LTC Research Influencing Practice

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Conflicts of Interest

• Dr. Nace does not have any current conflicts of interest to report.
Objective

• Discuss five articles that have the potential to change LTC practice.
Methods

- **5 LTC focused** articles
- Potential **practical** implications
- Selection period **Sept 2015 to Sept 2016**
- English language
- Identified using an expanding search strategy
  - *Top rank medicine journals > JAMDA & JAGS > OVID Core > Pub Med*
What Do I Do with Those Dementia Medications?

- Do I Continue the Cholinesterase Inhibitor?
- Do I Add Memantine?
# Current State of Knowledge

## Cholinesterase Inhibitors (ACI) in NF

### What We Know

- **NF Residents w/Dementia**
  - Increased AD severity
  - Greater functional impairment
  - More medications

### What We Don’t

- Benefits in NF Population
- Risks of Drug Withdraw in NF Residents
• ACI do not impact mortality
• ACI do not increase survival
• ACI are not disease modifiers
• ACI have limited benefit
• Temporary stabilizers

Don’t prescribe cholinesterase inhibitors for dementia without periodic assessment for perceived cognitive benefits and adverse gastrointestinal effects.
A Randomized Placebo-Controlled Discontinuation Study of Cholinesterase Inhibitors in Institutionalized Patients with Moderate to Severe Alzheimer Disease

Herrmann N, O’Regan J, Ruthirakuhan M, Kiss A, Eryavec G, Williams E, Lanctot KL.

J Am Med Dir Assoc
2016;17(2):142-147.
Design

• 8 week placebo controlled, double-blind RCT
  – Continued ACI vs ACI withdrawal

• 2 NF in Canada

• Inclusion criteria
  – >55 yr with probable AD
  – ≤ 15 on MMSE
  – ≥ 2 years on donepezil, rivastigmine, galantamine
  – ACI dose stable ≥ 3 mos
  – Concomitant psychotropics stable ≥ 1 mos
Outcome Measures

- Clinicians Global Impression
- **Clinicians Global Impression of Change (CGIC)**
- MMSE
- Severe Impairment Battery
- Udvalg (side effects)
- Neuropsychiatric Inventory-NH
- Cornell Depression Scale for Dementia
- Apathy Evaluation Scale
- Cohen-Mansfield Agitation Inventory
- ADCS-ADL-sev
- QUALID (QOL)

CGIC – primary outcome
Results

• 40 subjects with moderate to severe AD

• No significant difference in CGIC decline
  – 6 worsened in continuation grp
  – 7 worsened in withdrawal grp
  – Baseline hallucinations predicted CGIC decline
  – Baseline delusions trended to predict CGIC decline

• No difference in adverse event rates

• No difference in other measures
Results

- Limitations
  - Sample size
  - Duration of follow up = 6 weeks
  - Mostly male population

- Differs from meta-analysis by same authors of 5 studies of ACI withdraw among community dwellers
  - Mostly earlier stage disease
Summary

• ACI discontinuation is safe and well tolerated in NF residents
  – with moderate to severe AD
  – who have been stable, and treated for ≥ 2 yrs
  – without psychotic features
    (hallucinations/delusions) at baseline

• Supports prior work showing ACI can attenuate behavioral symptoms
## Criteria for Attempting ACI Withdraw

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the resident have moderate to severe dementia?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has the resident been on an ACI for $\geq$ 2 years?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has the ACI dose been stable $\geq$ 3 months?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the resident free of psychotic features (hallucinations, delusions)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have other psychotropic medications been stable $\geq$ 1 month?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- ACI = acetylcholinesterase inhibitor
## Current State of Knowledge
### Combination Therapy with Memantine

<table>
<thead>
<tr>
<th>What We Know</th>
<th>What We Don’t</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Memantine approved for moderate to severe AD</td>
<td>• Are there benefits with combination therapy?</td>
</tr>
<tr>
<td>• ACI approved for all stages of AD</td>
<td></td>
</tr>
<tr>
<td>• Conflicting results for combination therapy trials</td>
<td></td>
</tr>
</tbody>
</table>
Combination Therapy Showed Limited Superiority Over Monotherapy for Alzheimer Disease: A Meta-analysis of 14 Randomized Trials

Tsoi KKF, Chan JYC, Leung NWY, Hirai HW, Wong SYS, Kwok TCY.

