Dementia and Antipsychotics in the Long Term Care Setting: A Quality Improvement Initiative
Welcome and Acknowledgments

- Vanderbilt University Medical Center
- Vanderbilt University Center for Quality Aging
- Qsource
Training Series Overview

- Session #3: Psychopharmacology in the Nursing Home
- Session #4: Principles of Non-pharmacologic Management & the Formulation of Behavioral Care Plans
- Session #5: The Implementation of Behavioral Strategies & the Management of Pharmacologic Interventions
- Session #6: Addressing Barriers to Change: the Perspective of Psychiatry, Nursing, and Medical Directors
Webinar Assistants

- Chat Monitor: Britt Kuertz, RDN
  Brittany.t.kuertz@vanderbilt.edu
  615-936-1499

- Moderator: Emily Hollingsworth, MSW
  Emily.k.hollingsworth@vanderbilt.edu
  615-936-2718
Chat Question

- How many people are in the room with you to view this webinar?

(Please answer in the chat pane, and be sure to include your full facility name)
Psychopharmacology in the Nursing Home
Warren Taylor, MD

Director, Mood Disorders Program
Psychiatry Department, Vanderbilt University

Researcher, Center for Cognitive Medicine
Paul Newhouse, MD

Director, Vanderbilt Center for Cognitive Medicine,
Jim Turner Chair in Cognitive Disorders
Department of Psychiatry,
Vanderbilt University
Objectives

- Describe the psychototropic drug treatment of the elderly patient
- Address on- and off-label uses of psychototropic drugs
- Review the efficacy, risk data, and dosing strategies for antipsychotics and antidepressants in elderly patients
- Explain the appropriate and inappropriate use in dementia and geriatric depression
- Discuss the discontinuation strategies for antipsychotics
Psychototropic Drug Management of AD

- Monotherapy is an ideal
- Polytherapy is common
  - “Rational coprescribing”
  - Combinations may improve efficacy but increase risk of adverse events
  - Complex regimens decrease compliance
Cumulative Prevalence of Neuropsychiatric Symptoms

Behavioral Symptoms that *May* be Responsive to Pharmacologic Intervention

- Behaviors that are fairly continuous and unresponsive to behavioral interventions
  - *e.g.* Agitation, anxiety

- Behaviors that may occur in response to certain environmental stressors
  - *e.g.* Bathing, examination, activities

- Behaviors that are similar to major psychiatric disorders
  - *e.g.* Psychosis
Cholinergic System Stimulation Improves Behavioral Disturbances in Alzheimer’s Disease

- Analysis of behavioral effects of acetylcholinesterase (AchE) inhibitors in AD studies show:
  - decreased apathy
  - decreased anxiety
  - decrease in hallucinations

- Withdrawal of AchE inhibitors found to produce behavioral disturbances
Significant differences were observed for the domains of depression, anxiety, and apathy ($P \leq 0.0166$).

Adapted with permission from Feldman et al. *Neurology.* 2001;57:613-620.
Anticholinesterase Discontinuation Worsens Behavior in AD

Randomization to donepezil continuation or placebo

Neuropsychiatric Inventory total score (NPI) (n ~ 96)

Holmes et al, 2004
Acetylcholinesterase inhibitors may help memory and cognition, but do not help with behavioral disturbances

A. TRUE
B. FALSE
Antipsychotics

- **Indications:**
  - Hallucinations, delusions, aggression, severe anxiety
  - Therapeutic efficacy is *modest* rather than striking
  - May actually *worsen* behavior

- **Adverse Effects:**
  - Extrapyramidal symptoms
  - Sedation
  - Confusion
  - Cardiovascular effects
  - *Increased risk of death*
# Deaths Due to Antipsychotics in Long-Term Care

## Table 2: Death within 180 days after start of treatment with antipsychotic drugs* in elderly patients in nursing homes

