)</td>
<td>95</td>
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<tr>
<td>Metabolism</td>
<td>Hepatic (CYP2C19, CYP3A4)</td>
<td>Hepatic (CYP2C19, CYP3A4)</td>
<td>Hepatic (CYP2C19, CYP3A4)</td>
<td>Non-enzymatic reduction, Hepatic (CYP2C19, CYP3A4)</td>
<td>Hepatic (CYP2C19, CYP3A4)</td>
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<tr>
<td>Urinary excretion of oral dose (%)</td>
<td>77</td>
<td>80</td>
<td>14-23</td>
<td>30-35</td>
<td>71-80</td>
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</table>
## Comparison of Common Side Effects of Second Generation Atypical Antipsychotics

<table>
<thead>
<tr>
<th>Atypical Antipsychotic</th>
<th>Brand Name</th>
<th>Weight Gain</th>
<th>Constipation</th>
<th>Hyperprolactinemia</th>
<th>Nausea/Vomiting</th>
<th>Orthostasis</th>
<th>Dizziness</th>
<th>Akathisia</th>
<th>EPS</th>
<th>Somnolence</th>
<th>Tachycardia</th>
<th>↑ BG</th>
<th>↑ Lipids</th>
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<tbody>
<tr>
<td>Aripiprazole</td>
<td>Abilify</td>
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**Key**

- **---**: Almost No Effect
- **One ***: 0-10% incidence
- **Two ****: 10-20% incidence
- **Three *****: 20-30% incidence
- **Four ******: >30% incidence

Never Compare Your Children

- Atypical antipsychotics have incredibly wide variability in properties

- Antihistamines
  - Diphenhydramine, doxylamine are on Beer’s List
  - Fexofenadine, loratadine are not on Beer’s List
  - All four are antihistamines
  - Different properties distinguish medications

*Atypicals are effectively a class in name only*
Agitation in Dementia
Antipsychotics are associated with increased mortality in people with dementia and behavioral disturbances or psychotic symptoms (relative risk compared with placebo: 1.6-1.7)
• Four antipsychotics evaluated
  o Risperidone
  o Olanzapine
  o Quetiapine
  o Aripiprazole

• Causes of death
  o Cardiac related (heart failure, sudden death)
  o Infections (mostly pneumonia)
Where Did the FDA Get the Data?

- 17 trials, 5106 patients evaluated
  - Pooled, all retrospective studies
  - Mostly unpublished
  - No list of trials used for evaluation

- Started in 2003 with risperidone and cerebrovascular adverse effects (CVAE)

• FDA issued a warning entitled ‘Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia”

• Data from 3 trials
  o Patients aged 73-97
  o Serious CVAE risperidone- 12 (n=744)
  o Serious CVAE placebo- 4 (n=562)

• Janssen says no cause-effect relationship established
  o Cannot be fully ruled out either

• Janssen provided data from 6 trials this time
  o 3 published, 3 unpublished

• Serious CVAE
  o Risperidone- 15 (n=1009, 1.5%)  
  o Placebo- 4 (n=712, 0.6%)  
  o P= 0.27
More CVAE

• Olanzapine had 5 trials evaluated
  o Relative risk 1.8
  o P = 0.36 \rightarrow not statistically significant

• Quetiapine had 2 trials evaluated
  o Quetiapine CVAE - 0.9%
  o Placebo CVAE - 1.9%
  o Relative risk - 0.5

• The warning for risperidone was subsequently added for olanzapine and aripiprazole
• FDA trial data still unreleased

• JAMA 2005 article evaluated 15 trials (9 unpublished)
  o Risperidone- 5
  o Olanzapine- 5
  o Quetiapine- 3
  o Aripiprazole- 3

• Combined mortality risk OR 1.54 (95% CI, 1.06-2.23)

*No drug individually reached statistical significance!*
Causes of Death

- Dementia in elderly on antipsychotics
  - Cardiac related (heart failure, sudden death)
  - Infections (mostly pneumonia)

- Age greater than 65
  - #1- Disease of the heart
  - #4- Cerebrovascular
  - #8- Influenza and pneumonia

- People with dementia
  - #1- Bronchopneumonia → 38.4%
  - #2- Ischemic heart disease → 23.1%

Are patients on antipsychotics just dying statistically how they are expected to die?

Don’t Forget Delirium

• 14-56% of elderly inpatients

• 22-89% have delirium superimposed on dementia

• Delirium is an independent risk factor for mortality
  ○ Gonzalez et al → delirium 3x increased mortality rate over non-delirium patients

• Treatment of choice for agitation associated with delirium ... antipsychotics
• Hypoactive delirium increased mortality rate over hyperactive delirium
  - Antipsychotics not generally used for hypoactive variant

Antipsychotics may be a red herring for increased mortality in already vulnerable patient population
Behavioral Disturbances in Dementia

• Neuropsychiatric symptoms in 60-98% of people with dementia (behavioral and psychological symptoms of dementia, BPSD)

• Associated complications
  o Increased hospitalizations
  o Increased hospital length of stay
  o Increased nursing home placement
  o Decreased caregiver employment/income
  o Caregiver stress/depression
  o Up to 1/3 the cost of Alzheimer’s care

• An estimated 1/3 of AD patients have severe symptoms

• Present in dementia types other than AD

JAMA. 2005;293:596-608
How do we treat this?