J Am Med Dir Assoc
2016;17(9):863.e1-863.e8.
Design

• Meta-analysis – *through 2015*

• Study inclusion criteria
  – RCT
  – Alzheimer Disease
  – Compared effectiveness of combination therapy against monotherapy
  – Measured change in assessment scores, or adverse events, from baseline to study endpoints
  – Full text and details available
  – Included advanced dementia stages
Results

• 4485 abstracts identified
  – 14 studies eligible
  – 7 > moderate to severe
  – 7 > mild to moderate

• 5019 patients

• 42% male

• 72-86 years of age

• Baseline MMSE 9-21
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Mean Difference</th>
<th>95% CI</th>
<th>Significant?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cognition</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMSE (Monotherapy with NMDA)</td>
<td>0.54</td>
<td>-0.19, +1.28</td>
<td>NS</td>
</tr>
<tr>
<td>MMSE (Monotherapy with ACI)</td>
<td>-0.02</td>
<td>-0.69, +0.66</td>
<td>NS</td>
</tr>
<tr>
<td>MMSE (Any Monotherapy)</td>
<td>0.06</td>
<td>-0.52, +0.65</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADCS-ADL (Monotherapy with NMDA)</td>
<td>-0.39</td>
<td>-1.01, +0.23</td>
<td>NS</td>
</tr>
<tr>
<td>ADCS-ADL (Monotherapy with ACI)</td>
<td>-0.14</td>
<td>-1.23, 0.95</td>
<td>NS</td>
</tr>
<tr>
<td>ADCS-ADL (Any Monotherapy)</td>
<td>-0.15</td>
<td>-1.08, +0.78</td>
<td>NS</td>
</tr>
</tbody>
</table>
### Division of Geriatric Medicine

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Mean Difference</th>
<th>95% CI</th>
<th>Significant?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropsychiatric &amp; Behavior</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPI (Monotherapy with ACI)</td>
<td>-1.85</td>
<td>-4.83, +1.13</td>
<td>NS*</td>
</tr>
<tr>
<td>Global Changes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIBIC-plus (Monotherapy with ACI)</td>
<td>0.01</td>
<td>-0.25, +0.28</td>
<td>NS</td>
</tr>
</tbody>
</table>

- Adverse events not different

- *Combination therapy was better on neuropsychiatric and behavior symptoms when restricted to studies of moderate to severe AD (excluding the mild to moderate AD studies)
Summary

- Combination therapy beneficial on neuropyschiatric and behavioral symptoms in those with moderate to severe disease
- No clear benefit to combination therapy in for other outcomes
- No major adverse events with combination therapy compared to monotherapy
- Combination therapy increases costs with limited benefit in most cases
Summary

• Careful assessment of individuals with moderate to severe disease
  – In absence of behavioral and psychological symptoms of dementia, combined therapy not likely to benefit

• Combined therapy not likely to benefit those with mild to moderate disease
What Is This Patient’s Risk of 30 Day Readmission?

Who Should I Follow More Closely?
Current State of Knowledge

30 Day Readmissions

**What We Know**

- 20% of hospitalized Medicare pts are discharged to SNFs
- 23.5% of these are readmitted w/i 30 days
- SNF transfers have greater severity of illness c/w community discharges

**What We Don’t**

- No prediction tools for patients discharged to SNFs
- HOSPITAL Score developed, but not validated for SNF patients
Validation of the HOSPITAL Score for 30-Day All-Cause Readmissions of Patients Discharged to Skilled Nursing Facilities

Kim LD, Kou L, Messinger-Rapport BJ, Rothberg MB.

*J Am Med Dir Assoc*

2016;17(9):863.e15-863.e18.
Design

- Validation study
- HOSPITAL score developed in Boston
- Retrospective collection of administrative and clinical data
- Outcome was readmission w/i 30 days to Cleveland Clinic Health System hospital
- Variable was HOSPITAL score
<table>
<thead>
<tr>
<th>Attribute</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin &lt; 12 g/dL at discharge</td>
<td>1</td>
</tr>
<tr>
<td>Discharge from oncology service</td>
<td>2</td>
</tr>
<tr>
<td>Na &lt; 135 mEq/L at discharge</td>
<td>1</td>
</tr>
<tr>
<td>Any ICD9 coded procedure</td>
<td>1</td>
</tr>
<tr>
<td>Non-elective admission</td>
<td>1</td>
</tr>
<tr>
<td>Number hospital admissions in prior yr</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1-5</td>
<td>2</td>
</tr>
<tr>
<td>&gt;5</td>
<td>5</td>
</tr>
<tr>
<td>Length of stay ≥ 5 days</td>
<td>2</td>
</tr>
</tbody>
</table>

Total = ____  (Low Risk = 0-4; Intermediate Risk = 5-6; High Risk = ≥ 7)
Results

- 4208 discharges
- Mean age = 71.6
- 45.9% = African American
- Medicare primary payor = 75%
- 30-day readmit rate = 30.9%
Results

Low Risk: 15.40%
Intermediate Risk: 28.10%
Hi Risk: 40.90%

c-statistic = 0.65
Summary

• HOSPITAL Score stratifies NF patients regarding all-cause 30-day readmission risk

• Can be used by clinicians to identify those who may need “extra attention” in order to prevent readmissions

• Helpful given SNF VPB, 5 Star Measures, & narrowed network providers
Long Acting Opioids & Long Stay Residents

Always Start the Game in the First Inning
## Current State of Knowledge
### Long Acting Opioids (LAO)

### What We Know
- LAO opioids should not be started in opioid naïve patients
- FDA warnings, particularly about fentanyl patches
- In 2004-2005, 39% of RI NF residents started on LAO had not used any opioid in prior 60 days

### What We Don’t
- What is happening nationally with LAO prescribing?
- Has there been any improvement in LAO prescribing?
New Initiation of Long-Acting Opioids in Long-Stay Nursing Home Residents

Pimentel CB, Gurwitz JH, Tjia J, Hume AL, Lapane KL.