<table>
<thead>
<tr>
<th></th>
<th>Haloperidol (n=5904; 683 person years)</th>
<th>Aripiprazole (n=1849; 465 person years)</th>
<th>Olanzapine (n=22 919; 5741 person years)</th>
<th>Quetiapine (n=15 776; 3945 person years)</th>
<th>Risperidone (n=27 936; 6720 person years)</th>
<th>Ziprasidone (n=1061; 235)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>745</td>
<td>122</td>
<td>2104</td>
<td>1120</td>
<td>2434</td>
<td>73</td>
</tr>
<tr>
<td>Rate (95% CI)</td>
<td>109.1 (101.4 to 117.0)</td>
<td>26.2 (21.8 to 31.1)</td>
<td>36.7 (35.1 to 38.2)</td>
<td>28.4 (26.8 to 30.1)</td>
<td>36.2 (34.8 to 37.7)</td>
<td>31.1 (24.4 to 38.6)</td>
</tr>
<tr>
<td>Cause specific mortality:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Circulatory system</td>
<td>351</td>
<td>57</td>
<td>1045</td>
<td>542</td>
<td>1230</td>
<td>37</td>
</tr>
<tr>
<td>Rate (95% CI)</td>
<td>51.4 (46.2 to 56.9)</td>
<td>12.3 (9.3 to 15.6)</td>
<td>18.2 (17.1 to 19.3)</td>
<td>13.7 (12.6 to 14.9)</td>
<td>18.3 (17.3 to 19.3)</td>
<td>15.8 (11.1 to 21.2)</td>
</tr>
<tr>
<td>Cerebrovascular diseases</td>
<td>81</td>
<td>6</td>
<td>192</td>
<td>102</td>
<td>263</td>
<td>11</td>
</tr>
<tr>
<td>Rate (95% CI)</td>
<td>11.9 (9.4 to 14.6)</td>
<td>1.3 (0.5 to 2.5)</td>
<td>3.3 (2.9 to 3.8)</td>
<td>2.6 (2.1 to 3.1)</td>
<td>3.9 (3.5 to 4.4)</td>
<td>4.7 (2.3 to 7.9)</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>129</td>
<td>26</td>
<td>320</td>
<td>151</td>
<td>342</td>
<td>13</td>
</tr>
<tr>
<td>Rate (95% CI)</td>
<td>18.9 (15.8 to 22.3)</td>
<td>5.6 (3.6 to 7.9)</td>
<td>5.6 (5.0 to 6.2)</td>
<td>3.8 (3.2 to 4.5)</td>
<td>5.1 (4.6 to 5.6)</td>
<td>5.5 (2.9 to 9.0)</td>
</tr>
<tr>
<td>Other</td>
<td>265</td>
<td>39</td>
<td>739</td>
<td>427</td>
<td>862</td>
<td>23</td>
</tr>
<tr>
<td>Rate (95% CI)</td>
<td>38.8 (34.3 to 43.6)</td>
<td>8.4 (6.0 to 11.2)</td>
<td>12.9 (12.0 to 13.8)</td>
<td>10.8 (9.8 to 11.9)</td>
<td>12.8 (12.0 to 13.7)</td>
<td>9.8 (6.2 to 14.2)</td>
</tr>
</tbody>
</table>

*Rate expressed per 100 person years.

Huybrechts et al, BMJ 2012
OBRA Guidelines: Antipsychotics

- Use **only** if patients exhibit symptoms that impair functioning or cause danger to themselves or others, and/or interfere with provision of care.

- Agitated behavior is an insufficient reason to use an antipsychotic medication (i.e. must be psychotic or aggressive).

- Considered **unnecessary** if initiated as treatment in the absence of documentation of the approved indications.

- Use requires **approved** diagnosis and symptoms.

