A PERSPECTIVE ON CMS'S ANTIPSYCHOTIC REDUCTION INITIATIVE

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ASCP
National Harbor MD November 8th, 2012
Dr Gifford has no financial, other relationship or other support from the pharmaceutical industry related to antipsychotic medications.

Dr Gifford will be discussing the evidence related to the off-label use of antipsychotic medications.
Learning Objectives

- Able to describe the magnitude of the risks and benefits of antipsychotics for individuals with dementia residing in nursing homes
- Interpret and use the CMS quality measures on the use of antipsychotic medication in your practice
- Strategies to safely reduce the use of these medications in long term care setting
National Priority

- CMS is making the reduction of off-label use of antipsychotic medications a national priority.
- Don Berwick, Director of CMS has asked professional associations to work together and with CMS to reduce the off-label use of antipsychotic medications in nursing homes.
## Antipsychotic Medications

<table>
<thead>
<tr>
<th>Conventional</th>
<th>Atypical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compazine</td>
<td>Aripiprazole</td>
</tr>
<tr>
<td>Haldol</td>
<td>Asenapine</td>
</tr>
<tr>
<td>Loxitane</td>
<td>Clozapine</td>
</tr>
<tr>
<td>Mellaril</td>
<td>Iloperidone</td>
</tr>
<tr>
<td>Moban</td>
<td>Olanzapine</td>
</tr>
<tr>
<td>Navane</td>
<td>Paliperidone</td>
</tr>
<tr>
<td>Orap</td>
<td>Quetiapine</td>
</tr>
<tr>
<td>Prolixin</td>
<td>Risperidone</td>
</tr>
<tr>
<td>Prolixin</td>
<td>Ziprasidone</td>
</tr>
<tr>
<td>Stelazine</td>
<td></td>
</tr>
<tr>
<td>Thorazine</td>
<td></td>
</tr>
<tr>
<td>Trilafon</td>
<td></td>
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</tbody>
</table>
FDA approved diagnoses

- Schizophrenia
- Bi-polar Disorder
- Irritability associated with Autistic Disorder (Aripiprazole & Risperidone)
- Treatment Resistant Depression (Olanzapine)
- Major Depressive Disorder (Quetiapine)
- Tourettes (Orap)

When prescribed to a patient without an FDA approved diagnosis; the prescription is considered as an “off-label use”, which is allowed by FDA and Medical Boards
Common Off-label uses

- Dementia with behavior difficulties
  - Agitation
  - Abusive, violent
  - Wandering
- Acute Delirium
- Obsessive-compulsive disorder
- Psychotic symptoms (e.g. hallucinations, delusions) with neurological diseases
  - Parkinson’s disease
  - Stroke
Effectiveness in Dementia

- Antipsychotic effect takes 3-7 days to start working
  - Very sedating medication so acute effect is most likely due to sedating effect not antipsychotic effect
- In RCTs, recipients do a little bit better than placebo but the effect beyond 3 months is unclear
  - Not everyone who receives the meds improve
  - A large number of people getting the placebo improve
  - The net effect is that 10 to 20 people out of 100 who receive the medication improve due to the medication
Effectiveness in Dementia is weak
Meta-Analysis (JAMA 2011)

- Aripiprazole, Olanzapine, and Risperidone had a small but statistically significant effect (12 – 20%) when compared to placebo
- Quetiapine did not have a statistically significant effect
- Antipsychotics led to an average change/difference on the NeuroPsychiatric Inventory (NPI) of
  - 35% from a patient’s baseline
  - 3.41 point difference from placebo group
    (note: a 30% change and 4.0 difference is the minimum threshold needed for a clinically meaningful result)
- No conclusive evidence was found regarding the comparative effectiveness of different antipsychotics

Source: JAMA 306:1359-69 2011; Meta-analysis 38 RCTs in dementia
# Antipsychotic vs Placebo Results