• No FDA approved options

• Antidepressants
• Mood stabilizers
• Cholinesterase inhibitors
• Other

• Use of antipsychotics has been steadily increasing despite warnings
Antidepressants for BPSD

• Very few studies comparing serotoninergic drugs to placebo

• Efficacy pretty questionable
  o Fluoxetine (Prozac)
  o Sertraline (Zoloft)
  o Trazodone (Desyrel)

• Depressive symptoms may improved, but not BPSD

• Citalopram has some positive data ...
Citalopram for BPSD

• Pollock et al
  o 85 hospitalized patients; 17 days
  o Citalopram 20 mg/day vs. perphenazine vs. placebo
  o Various types of dementia
  o MMSE mean score 8.5

• Primary outcome: neurobehavioral rating scale change from baseline to day 17

### Pollock et al Efficacy Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Citalopram (n=31)</th>
<th>Perphenazine (n=33)</th>
<th>Placebo (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in NBRS</td>
<td>-10</td>
<td>-7.2</td>
<td>-2.3</td>
</tr>
</tbody>
</table>

- Citalopram vs. placebo, p < 0.002
- No differences in EPS symptoms noted (no #’s given)
- Only 39 patients (45%) completed the study
  - 24 withdrew for lack of efficacy
Effect of Citalopram on Agitation in Alzheimer’s Disease - The CitAD Randomized Controlled Trial

• 186 patients → MMSE 5-28; clinically significant agitation; 9 wks
  o 94 citalopram; start at 10 mg titrated up to 30 mg/day
  o 92 placebo
  o 2/3 on cholinesterase inhibitors; 2/5 on memantine (Namenda)

• Primary outcomes
  o NBRS agitation subscale
  o Modified Alzheimer Disease Cooperative Study-CGI of change

• Safety
  o MMSE
  o GUG (measure assessing mobility and gait)
## CitAD Trial Efficacy Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Citalopram</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>NBRS agitation</td>
<td>4.33</td>
<td>5.26</td>
</tr>
</tbody>
</table>

- Difference of 0.93 statistically significant (p=0.004)
- ADCS-CGIC estimated treatment effect ➔ 2.13 (p=0.007)
- Secondary outcomes ➔ favored or trended toward favoring citalopram
CitAD Trial Safety Outcomes

• MMSE→ greater cognitive worsening with citalopram (p=0.003)

• QTc interval→ greater increase with citalopram (18.1 msec)

• Falls→ more frequent with citalopram

• Anorexia→ increased with citalopram

• Diarrhea→ increased with citalopram
CitAD Trial Final Thoughts

• Efficacy for BPSD fairly robust

• 30 mg/day dose higher than FDA recommended dose in the elderly

• Adverse effects quite troubling

• Same question as with atypicals ... does benefit outweigh risks???
## Mood Stabilizers for BPSD

### Valproic acid (Depakote)

<table>
<thead>
<tr>
<th>Participants</th>
<th>Intervention</th>
<th>Primary outcome</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tariot et al 2005</td>
<td>128 nursing home patents</td>
<td>VPA 500-1000 mg/day x 6 weeks</td>
<td>Agitation factor of BPRS</td>
</tr>
<tr>
<td>Herrmann et al 2007</td>
<td>14 nursing home patients</td>
<td>VPA x 6 wks, 2 wk washout, VPA x 6 wks</td>
<td>NPI CMAI</td>
</tr>
<tr>
<td>Tariot et al 2001</td>
<td>172 nursing home patients</td>
<td>VPA titrated to 20-30 mg/kg/day</td>
<td>CMAI MMSE</td>
</tr>
</tbody>
</table>
### Valproic acid (Depakote)

<table>
<thead>
<tr>
<th>Safety</th>
</tr>
</thead>
</table>
| **Tariot et al 2005** | Inc. diarrhea with VPA  
Dec. platelets with VPA |
| **Herrmann et al 2007** | Inc. agitation on CMAI;  
mean AE  
VPA=4  
PBO=1 |
| **Tariot et al 2001** | Dropouts:  
VPA= 22%  
PBO= 4%  
Inc. thrombocytopenia, somnolence with VPA |

- Other studies have similar results
  - Little to no efficacy
  - Considerably increased side effects

- VPA not recommended for BPSD
Carbamazepine for BPSD

• Two small trials
  o Tariot et al 1998 → n=51
  o Olin et al 2001 → n=21

• 1 positive study, 1 negative study

• AE significantly worse for CBZ in one study, mild in one study

• Chloral hydrate was rescue med in each study 😞

• CBZ not recommended based on
  o Questionable efficacy
  o AE profile (use with caution on Beer’s List)
  o Significant DDI potential
Cholinesterase inhibitors for BPSD

• Conflicting results from trials (majority positive)
• Majority of trials in only Alzheimer’s patients
• Inc. adverse effects with treatment groups
• Does statistical significance = clinical significance?
  o Few of the trials required significant neuropsychiatric symptoms (mainly mild)

• Longest cholinesterase study (Courtney et al)
  o Donepezil 5 or 10 mg vs. placebo
  o MMSE improved by 0.8 at year 2
  o No differences at year 3
    ➢ BPSD symptoms
    ➢ Institutionalization
    ➢ Disability progression

JAMA. 2005;293:596-608
Memantine (Namenda)

- Inconsistent efficacy

- MAIN-AD Trial → Compared memantine to atypical antipsychotics
  - 199 nursing home patients
  - No significant difference in any measure
  - Trend towards atypicals at weeks 12 and 24
  - Atypicals less likely to experience symptom relapse

Atypical Antipsychotics

• More studies than other off label agents

• Safety data better than 1\textsuperscript{st} generation antipsychotics

• Most studied agents
  o Risperidone
  o Olanzapine
  o Quetiapine
  o Aripiprazole