J Am Geriatr Soc
(epub ahead of print)
Design

- Analysis of NF residents via 4 national data sets
- Long stay NF residents (> 90 d)
  - Minimize Part A covered meds
  - Minimize uncaptured acute care meds
- Jan 1 to Dec 31, 2011
- 22,253 met inclusion criteria
- Opioid naïve = no short acting opioid w/i 60 days
Results

• Mean age = 75, 71% female
• 73% mild to mod functional impairment
• 19% mod to severe cognitive impairment
• 83% had pain in prior 5 days
  – 25% had constant pain
  – 45% had frequent pain
  – 26% had occasional pain
Results

When LAO Are Prescribed Following Admission

- ≤ 7 Days: 31%
- ≤ 30 Days: 55%
- ≤ 60 Days: 72%
- ≤ 90 Days: 81%
New Initiation of LAO in Long-Stay Nursing Home Residents By Look Back Period

Overall 9.4% of LAO Prescriptions W/I 30 days Were in Opioid Naïve Patients

J Am Geriatr Soc 2016;64(9):1772-1778
Results

Most Common Long Acting Opioids Started in Opioid Naïve Residents

- 51.9% Fentanyl Patch
- 28.2% Morphine
- 17.2% Oxycodone
- 2.7% Others
Summary

- Rate of LAO use in opioid naïve residents may be declining…BUT
- > 9% of NF residents started on LAO in the first 30 days are opioid naïve
- 18.5% of NF residents prescribed LAO at any point, are opioid naïve
- Fentanyl patches comprise the largest category of potentially inappropriate LAO starts
  - May be particularly true in hospice patients
Delusions About Reducing Antipsychotics

Can We Really Make a Difference?
## Current State of Knowledge

### Antipsychotic (AP) Review

#### What We Know

- Behavioral problems impact 90% of patients with dementia.
- AP medications have modest benefits, but also significant risks.
- AP usage should be regularly reviewed and dose reductions attempted.

#### What We Don’t

- Is AP review effective in reducing AP use?
- Can nonpharmacological interventions reduce agitation among residents with dementia?
- Does exercise reduce depression?
Impact of Antipsychotic Review & Nonpharmacological Intervention on Antipsychotic Use, Neuropsychiatric Symptoms, & Mortality in People with Dementia Living in Nursing Homes: A Factorial Cluster-Randomized Controlled Trial by the Well-Being & Health for People with Dementia (WHELD) Program

Ballard C, Orrell M, YongZhong S, Moniz-Cook E, et al.

Design

- Cluster randomized 9 month trial in 16 NF
- Residents with stage 4 dementia or greater
- 8 NF assigned to AP review
- 8 NF assigned to increased social interaction
- 8 NF assigned to exercise intervention
- All received person centered care training

Outcomes
- Primary = AP use.
- Secondary = Mortality & Neuropsych measures
Results

- 277 participants
  - 195 (70%) completed the study
- Mean age = 85, Female = 74%
- Dementia (CDR) Severity
  - Mild – 12%
  - Mod – 40%
  - Sev – 47%
- 18% were taking AP
## Results

<table>
<thead>
<tr>
<th></th>
<th>AP Review</th>
<th>No AP Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number on AP at Start</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Number Discontinued</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>New AP Starts</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Final AP Use</td>
<td>13</td>
<td>23</td>
</tr>
</tbody>
</table>

- 50% reduction over 9 months
- 3 residents discontinued had worsening of NPI scores, but these residents had baseline scores above 14
### Results

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>No AP Review or Social Interaction</td>
<td>35%</td>
</tr>
<tr>
<td>AP Review</td>
<td>28%</td>
</tr>
<tr>
<td>AP Review and Social Interaction</td>
<td>19%</td>
</tr>
</tbody>
</table>

- In regression analysis, strongest association with mortality was social interaction.
- Exercise did not impact mortality
Results

- AP Review alone had worse NPI scores
  - However, 3 residents were above 14 at baseline

- Group with AP Review & Social Interaction did not worsen

- Exercise improved NPI scores, but not depression
Summary

• AP Review effective >>> reduced AP use by 50%
  – Even in population with low prevalence of AP use at baseline (18%)

• Mortality reduced with AP Review and Social Interaction

• Social Interaction didn’t improve agitation or total NPI scores

• Exercise helped NPI scores, but not depression
Summary

• AP review is effective and should be part of a facility QAPI program
• May be harder in facilities with lower rates of AP use, but still worth attempting
• Non-pharmacological interventions complement AP review efforts, particularly when AP use is low