**Figure 1.** Controlled Trials of Patients Taking Atypical Antipsychotic Medications vs Placebo

<table>
<thead>
<tr>
<th>Source</th>
<th>Dose, mg/d</th>
<th>Standardized Mean Difference (95% CI)</th>
<th>Favors Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aripiprazole</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mintzer et al.</td>
<td>2, 5, 10</td>
<td>0.16 (0.05 to 0.37)</td>
<td>Placebo</td>
</tr>
<tr>
<td>De Deyn et al.</td>
<td>10 (mean)</td>
<td>0.06 (0.21 to 0.34)</td>
<td>Treatment</td>
</tr>
<tr>
<td>Streim et al.</td>
<td>8.6 (mean)</td>
<td>0.36 (0.11 to 0.61)</td>
<td>Treatment</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td>0.20 (0.04 to 0.35)</td>
<td></td>
</tr>
<tr>
<td><strong>Olanzapine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De Deyn et al.</td>
<td>1, 2.5, 5, 7.5</td>
<td>0.14 (0.05 to 0.34)</td>
<td>Placebo</td>
</tr>
<tr>
<td>Deberdt et al.</td>
<td>5.2 (mean)</td>
<td>-0.02 (-0.27 to 0.23)</td>
<td>Treatment</td>
</tr>
<tr>
<td>Schneider et al.</td>
<td>5.5 (mean)</td>
<td>0.15 (-0.11 to 0.40)</td>
<td>Treatment</td>
</tr>
<tr>
<td>Street et al.</td>
<td>5, 10, 15</td>
<td>0.30 (0.03 to 0.63)</td>
<td>Treatment</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td>0.12 (0 to 0.25)</td>
<td></td>
</tr>
<tr>
<td><strong>Quetiapine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schneider et al.</td>
<td>56.5 (mean)</td>
<td>0.15 (-0.11 to 0.42)</td>
<td>Placebo</td>
</tr>
<tr>
<td>Taric et al.</td>
<td>97 (median)</td>
<td>0.22 (-0.03 to 0.47)</td>
<td>Treatment</td>
</tr>
<tr>
<td>Taric et al.</td>
<td>96.9 (median)</td>
<td>0 (-0.29 to 0.30)</td>
<td>Treatment</td>
</tr>
<tr>
<td>Zhong et al.</td>
<td>100, 120, 200</td>
<td>0.04 (-0.21 to 0.28)</td>
<td>Placebo</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td>0.11 (-0.02 to 0.24)</td>
<td></td>
</tr>
<tr>
<td><strong>Risperidone</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brodaty et al.</td>
<td>0.95 (mean)</td>
<td>0.46 (0.23 to 0.69)</td>
<td>Placebo</td>
</tr>
<tr>
<td>Deberdt et al.</td>
<td>1 (mean)</td>
<td>-0.13 (-0.38 to 0.12)</td>
<td>Treatment</td>
</tr>
<tr>
<td>De Deyn et al.</td>
<td>1.1 (mean)</td>
<td>0.12 (-0.14 to 0.38)</td>
<td>Treatment</td>
</tr>
<tr>
<td>Katz et al.</td>
<td>0.5, 1.2</td>
<td>0.32 (0.11 to 0.53)</td>
<td>Treatment</td>
</tr>
<tr>
<td>Mintzer et al.</td>
<td>1.03 (mean)</td>
<td>-0.01 (-0.21 to 0.18)</td>
<td>Treatment</td>
</tr>
<tr>
<td>Schneider et al.</td>
<td>0.95 (mean)</td>
<td>0.40 (0.13 to 0.68)</td>
<td>Placebo</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td>0.19 (0 to 0.38)</td>
<td>Placebo</td>
</tr>
</tbody>
</table>

Source: JAMA, September 28, 2011; Vol 306, No. 12; Meta-analysis 18 RCTs in Dementia
## Effectiveness of Antipsychotics in Dementia

<table>
<thead>
<tr>
<th>Drug</th>
<th>% improvement in symptom scale</th>
<th>% treatment discontinuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>olanzapine</td>
<td>32%</td>
<td>24%</td>
</tr>
<tr>
<td>quetiapine</td>
<td>26%</td>
<td>16%</td>
</tr>
<tr>
<td>risperidone</td>
<td>29%</td>
<td>18%</td>
</tr>
<tr>
<td>placebo</td>
<td>21% (p=0.22 for trend)</td>
<td>5% (p=0.009 for trend)</td>
</tr>
</tbody>
</table>

Effectiveness in Treating Aggression in Dementia (Cochararane Review 2012)

Evaluated 16 placebo controlled trials with atypical antipsychotics although only 9 had sufficient data to contribute to a meta-analysis and only 5 have been published in full in peer reviewed journals. No trials of amisulpiride, sertindole or zotepine were identified which met the criteria for inclusion.

Conclusions:

- Statistically significant improvement in aggression with risperidone and olanzapine when compared to placebo.
- Statistically significant improvement in psychosis with risperidone.
- Risperidone and olanzapine treated patients had a significantly higher incidence of serious adverse cerebrovascular events (including stroke), extrapyramidal side effects and other adverse outcomes.
- Significant increase in drop-outs in risperidone (2 mg) and olanzapine (5-10 mg) treated patients.
- Data were insufficient to examine impact upon cognitive function.