Antipsychotics should not be used when the following symptoms are the ONLY criteria:

- Wandering
- Poor self-care
- Anxiety/restlessness
- Impaired memory
- Uncomplicated depression
- Unsociability
- Fidgeting
- Nervousness
- Uncooperativeness
- Agitation without any danger to resident or others
Allowed Diagnosis for Antipsychotic Use in LTC

- Schizophrenia
- Schizo-affective Disorder
- Schizophreniform Disorder
- Delusional Disorder
- Psychotic Mood Disorder
- Acute Psychotic Episodes
- Brief Reactive Psychosis
- Atypical Psychosis
- Tourette's Disorder
- Huntington’s Disease
- “Organic” mental syndromes IF certain criteria are met
**Atypical Antipsychotics**

**Olanzapine (Zyprexa)**
- Moderately anticholinergic
- Requires starting at quite low doses (1.25-5 mg per day)
- May produce weight gain, glucose intolerance

**Quetiapine (Seroquel)**
- Wide dosage range; start at 25-75 mg per day
- Watch for sedation, orthostatic hypotension

**Risperidone (Risperdol)**
- May be better tolerated at low doses than standard neuroleptics but will produce EPS above ≈3 mg/day
Atypical Antipsychotics (2)

Aripiprazole (Abilify)
- Starting dose 2.5 mg qhs
- Dose can be slowly escalated to ~20 mg/day

Ziprasidone (Geodon)
- Little data in dementia

Clozapine
- May be helpful for patients who cannot tolerate standard neuroleptics (e.g. Parkinson’s Disease
- Very low doses often effective (12.5-50 mg/day)
- Requires weekly leukocyte monitoring
Antipsychotic Dose Reduction

- Must attempt a gradual reduction every 6 months unless:
  - The patient has one of the 10 approved conditions
  - If the diagnosis is an “Organic Mental Syndrome”

  PLUS:
  - Two previous attempts have been made in the last year to establish the dose is reduced to the lowest level to control symptoms

  Document justification including:
  - Diagnosis, symptoms, differential diagnosis, consideration of medical causes, risk/benefit analysis
CATIE Atypical Antipsychotic Study in Alzheimer’s Disease

Schneider et al, NEJM 355: 1525, 2006
Polling Question

Antipsychotic medications are required to have a dose reduction and withdrawal plan in place

A.  TRUE

B.  FALSE
**Use of Antidepressants in Dementia: Trazodone**

- May help control anxiety-related agitation, aggression, excess vocalization, and improve sleep
- Large therapeutic range (25-400 mg/day)
- Short half life may necessitate frequent dosing, up to every two hours
- May be combined with antipsychotics

*Newhouse 2000*
Use of Antidepressants in Dementia: Selective Serotonin Reuptake Inhibitors (sertraline, citalopram, etc.)

- Effective for the treatment of depression

- May also be useful for:
  - Irritability/Hostility
  - Excess Vocalization
  - Anxiety

- Can be used in combination with neuroleptics and cognitive enhancers

Newhouse 2000
Potential Antidepressant Risks

- **Falls / Fractures**
  - Concern led to SSRIs being placed on Beers Criteria

- **Stroke**
  - Annualized rate of 4 v 3 per 1000 person years

- **Limitations of studies:**
  - Comparing antidepressant users vs. non-users
Antidepressant Use for Agitation in Dementia: Guidelines

- **Anxiety/Nonaggressive Agitation**
  - Trazodone: 12.5-50 mg bid-tid initially; up to q2hrs if needed; target specific times (e.g. 30 minutes prior to care)

- **Irritability/Disinhibition/Vocalization**
  - SSRIs: Initiate at ¼ to ½ normal dose for at least seven days before raising dose to normal clinical range
Antipsychotics should never be used to treat depression in the elderly

A. TRUE

B. FALSE
Anticonvulsants In Dementia: Treatment of Agitation in Dementia

Valproic Acid/Valproate

- Small trials supportive of efficacy, but larger trials equivocal or negative.
- Dose starts at 125-250 mg twice a day
- Available in liquid formulation for better compliance

“Chronic Divalproex Sodium to Attenuate Agitation and Clinical Progression of Alzheimer Disease” Tariot et al, 2011
Benzodiazepines

- May be useful for short-term management of anxiety or for rapid control of agitation

- Short acting agents are less problematic
  - lorazepam (0.25-0.5 mg)
Benzodiazepine Risks

- Sedation
- Paradoxical excitation / disinhibition
- Ataxia / Falls
  - Increased hip fracture risk
- Long-term use
  - Increased risk of further cognitive decline
  - Withdrawal
Sedatives / Sleep Aids

- Concerns about risk of falls with sedatives
- Insomnia itself associated with falls risk!