• Efficacy data generally shows modest improvement

• Studies generally range from 24 hr to 12 weeks
# Atypicals for BPSD

<table>
<thead>
<tr>
<th>Participants</th>
<th>Intervention</th>
<th>Primary Outcome</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Street et al 2000</td>
<td>206 NH patients; MMSE= 7</td>
<td>OLZ 5/10/15 vs. PBO x 6 wks</td>
<td>3 NPI core symptoms</td>
</tr>
<tr>
<td>Meehan et al 2002</td>
<td>331 NH or hospitalized patients; MMSE= 11</td>
<td>IM OLZ 2.5/5 vs. Ativan 1mg vs. PBO x 24 hr</td>
<td>PANSS-EC ACES</td>
</tr>
<tr>
<td>Brodaty et al 2003</td>
<td>345 NH patients</td>
<td>RIS vs. PBO x 12 wks</td>
<td>CMAI</td>
</tr>
<tr>
<td>Zhang et al 2007</td>
<td>333 institution patients; MMSE= 5.3</td>
<td>SER 100/200 vs. PBO x 10 wks</td>
<td>PANSS-EC</td>
</tr>
<tr>
<td>Mintzer et al 2007</td>
<td>487 institution patients</td>
<td>ARP 2/5/10 vs. PBO x 10 wks</td>
<td>NPI-NH (psychosis) CMAI was 2nd</td>
</tr>
</tbody>
</table>

[Neuropsychopharmacology, 2002 Apr;26(4):494-504.](https://doi.org/10.1038/s001380202092)  
<table>
<thead>
<tr>
<th>Study</th>
<th>Findings</th>
</tr>
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<tbody>
<tr>
<td>Street et al 2000</td>
<td>Inc. somnolence and gait disturbance</td>
</tr>
<tr>
<td>Meehan et al 2002</td>
<td>No marker statistically significant</td>
</tr>
<tr>
<td>Brodaty et al 2003</td>
<td>Somnolence and URI- RIS; agitation- PBO; EPS not stat significant</td>
</tr>
<tr>
<td>Zhang et al 2007</td>
<td>Inc. somnolence- SER; more deaths- SER, but not statistically significant</td>
</tr>
<tr>
<td>Mintzer et al 2007</td>
<td>CV SE: ARP= 7, PBO= 0</td>
</tr>
</tbody>
</table>
Where does this leave us?

• Atypicals work pretty well, but aren’t the safest
  o Are they as unsafe as reported, however???
  o Individual drugs don’t show a statistically significant risk
  o Each atypical has a VERY different receptor profile

• Other options don’t work as well and/or aren’t safe

• Large, robust trials in this area are difficult
  o Older patients
  o High mortality
  o High morbidity
  o Small clinical benefit

• These patients are really sick and complicated!
Potential future directions

• Use/study meds that show promise

• Study who specifically has highest risk using atypicals
  o Type of dementia
  o Severity of dementia
  o Medical comorbidity
  o Genetic factors
  o Dose of medication
  o DDI

• Duration of treatment
  o Emergent vs. prophylactic
  o When/how to taper down medication
  o Monitoring for efficacy AND beginnings of clinical worsening
Conclusion

• Very little positive news regarding treatment of BPSD
• Atypical antipsychotics may not be safe as Tylenol, but are not poison

• Using atypicals for BPSD considering warnings cannot be taken lightly

• Strongly keep in mind
  o Duration of treatment
  o Choice of agent
  o Dose
  o How/what to monitor

• Always keep in mind the benefits vs. risk of untreated BPSD
Atypicals versus Blackberry

• Iphone
• Samsung
• Other
• BlackBerry
  o They still make these?
  o Why do you still have that?
  o You should upgrade

• By what measure can we say that there are better options than atypicals ... or BlackBerries?
Argument Against Antipsychotic use for BPSD

Austin De La Cruz, Pharm.D.
Clinical Assistant Professor
University of Houston College of Pharmacy
Michael E. DeBakey VA Medical Center
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Mental Health Care for Elderly

• The U.S. Census Bureau projects that the number of adults ≥ 65 old will increase from 40.3 million → 72.1 million between 2010-2030

**Question**: How are we going to address the mental health needs of our growing geriatric population?

• Institute of Medicine report- *The Mental Health and Substance Use Workforce for Older Adults: In Whose Hands?*
  - Highlighted the significant lack of providers with expertise necessary to address the mental health (MH) needs of older adults
  - The committee focused on the importance of proper treatment, care, and management of MH conditions
    - Improve care through general psychiatrists, psychologists, social workers, psychiatric nurses, and substance use counselors

Institute of Medicine. 2012
• Missing from report: Care from pharmacists!
  o Pharmacists can play a huge role when it comes to the management of MH conditions in our elderly population
  o Starting with appropriate pharmacotherapy recommendations
Compared to younger adults, older adults are...

1. Less likely to receive psychiatric care

**Question:** Why are older adults receiving less specialized care?

- Primary care provider/long term care facility manages psychotropic medications
- Psychiatrists may not accept Medicare

2. Are more likely to receive prescriptions for psychotropic medications

**Question:** Why are older adults receiving more psychotropics?

- Improved diagnosing?
- Updated guidelines to support the increased use?
- Surge in FDA approved medications for the elderly?
Overprescribing of Antipsychotics

Current State:
• 1 in 4 nursing home residents receive at least 1 AP
• 83% of atypical APs prescribed for geriatric nursing home residents were for off-label conditions
  o 88% of those APs were for dementia related psychosis
➢ Current Black Box Warning
  • The strictest warning put in the labeling of prescription drugs by the FDA when there is reasonable evidence of an association of a serious hazard with the drug

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS
Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. This antipsychotic is not approved for the treatment of patients with dementia-related psychosis