Source: Cochrane Review 2012; Meta-analysis 16 RCTs in dementia
Associated with adverse outcomes

- Off-label use of antipsychotics in nursing facility residents are associated with an increase in:
  - Death
  - Hospitalization
  - Falls & fractures
  - Venothrombolic events

- Conventional antipsychotics are worse than atypical antipsychotics
## Dose for Antipsychotics Used in Dementia

<table>
<thead>
<tr>
<th>Medication</th>
<th>Low Dose</th>
<th>Normal Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>&lt;2 mg/d</td>
<td>2-15 mg/d</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>&lt;5 mg/d</td>
<td>5-10 mg/d</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>&lt;50 mg/d</td>
<td>50-100 mg/d</td>
</tr>
<tr>
<td>Risperidone</td>
<td>&lt;1 mg/d</td>
<td>1-2 mg/d</td>
</tr>
</tbody>
</table>
Effectiveness with Low Dose

- Low dose **Resperidone** (<1 mg/d) has small positive effective but also has increase risk of adverse events.
- Low dose **Olanzapine** (5 mg/d) has no positive effect but does have increase risk of adverse events.
- Low dose **Aripiprazole** and **Quetiapine** effectiveness are unknown but Quetiapine at normal dose ineffective.

Source: Cochrane Review 2012; Meta-analysis 16 RCTs in dementia.
Odds of having an adverse event after receiving an Respiridone 1 mg/d compared to placebo

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Odd Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>1.25</td>
<td>0.73 to 2.16</td>
</tr>
<tr>
<td>Somnolence</td>
<td>2.40</td>
<td>1.70 to 3.20</td>
</tr>
<tr>
<td>Falls</td>
<td>0.84</td>
<td>0.63 to 1.14</td>
</tr>
<tr>
<td>Extrapyramidal disorder</td>
<td>1.78</td>
<td>1.00 to 3.17</td>
</tr>
<tr>
<td>UTI</td>
<td>1.40</td>
<td>0.92 to 2.13</td>
</tr>
<tr>
<td>Edema</td>
<td>2.75</td>
<td>1.51 to 5.03</td>
</tr>
<tr>
<td>Abnormal Gait</td>
<td>5.31</td>
<td>2.24 to 12.62</td>
</tr>
<tr>
<td>Urinary Incontinence</td>
<td>13.6</td>
<td>1.81 to 101</td>
</tr>
<tr>
<td>CVA</td>
<td>3.64</td>
<td>1.72 to 7.69</td>
</tr>
<tr>
<td>Drop outs</td>
<td>1.43</td>
<td>1.01 to 2.03</td>
</tr>
</tbody>
</table>

Source: Cochrane Review 2012; Meta-analysis 4 RCTs in dementia
Odds of having an adverse event after receiving an Olanzapine 5-10 mg/d compared to placebo

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Odd Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>2.31</td>
<td>0.66 to 8.13</td>
</tr>
<tr>
<td>Somnolence</td>
<td>3.72</td>
<td>1.90 to 7.25</td>
</tr>
<tr>
<td>Falls</td>
<td>1.52</td>
<td>0.79 to 2.91</td>
</tr>
<tr>
<td>Abnormal Gait</td>
<td>4.76</td>
<td>1.67 to 13.57</td>
</tr>
<tr>
<td>Urinary Incontinence</td>
<td>9.60</td>
<td>1.27 to 72.85</td>
</tr>
<tr>
<td>CVA</td>
<td>5.24</td>
<td>0.29 to 95.69</td>
</tr>
<tr>
<td>Drop outs</td>
<td>3.34</td>
<td>1.69 to 6.59</td>
</tr>
</tbody>
</table>

Source: Cochrane Review 2012; Meta-analysis 3 RCTs in dementia
Net effectiveness

“For every 100 patients with dementia treated with an antipsychotic medication, only 9 to 25 will benefit and 1 will die”

Drs Avorn, Choudhry & Fishcher
Harvard Medical School

Dr Scheurer
Medical University of South Carolina

FDA Black Box Warning

- Issued in 2005
- 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. [Name of Antipsychotic] is not approved for the treatment of patients with dementia-related psychosis.
F-Tag associated with off-label use

- F-Tag 329: Unnecessary Drugs
  - Residents should have drug regimens that are free of unnecessary drugs defined as
    - There is an excessive dose including duplicate therapy
    - There is an excessive duration of being on the drug
    - There is inadequate monitoring of the drug
    - There is inadequate indication for the use of the drug
    - There are adverse consequences
    - A combination of the reasons above