Table 3. Adjusted Associations Between Baseline Explanatory Variables and 6-Month Outcome Variables (N = 34,163 Subjects)

<table>
<thead>
<tr>
<th>Explanatory Variable</th>
<th>Observations n</th>
<th>Falls Odds Ratio (95% Confidence Interval)</th>
<th>Hip Fracture Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2,149</td>
<td>1.52 (1.38–1.66)</td>
<td>0.99 (0.77–1.26)</td>
</tr>
<tr>
<td>No</td>
<td>32,014</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Hypnotic use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>882</td>
<td>1.13 (0.98–1.30)</td>
<td>0.85 (0.58–1.22)</td>
</tr>
<tr>
<td>No</td>
<td>33,281</td>
<td>Ref</td>
<td>Ref</td>
</tr>
</tbody>
</table>

Avidan AY et al. JAGS, 2005.
Medical Issues: Pain Control

- Undiagnosed/untreated pain (musculoskeletal or visceral) may be a significant factor exacerbating behavioral disturbances in AD, particularly in long-term care.

- May produce irritability, agitation, aggression, poor compliance, poor ADL performance, etc.

- Routine prophylactic acetaminophen use in institutionalized AD patients improved social interaction and ADLs (Chibnall, et al, 2005).

- More severe or chronic pain should prompt trial of opiates or similar agents (e.g. fentanyl patch).
Agitation scores over 3 months in pain managed group vs usual care (n= 352)

Husebo et al, BMJ, 2011
Medical Issues: Constipation

- Constipation: often missed contributor
  - Presence increases the odds of both verbal and physical aggression (OR: 1.3)

- Common side effect in many medications

- Need to monitor, treat when needed
## Medical Issues: Delirium

<table>
<thead>
<tr>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute onset / change</td>
<td>Gradual onset / change</td>
</tr>
<tr>
<td>Fluctuating symptoms</td>
<td>More consistent symptoms</td>
</tr>
<tr>
<td>Marked psychomotor changes</td>
<td>Psychomotor activity changes slowly progressive</td>
</tr>
<tr>
<td>(hyperactive or hypoactive)</td>
<td></td>
</tr>
<tr>
<td>Altered &amp; changing</td>
<td>Consciousness not</td>
</tr>
</tbody>
</table>
Psychotropic Medication Summary for Behavioral Disturbances in Dementia

Modified from Singer, 2001
Abnormal Behavior in AD

Behavioral Problems are the most problematic aspect of dementia

1. Institute environmental modifications first
   - Change where the patient is, what the environment is like, etc.
   - While also evaluating medical issues

2. Institute behavioral modifications second
   - Change how caregivers approach or handle patient, etc.

3. Institute pharmacological interventions third
   - Targeted or generalized medication depending on the type and scope of the problem
Session Summary

- All psychotropic medications may play an important role in managing behavioral disturbances in dementia.

- These medications all have risks. Thus it is important to have ongoing re-evaluations of their continuing need in each patient.

- The re-evaluation and attempt to reduce dosage is particularly important for antipsychotics.

- Do not ignore environmental or behavioral factors that can lead to improvement!

*There will be a second presentation of Session #3 on Wednesday, December 16th at 10AM CST (11AM EST)*
Two options for attending Session #4:

- January 12\(^{th}\) (Tuesday) 1pm CST / 2pm EST
- January 28\(^{th}\) (Thursday) 10am CST / 11am EST
Contact Information

- Emily Hollingsworth
  Emily.K.Hollingsworth@vanderbilt.edu

- Britt Kuertz
  Brittany.T.Kuertz@vanderbilt.edu

- Project Website:
  www.VanderbiltAntipsychoticReduction.org

- Vanderbilt Center for Quality Aging 615-936-1499
  www.vanderbiltcqa.org for other resources