Use of Atypical Antipsychotics

• Indicated

<table>
<thead>
<tr>
<th>Antipsychotic FDA Approved Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
</tr>
<tr>
<td>Schizoaffective disorder</td>
</tr>
<tr>
<td>Suicidal behaviors in schizophrenia or schizoaffective disorder</td>
</tr>
</tbody>
</table>

• Off-label

<table>
<thead>
<tr>
<th>Non-FDA Approved Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia</td>
</tr>
<tr>
<td>Pain</td>
</tr>
</tbody>
</table>
Age Related Changes in the Elderly
Considerations for Elderly

• In order to provide the best form of pharmacotherapy for our elderly patients, always consider:
  o Pharmacokinetic profile
  o Pharmacodynamics profile
  o Adverse drug reactions
  o Contraindications
  o Warnings/precautions
  o Drug-drug interactions
  o Patient’s co-morbidities
  o Pharmacotherapy history
  o Treatment guidelines
  o Use of non-prescription/OTC
  o Age group
  o Gender
  o Compliance
  o Current state of health
  o Allergies
Pharmacodynamic Changes of Aging

- **Pharmacodynamics**: how a specific drug affects the body
- Elderly patients are more susceptible to antipsychotic side effects

<table>
<thead>
<tr>
<th>Receptor antagonism</th>
<th>Pharmacodynamic effects</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dopamine D&lt;sub&gt;2&lt;/sub&gt;</strong></td>
<td>Parkinsonian like features (e.g. bradykinesia, tremor)</td>
<td>• ↑ risk of instability and falls</td>
</tr>
<tr>
<td><strong>Serotonin 5-HT&lt;sub&gt;2c&lt;/sub&gt;</strong></td>
<td>Weight gain</td>
<td>• Weight gain ↑ the risk of newly diagnosed diabetes, CV related mortality, and poor adherence</td>
</tr>
</tbody>
</table>
| **Acetylcholine muscarinic**  | Dry mouth, constipation, tachycardia, blurred vision, urinary retention | • Constipation should be closely monitored  
• Caution with concomitant glaucoma and BPH |
| **Histamine**                | Over sedation                                                 | • May lead to cognitive, perceptual, and motor dysfunction            |
| **Alpha-adrenergic**         | Orthostatic hypotension                                       | • Hypotension may ↑ the risk of dizziness and falls                   |

# Pharmacokinetic Changes of Aging

<table>
<thead>
<tr>
<th>PK parameter</th>
<th>Altered physiology</th>
<th>Outcome</th>
<th>Antipsychotic effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absorption</strong></td>
<td>↓ Gastric secretion ↓ Gastric pH ↓ GI motility ↓ GI blood flow</td>
<td>• Decreased absorption ability • Onset of action may be delayed • Elevated gastric pH</td>
<td>• Delayed onset may lead to a additional/unneeded dose titrations</td>
</tr>
<tr>
<td><strong>Distribution</strong></td>
<td>↓ Total body water ↓ Lean body weight ↓ Albumin ↑ Body fat</td>
<td>• Increased $V_d$ of lipid soluble drugs • Decreased $V_d$ of water soluble drugs • Increased free fraction</td>
<td>• Antipsychotics are highly lipophilic (e.g. haloperidol) • Acidic APs may accumulate (e.g. risperidone)</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
<td>↓ Enzyme induction ↓ Hepatic mass ↓ Hepatic blood flow ↓ Oxidase system</td>
<td>• Decreased hepatic clearance of meds • Potential for drug interactions</td>
<td>• Majority of APs are metabolized through CYP enzymes</td>
</tr>
<tr>
<td><strong>Elimination</strong></td>
<td>↓ Renal blood flow ↓ GFR</td>
<td>• Accumulation of renally cleared drugs</td>
<td>• Many APs are renally cleared (e.g. paliperidone)</td>
</tr>
</tbody>
</table>

Susceptibility in the elderly

- Patients regularly have comorbid medical illnesses
  - Antipsychotics may worsen outcomes of other disorder
    - Parkinson’s disease, diabetes, hypercholesterolemia etc.
  - **Polypharmacy is the rule, not the exception**
    - 90% of individuals ≥ 65 years old have at least 1 prescription drug
    - 40% of individuals ≥ 65 years old have at least 5 prescription drugs
  - Drug-drug interactions more likely

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Substrates</th>
<th>Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP1A2</td>
<td>clozapine, olanzapine, asenapine, haloperidol</td>
<td></td>
</tr>
<tr>
<td>CYP3A4</td>
<td>clozapine, risperidone, ziprasidone</td>
<td></td>
</tr>
<tr>
<td>CYP2D6</td>
<td>clozapine, olanzapine, risperidone, aripiprazole, asenapine, haloperidol, thioridazine, perphenazine, fluphenazine</td>
<td>asenapine, perphenazine, thioridazine</td>
</tr>
</tbody>
</table>


National Center for Health Statistics.
Behavioral and Psychological Symptoms of Dementia (BPSD)
BPSD

- No specific diagnostic criteria for BPSD
- Antipsychotics are used off-label

Common symptoms
- Anxiety
- Apathy
- Depression
- Disinhibition
- Dysphoria
- Euphoria
- Hypersexuality
- Irritability
- Lability
- Obsessive-compulsive
- Psychomotor disturbance
- Sleep/wake disturbance
- Sundowning

Symptoms leading to intervention
- Agitation
- Delusions
- Hallucinations
- Physical aggression
Clinical Course of BPSD

Prior to diagnosis
- Depression
- Apathy
- Social withdrawal

Dementia
- Frequency and intensity of agitation and aggression may worsen

End stages
- Episodes of agitation and aggression may diminish
Which way to go?