- Specific conditions for antipsychotic drugs
  - The facility must ensure that residents have not used antipsychotics previously, are not given these drugs unless the drug therapy is necessary, and recorded in the clinical record
  - In an effort to decrease the use of antipsychotics residents must receive gradual dose reduction and alternate therapies, unless they are counter-indicated
Trends in F-Tag 329 unnecessary Meds

Trend in the percent of facilities cited for F-Tag 329

% of Facilities Cited for F-Tag 329

Trends in use following FDA Black Box

- 1990s there was a shift from conventional to atypical antipsychotics
  - Atypical antipsychotics have lower rates of Parkinsonism and Tardive Dyskinesia
- The outpatient use of antipsychotics started to decrease before the FDA black box warning
- 5% increase in the use of antidepressants, anxiolytics, and anticonvulsants after the FDA black box warning
Patients with dementia who use antipsychotic medication.
OIG Report 2011

- OIG report
  - Reviewed 600 medical records
  - Medicare claims data for Part B and Part D and MDS data from January 1st to July 31st, 2007 was used to identify payments for atypical antipsychotic drug use for elderly nursing home residents

- Major Findings
  - 14% of elderly nursing home residents had Medicare claims for atypical antipsychotic drugs
    - Off-label conditions accounted for 83% of these claims
  - Over ½ of the Medicare claims for antipsychotic drugs for elderly nursing home resident were incorrect
  - Medicare reimbursement criteria was not met for 726,000 of the 1.4 million claims
  - 22% of the atypical antipsychotic drugs were not administered in accordance with CMS standards
CMS quality measures

- % started on medication following admission
  - % of individuals in a facility for ≤100 days who were not admitted on the medication but who have it started during their 100 day stay excluding individuals with schizophrenia, Tourette's and Huntington's disease

- % long stay residents who receive the medication
  - % of individuals in a facility for >100 days who are receiving the medication excluding individuals with schizophrenia, Tourette's and Huntington's disease
CMS measures

- Failure to include other FDA approved diagnoses such as bipolar disorder
- % Started during 100 days\(^1\) = 3%
- % Receiving medication long stay\(^1\) = 24%
- % Receiving medication on admission\(^2\) = 12%

\(^1\)Source: CMS Nursing home compare reported July 2012 using data from 4\(^{th}\) Quarter 2011
\(^2\)Source: MDS 2.0 data 2010 analysis of admission assessments excluding schizophrenia and bipolar disorder
Off-Label Use of Antipsychotic Meds

Percentage of Off-label Antipsychotic Usage among Long-Stay Residents in Nursing Facilities

Source: CMS analysis of MDS 3.0 data, 4th Quarter 2011.
Off-Label Use of Antipsychotics
AHCA Quality Initiative Goals

- **Reduce Hospital Readmissions**
  - By March 2, 2015 at 12:00 p.m., reduce the number of hospital readmissions within 30 days during a SNF stay by 15 percent.

- **Increase Staff Stability:**
  - By March 2, 2015 at 12:00 p.m., reduce turnover among clinical staff (RN, LVN, CNA) by 15 percent.

- **Reduce the Off-Label Use of Antipsychotics:**
  - By December 31, 2012 at 12:00 p.m., reduce the off-label use of antipsychotics by 15 percent.

- **Increase Resident Satisfaction:**
  - By March 2, 2015 at 12:00 p.m., increase the number of customers who would recommend the facility to others up to 90%.
AHCA Strategies to reduce use of antipsychotics in nursing facilities

- Phase I: immediate steps facilities can take that will show results in the near term
  - Focus on withdrawal or gradual dose reduction of antipsychotics

- Strategies
  - Identify residents with off-label use of antipsychotics
  - Review records to assure compliance with CMS SOM
  - Use evidence based approaches for gradual dose reduction (GDR) to discontinue patients from antipsychotics
    - Work with the medical director and consultant pharmacist to guide the GDR process and promote GDR to physicians, staff and families.
  - Educate families about prevalence of dementia, use of antipsychotics and alternate treatment options
Immediate steps to reduce antipsychotics

- No role for PRN only antipsychotic medications
- Evaluate the need for continuing antipsychotics at admission & those on very low doses
- Evaluate need for antipsychotics started on residents during the evening/night shift or over the weekend
- Look at discontinue or gradual dose reduction for residents on medications for greater than 12 weeks (3 months), particularly those with no change in dose or frequency
Evidence based for Discontinuing Meds at lose dose

- RCTs comparing low dose to placebo show
  - Resperidon to be minimally ineffective
  - Olanzapine to be not effective
  - Aripiprazole and Quetiapine unknowns as low dose not tested