BPSD Dementia

New Way
(hard)

No Antipsychotics

Old Way
(easy)

Antipsychotics!
# BPSD Guideline Recommendations

<table>
<thead>
<tr>
<th>1&lt;sup&gt;st&lt;/sup&gt; line</th>
<th><strong>American Psychiatric Association 2016</strong></th>
<th><strong>Journal of the American Board of Family Medicine 2012</strong></th>
<th><strong>World Federation Societies of Biological Pathways 2011</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Non-pharmacological intervention as part of a comprehensive txt plan</td>
<td>• Non-pharmacological intervention</td>
<td>• Non-pharmacological intervention (e.g. psychosocial intervention)</td>
</tr>
</tbody>
</table>
| When to use APs?    | • Only used when agitation or psychosis are severe, dangerous, and/or cause the patient significant distress | • After 7 days of non-pharmacological txt  
• Agitation/aggression: After failed non-pharm and ChEIs, memantine, or both | • Standard treatment with ChEIs, memantine, or both  
• Only used if behavior requires urgent attention (e.g. dangerous aggression)  
• Hyperactivity, psychosis, or apathy |
| Notes               | • Only use APs if risk/benefit assessment favors use and is discussed by clinician, patient, & family  
• If no response in 4 weeks= discontinue  
• If responded well = attempt taper at 4 mo.  
• Don’t use Haldol or LAI | • Start low and go slow  
• Agitation: trazodone, carbamazepine, valproate, citalopram, risperidone  
• Apathy: methylphenidate  
• Depression: citalopram, sertraline  
• If responded well= attempt taper at 4 mo. | • APs have a high rate of side effects and increased mortality rate  
• Result of neuroleptic treatment often is a symptom shift leading to new unsolved problems like EPS, falls and fractures |

Non-Pharmacologic Intervention

- **Non-pharmacologic interventions are the most appropriate initial strategy for managing problematic behaviors**

- Optimal management involves a multi-disciplinary approach to treatment

- Greater attempts are made to understand the individual’s experience of dementia & in turn develop strategies to improve the patient’s quality of life

- Therapy is now directed toward person-centered forms of care
  - Recognizing, redirecting, and defusing, or using the A-B-C approach

<table>
<thead>
<tr>
<th>Standard Therapies</th>
<th>Alternative Therapies</th>
<th>Brief Psychotherapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Behavioral therapy</td>
<td>• Art therapy</td>
<td>• Cognitive behavioral therapy</td>
</tr>
<tr>
<td>• Reality orientation</td>
<td>• Music therapy</td>
<td>• Interpersonal therapy</td>
</tr>
<tr>
<td>• Validation therapy</td>
<td>• Activity therapy</td>
<td></td>
</tr>
<tr>
<td>• Reminiscence therapy</td>
<td>• Aromatherapy</td>
<td></td>
</tr>
<tr>
<td>• Art therapy</td>
<td>• Bright-light therapy</td>
<td></td>
</tr>
<tr>
<td>• Music therapy</td>
<td>• Multi-sensory</td>
<td></td>
</tr>
<tr>
<td>• Activity therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Aromatherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Bright-light therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Multi-sensory</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sadowsky CH, Galvin JE, et al. *JABFM* 2012; (25)3
# Non-Pharmacologic Treatment

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Intervention</th>
</tr>
</thead>
</table>
| Agitation        | • Use distraction and re-direction of activities to divert patient from problem situations  
• Reduce excess stimulation and outings in crowded places  
• Use lighting to reduce confusion and restlessness at night |
| Disorientation   | • Provide patient with predictable routine & avoid relocation  
• Use calendars, clocks, color coded labels, and newspapers for orientation & time |
| Hallucinations   | • Do not be concerned if they are not distressing to the patient |
| Delusions        | • Redirect and distract the patient |
| Accident-prone   | • Provide a safe environment (grab bars near toilet, no slippery floors or rugs) |
| Wandering        | • Secure environment (doors, locks), inform neighbors, AASRP |
| Sleep disturbances | • Limit daytime napping  
• Strive for consistent bedtimes |

Sadowsky CH, Galvin JE, et al. *JABFM* 2012; (25)3
Clinical “Efficacy” for BPSD

• There is only **modestly convincing evidence** that the APs provide benefit for BPSD
  o Data has been **unsatisfactory** to gain FDA approval

• Many of the meta-analysis’ that highlight the effectiveness of APs include trials that have not been published in full or are not available for review

• Best evidence exists for risperidone (5 RCTs- 1761 patients)
  o Meta-analysis showed a “significant advantage” for risperidone in the treatment of aggression
    ➢ 1mg: -0.84 points on BEHAV-AD rating scale (95% CI -1.28 to 0.40)
    ➢ 2mg: -1.5 points on BEHAV-AD rating scale (95% -2.05 to 0.95)

• **Evidence of modest clinical effectiveness must be balanced against considerable risk of adverse events**

Symptom resolution ≠ improved QOL

• For any treatment, the impact of quality of life (QOL) should be the primary focus

• APs may have short-term/moderate benefits, but we cannot assume that symptom resolution = improved QOL
  o There is little to no data where BPSD trials included QOL measures

• Ballard CG, et al. observed QOL measures in residential and nursing home facilities for patients with BPSD. AP use was associated with..
  o Less engagement in activities (p=0.03)
  o Less time eating (p=0.01)
  o Less time performing work (p=0.04)

• “APs had a more detrimental impact on QOL that the symptoms for which they were prescribed”

Antipsychotic Safety
Antipsychotic Safety in BPSD

FDA Public Health Advisory

• Treatment of behavioral disorders in elderly patients with dementia with atypical APs is associated with increased mortality (April 2005)
  1. Analyses of 17 placebo controlled trials showed significant increases in mortality in the SGA treated group vs. placebo group
     ➢ 1.6-1.7 fold increase in mortality
  2. Meta-analysis by Schneider et al. confirmed previous SGA results
     ➢ 1.5 fold increase in mortality
  3. DART-AD: The Dementia Antipsychotic withdrawal trial
     ➢ Increased long term risk of mortality at 12 months
     ➢ Highest risk if continued therapy for 24, 36, and 48 mo.
     ➢ Discontinuation did not result in worsening of behavioral symptoms over 6 mo’s

Center for Drug Evaluation and Research. [FDA public health advisory]. 2005 Apr 11
Antipsychotic Safety in BPSD

First Generation Antipsychotics (FGAs)

• Two observational epidemiological studies examined risk of death in patients treated with FGAs
  1. Gill et al. compared risk for death with use of a FGAs vs. SGA
     ➢ FGAs showed a marginally higher risk of death compared with SGAs
       o Causes of death not reported in study
  2. Schneeweiss et al. compared all cause mortality with FGA vs. SGA
     ➢ Risk of death for patients receiving FGAs was comparable to, or possibly greater than, SGAs
       o Highest relative risk were cancer and cardiac disease

• Based on the data from the two studies, the FDA extended all cause mortality BBW to include all antipsychotics (June 2008)

Gill SS et al. Ann Intern Med. 2007;146:775-786
Schneeweiss S et al. CMAJ. 2007;176:627-632.
Crude Death Rates

- Retrospective case-control study conducted at the VA from 1998-2009
  - 90,786 participants ≥65 years of age with a dementia diagnosis
- *JAMA Psychiatry* 2015

### Table 2. Crude Death Rates During a 180-Day Observation Period Among Patients With Dementia Starting Therapy With a New Medication

<table>
<thead>
<tr>
<th>Medication</th>
<th>No. of Paira</th>
<th>Death, No. (%)</th>
<th>Nonusers</th>
<th>Risk Difference, % (95% CI)b</th>
<th>NNH (95% CI)b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Users</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>1921</td>
<td>398 (20.7)</td>
<td>162 (8.4)</td>
<td>3.8 (1.0 to 6.6)c</td>
<td>26 (15 to 99)</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>1908</td>
<td>265 (13.9)</td>
<td>187 (9.8)</td>
<td>2.5 (0.3 to 4.7)d</td>
<td>40 (21 to 312)</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>4621</td>
<td>545 (11.8)</td>
<td>378 (8.2)</td>
<td>2.0 (0.7 to 3.3)c</td>
<td>50 (30 to 150)</td>
</tr>
<tr>
<td>Risperidone</td>
<td>6338</td>
<td>883 (13.9)</td>
<td>538 (8.5)</td>
<td>3.7 (2.2 to 5.3)c</td>
<td>27 (19 to 46)</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>901</td>
<td>110 (12.2)</td>
<td>65 (7.2)</td>
<td>4.1 (−1.0 to 9.2)</td>
<td>NAe</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>29 704</td>
<td>2472 (8.3)</td>
<td>2367 (8.0)</td>
<td>0.6 (0.3 to 0.9)c</td>
<td>166 (107 to 362)</td>
</tr>
</tbody>
</table>

**Conclusions and Relevance** The absolute effect of antipsychotics on mortality in elderly patients with dementia may be higher than previously reported and increases with dose.

Pneumonia

- Pneumonia- one of the leading causes of death in trials

**Without Alzheimer's**

- Knol W, et al. found that APs were associated with a 60% increased risk of pneumonia in the elderly
- Three other studies found a dose related increased risk of pneumonia in elderly taking both FGAs and SGAs

**With Alzheimer's (MEDALZ Study- 8/30/16)**

- 60,584 participants showed that APs raise the risk for pneumonia in patients both with and without AD
  - Risk is highest at the start of treatment and remains elevated with long term use
  - AD cohort- AP users had a 2-fold relative risk for pneumonia

Cardiovascular

• Many APs are associated with QTc changes
  o Some APs block K⁺ channels and are linked to prolongation of the QT interval
    ➢ Risk factor for ventricular arrhythmia torsade de pointes & sudden cardiac death

• EKG monitoring is usually not taken into consideration
  o Donepezil + Risperidone= **MAJOR**

<table>
<thead>
<tr>
<th>No effect</th>
<th>Low effect</th>
<th>Moderate effect</th>
<th>High effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>aripiprazole</td>
<td>asenapine</td>
<td>chlorpromazine</td>
<td>Any IV antipsychotic</td>
</tr>
<tr>
<td>lurasidone</td>
<td>clozapine</td>
<td>haloperidol</td>
<td><strong>Any antipsychotic exceeding max dose</strong></td>
</tr>
<tr>
<td></td>
<td>fluphenazine</td>
<td>iloperidone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>perphenazine</td>
<td>quetiapine</td>
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<td></td>
<td>olanzapine</td>
<td>ziprasidone</td>
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<tr>
<td></td>
<td>paliperidone</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>risperidone</td>
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</tbody>
</table>

**New Safety Warning** (February 27, 2017)

- The FDA approved a labeling update for all APs adding a new warning to the prescribing information

- All APs can cause somnolence, postural hypotension, and motor and sensory instability that could lead to falls and subsequently fractures or other injuries
  - Perform fall risk assessments

**New Data** (January 4, 2017)

- “Antipsychotics have been linked to respiratory failure in a dose dependent manner in patients with COPD”

**New Safety Warning** (May 5, 2016)

- The FDA added a new warning to olanzapine- can potentially cause drug reaction with eosinophilia and systemic symptoms (DRESS), a rare but serious skin reaction
Antipsychotics Use in Schizophrenia

Schizophrenia

• One of the most complex and challenging psychiatric disorders
  o Between 25-50% of schizophrenic patients attempt suicide
    ➢ 10% of schizophrenic patients who attempt, succeed
• Mortality rate is 8x greater & life expectancy may be 20-30 years shorter than the general population

Question: Do antipsychotics increase mortality in schizophrenia?