- RCTs for withdrawal of medication show
  - No difference in outcomes between placebo and continued medication
  - About 75% remain off the drug after the trial
    - Less than 25% need to be restarted on the medication
  - Placebo group (drug withdrawal) have fewer adverse events
RCT to withdraw antipsychotics

100 w/Dementia on antipsychotics

54 Continue med

Outcomes
- 76% no change in behaviors
- NPI total worse 0.2
- Agitation worse 1.5
- QOL worse 0.6

Outcomes assessed over 3 months

46 Stopped med

Meds stopped abruptly and given a placebo

Outcomes
- 67% no change behaviors
- NPI better 1.3 p=0.46
- Agitation better 1.0 p=0.02
- QOL worse 0.4 p=0.44

Higher NPI scores associated with change in behaviors & restarting medication

RCT to withdraw antipsychotics

165 w/Dementia on antipsychotics

83 Continue med

- Outcomes (N=51)
  - Cognitive Fxn worse 6.2
  - NPI total worse 1.3
  - Verbal fluency worse 3.2
  - ADLs worse 1.8
  - Agitation 32%

82 Stopped med

- Outcomes (N=51)
  - Cognitive Fxn worse 5.7  p=0.9
  - NPI worse 4.5  p=0.4
  - Verbal Fluency better 0.6  p=0.002
  - ADLs worse 0.2  p=0.5
  - Agitation 34%

Meds stopped abruptly and given a placebo

Outcomes assessed @ 6 months

RCT to withdraw antipsychotics\(^1\)

165 w/Dementia on antipsychotics

- 83 Continue med
  - Survival: 90% who stayed on med, 70% ITT

- 82 Stopped med
  - Survival: 97% who stay off med, 77% ITT

Meds stopped and given a placebo

Only 7 restarted on meds

\(^1\)Ballard D et al Lancet Neurol 2009; 9:151-57
RCT to withdraw antipsychotics

58 w/Dementia on antipsychotics

- 29 Continue med
- 29 Stopped med

Meds tapered for 3 wks and given placebo 6 weeks then groups switched

Outcomes (N=35)
- BPRS worse 2.3
- Aggression worse 1.7
- Verbal fluency worse 3.2
- Verbal agitation worse 2.1
- Abnl Movements worse 1.2
- Activity worse 2.8

Outcomes (N=35)
- BPRS worse 2.1  p=0.10
- Aggression worse 1.7  p=0.87
- Verbal Fluency better 0.6  p=0.002
- Verbal agitation worse 1.9  p=0.23
- Abnl movements worse 2.1  p=0.06
- Activity worse 2.8  p=0.88

Outcomes assessed @ 7 weeks & 14 weeks

Cohen-Manfield et al Arch Int Med 1999; 159:1733-1740
Verbally Agitated Behavior Scores

Clinical Practice Tools

- See ASCP, AMDA, AHCA, Advancing Excellence
- AHCA Tools to facilitate GDR/discontinuation:
  - Nursing Process
  - SBAR
- University of Iowa/Iowa Geriatric Education Center resources:
  - Videos
  - Pocket guides to evidence-based practices
  - Decision algorithms
  - Fact sheets for professionals & families
Primary Challenge is Changing Beliefs

- Most health care professionals and families believe:
  (1) dementia “behaviors” are abnormal & need to be treated
  (2) antipsychotics medications are effective
Strategies to reduce use of antipsychotics in nursing facilities

- **Phase II**: steps that will take longer to implement but need to be started now
  - Focus on implementing programs to minimize the off-label use of antipsychotics by promoting
    - Non-pharmacologic strategies to manage individuals with dementia
    - Changes to how we view dementia behaviors as attempts to communicate unmet needs

- **Strategies**
  - Staff training on interacting with individuals with dementia
  - Adopt policy on minimal use of medications with dementia residents
    - Educate families about this policy
  - Implement consistent assignment
  - Compare facility off-label antipsychotic use to others
    - Learn from other facilities
Dementia re-examined

- Experiencing the world in a different way
- What are “behaviors”?
  - Medical symptoms?
  - Predictable human responses to the situation perceived?
- Key questions to ask:
  - What is this person trying to tell me?
  - What is distressing this person?
  - What does he or she need to be in well-being?
Questions to ask for new Rx

- What did you do to try and figure out why the resident was doing <fill in the blank>?
- What is resident trying to communicate to us about their <fill in blank>?
- What is reason for resident doing <fill in blank>?
  - Unacceptable answer (Dementia or sun-downing)
- What did you try before requesting medications?
Contact Information

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