• Torniainen M, et al. determined that when compared to low, moderate, and high AP exposure, the highest overall mortality was among patients with no AP exposure

• Results support current clinical practice

BPSD Alternatives

- One of the main reasons for the widespread use of APs is the limited evidence for alternative treatments, however, alternative options have been studied!

1. **Antidepressants**
   - Trazodone
     - Equally effective for BPSD agitation when compared to haloperidol
   - Fluoxetine
     - Similar efficacy for BPSD agitation when compared to haloperidol
   - Citalopram
     - Both citalopram and risperidone equally improved BPSD agitation
   - Escitalopram
     - Both escitalopram and risperidone equally improved BPSD

2. **Carbamazapine**—efficacy in agitation and aggression

3. **Memantine**—modest improvement in BPSD

4. **Donepezil**—significant efficacy in BPSD

5. **Galantamine**—open label study showed BPSD improvement
Safety & Monitoring Guidelines
**Beers Criteria**

**What is the Beers Criteria?**

- A list of potentially inappropriate medications to be avoided in older adults

**Why is the criteria needed?**

- To decrease the inappropriate prescribing among elderly which will in turn decrease healthcare costs, morbidity, and mortality

**When do use the criteria?**

- The criteria is applicable to all older adults (≥ 65 year old) in ambulatory, acute, and institutionalized settings

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rationale</th>
<th>Recommendation</th>
<th>Quality of Evidence</th>
<th>Strength of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotics 1(^{st}) and 2(^{nd}) generation</td>
<td>↑ risk of CVA, rate of cognitive decline, and mortality in demented patients</td>
<td>Avoid, except for schizophrenia, bipolar disorder, or short term use as an antiemetic</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
</tbody>
</table>
Beers Criteria cont.

• “With increasing evidence of harm associated with antipsychotics and conflicting evidence on their effectiveness in delirium and dementia, the rationale to avoid was modified to...

• **Avoid** antipsychotics for behavioral problems of dementia or delirium unless **non-pharmacological options have failed** (or) **not possible**

  **AND**

The patient is **threatening substantial harm to self or others**

**Quality of evidence:** **Moderate**

  o Evidence is sufficient to determine risk of adverse outcomes but size of included studies limits the strength of evidence

**Strength of Recommendation:** **Strong**

  o Harms, adverse events, and risks clearly outweigh benefits
Questions to ask before AP trial

• What was the person trying to communicate through their behavior?

• What were the possible reasons for the person’s behavior that led to the initiation of the medication?

• What other approaches and interventions were attempted prior to the use of the antipsychotic medication?

• Was the family or representative contacted prior to initiating the medication?

• Was the medication clinically indicated and/or necessary to treat a specific condition and target symptoms as diagnosed and documented in the record?

• Was the medication adjusted to the lowest possible dosage to achieve the desired therapeutic effects?

• Were gradual dose reductions planned and behavioral interventions, unless clinically contraindicated, provided in an effort to discontinue the medication?

• Was the interdisciplinary team, including the primary care practitioner, involved in the care planning process?

• How does the staff monitor for the effectiveness and possible adverse consequences of the medication?
Monitoring Parameters

1) **General Physical Assessment**
   - Blood pressure, heart rate, temperature, and respiratory rate

2) **Weight/BMI measurement**
   - Baseline, every visit, 6 mo. after starting, and the quarterly once stable

3) **Fasting plasma glucose level or hemoglobin A1c**
   - Monitored more often if pre-diabetes/diabetes

4) **Lifestyle assessment**
   - Smoking, exercise, dietary habits, alcohol

5) **Lipid screening**
   - Fasting- annually if within normal limits

6) **Pregnancy Status**

7) **Sexual function inquiry**
   - If evidence of menstrual disturbance or libido/erectile disturbance

8) **EPS evaluation**
   - During treatment initiation, dosage change, and at each clinical visit

9) **Tardive dyskinesia evaluation**
   - Evaluate for abnormal movements using AIMS scale

10) **Vision questionnaire**
    - Might require slit lamp examination at 6 month intervals for quetiapine

11) **Prolactin level**
    - If evidence of galactorrhea/gynecomastia, libido disturbances

12) **Cardiac evaluation**
    - Personal history of heart disease or syncope, congenital long QT syndrome
Gradual Dose Reduction (GDR) - the stepwise tapering of a dose to determine if symptoms, conditions, or risks can be managed by a lower dose or through discontinuation

• “Residents who use APs drugs (should) receive GDR and behavioral interventions, unless clinically contraindicated, in an effort to discontinue these drugs.”

<table>
<thead>
<tr>
<th>Medication class</th>
<th>Frequency of GDR within 1st year of admission to LTC facility</th>
<th>Frequency of GDR after 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotics</td>
<td>2 separate quarters (at least 1 month between attempts)</td>
<td>Annually</td>
</tr>
<tr>
<td>Sedatives/hypnotics</td>
<td>Quarterly</td>
<td>Quarterly (until drug is D/C)</td>
</tr>
<tr>
<td>Other CNS medications (antidepressants, mood stabilizers)</td>
<td>2 separate quarters (at least 1 month between attempts)</td>
<td>Annually</td>
</tr>
</tbody>
</table>
Expert Consensus Guidelines

• Surveyed expert opinion on AP use in older patients (≥65 years of age)

• Antipsychotics are not 1st line for agitated dementia without delusions
  o May be used for agitated dementia with delusions
  o First line: Risperidone
  o Could also consider a mood stabilizer

• Experts (78%) did not recommend using APs in..
  1. Non-psychotic major depression (with or without agitation)
  2. Irritability
  3. Hostility
  4. Sleep disturbances

Looking Ahead
Overprescribing Trends

- In response to the OIG report, CMS established the *National Partnership to Improve Dementia Care in Nursing homes*
- Antipsychotic use was ↓ by from 23.9% to 16.3% (2011-2016)

*Percentage of long-stay nursing home residents who are receiving an antipsychotic medication (excluding those residents diagnosed with schizophrenia, Huntington's Disease or Tourette's Syndrome)*

Antipsychotic Use- Desired State

*National Partnership to Improve Dementia Care in Nursing homes*

- **Initial goal** = ↓ the inappropriate use of antipsychotics
- **Overall goal** = create environments that support person-centered care for individuals living with dementia
  1. Quality Innovation Network- Quality Improvement Organization
  2. MLN Connects2
  3. “Creating a Culture of Person-Directed Dementia Care”
  4. Advancing Excellence & CMS website

- **Available Toolkits**
  - [www.nursinghometoolkit.com](http://www.nursinghometoolkit.com)
  - [http://giic.rgps.on.ca/toolkit-libraries](http://giic.rgps.on.ca/toolkit-libraries)
  - [https://www.nhqualitycampaign.org./dementiaCare.aspx](https://www.nhqualitycampaign.org./dementiaCare.aspx)
  - Mount Sinai- “Non-Pharmacological Assessment and Management of Behavioural and Psychological Symptoms of Dementia in Primary Care”

Antipsychotic Use- Desired State cont.

• Despite decreased trends of AP use in long term care facilities, there still remains considerable room for improvement

• Pharmacists should be at the forefront and help decrease overuse
  o Education of providers
    • Safety
    • Efficacy
    • Guidelines
    • Available toolkits
  o A careful and thorough assessment with every intervention in order to determine if the benefits outweigh the risks
Conclusion

Antipsychotics...

1. ↑ the risk of mortality when used for BPSD and the risk increases over time
2. ↑ the risk for pneumonia in patients with (and without) Alzheimer’s disease
3. ↑ the risk of cerebrovascular events three-fold when used in Alzheimer’s disease
4. Only provide modest benefit over placebo for the treatment of psychosis and aggression in patients with dementia, per multiple meta-analyses
5. Only provide short term benefit, symptoms may return when a medication is discontinued

• All findings further support current treatment guidelines on setting a high threshold for initiating AP use for BPSD
• Reserve APs for patients that have not responded to multiple trials of non-pharmacologic therapies + severe aggression
  o Lowest effective dose for the shortest duration possible
Case Study

• DP is a 75 year old male nursing home resident who has been exhibiting daily disruptive behavior during and after changing clothes. Behavior has been happening for the past 3 weeks.

• He has lived in the nursing home for 2 years after his wife could no longer take care of him. He has advanced dementia and cannot communicate verbally with staff. He requires assistance with a majority of his activities of daily living.

• PMH: HTN, dementia, insomnia, severe arthritis RT knee, diabetes.

• Medication:
  o Methylprednisolone acetate 40mg intra-articular injection Q4M
  o Acetaminophen 325 mg PO Q4-6 hours PRN
  o Doxepin 3mg PO QHS
  o Lisinopril 10mg PO Qdaily
  o Metformin 1000mg PO QDaily

• Yesterday, he grimaced, moaned, and swung at the nurse while she was changing him. This is the second occurrence of agitation and aggression this week and the nurse states, “the patient needs to be restarted on Risperdal STAT!” He was also reported cursing at the other residents and throwing objects at staff after changing.
Case Study

- What would be an appropriate treatment option?
  A. Start risperidone 0.25mg PO Qdaily
  B. Start citalopram 10mg PO Qdaily
  C. Physical restraint only during changing
  D. Implement non-pharmacological treatment options to identify and treat the trigger

- The staff convened and developed a plan to prevent patient injury as well as injury to other residents and staff.
- Staff concluded that the patient’s arthritis pain could be contributing to his recent disruptive behavior.
- The team consulted with the patient’s son regarding the patient’s history. They discovered that the patient was a musician and enjoyed classical music. The next day, staff gave 650 mg of acetaminophen 30 minutes before and played Beethoven during the changing. In addition, cortisone injections were changed to Q3M. The patient stayed calm both during and after the changing.
Case Study #2

• KM is a 78 year old male nursing home resident who has returned to his nursing home after a two week psychiatric hospitalization

• He was diagnosed with dementia 3 years ago, and has lived in the nursing home for the last 2 months after his wife could no longer take care of him. He was exhibiting increased foul language toward his wife and children, and struck his wife twice; prompting his nursing home admission.

• KM was admitted to the psychiatric unit for similar aggressive behavior, this time towards nurses, other residents, and the activities coordinator. Prior to his psychiatric hospitalization he failed trials of behavioral modification, citalopram, trazodone, sertraline, and lorazepam. His current medications include donepezil and memantine for dementia, amiodarone for atrial fibrillation, simvastatin for hyperlipidemia, and Lisinopril for hypertension

• What would be an appropriate treatment option for KM?
  A. Start valproic acid 1000 mg PO Daily
  B. Start quetiapine 12.5 mg PO BID
  C. Discontinue all medications and try different non-pharmacological behavioral modification options
  D. Start carbamazepine 200 mg PO BID
QUESTIONS?