Geropsychopharmacology: Myth and Tradition vs. Evidence

Michael J. Rice, Ph.D, APRN-NP, FAAN
Professor
College of Nursing
University of Nebraska Medical Center
As of July 1st
Professor &
Endowed Chair of Psychiatric Nursing
College of Nursing
University of Colorado Anschutz Medical Center

Disclosure
- The speaker has no conflict of interest to disclose
- Off-label use of medications will be discussed in this presentation
- This session will be recorded and available on the APNA eLearning Center

Objectives
1. Review the myths of psychopharmacology in elders
2. Examine the evidence on the neurochemical changes associated with aging
3. Examine the evidence on current traditional use of psychotropics with the elderly
4. Examine the evidence based effectiveness of psychopharmacology with aging disorders

Geropsychopharmacology
- 21,526 older adults: median age of 84
- In Community
  - 1.1% on antipsychotics
- In Care Agency
  - 20 times more likely to be on Antipsychotics
  - Rochon et al. 2013

Antipsychotic Use with Elders: US

<table>
<thead>
<tr>
<th>Medication</th>
<th>Weighted Frequency</th>
<th>Percentage</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical</td>
<td>219,071</td>
<td>31.63</td>
<td>30.27, 33.00</td>
</tr>
<tr>
<td>olanzapine</td>
<td>76,626</td>
<td>11.06</td>
<td>10.14, 11.99</td>
</tr>
<tr>
<td>risperidone</td>
<td>72,762</td>
<td>10.85</td>
<td>9.76, 11.95</td>
</tr>
<tr>
<td>quetiapine</td>
<td>64,213</td>
<td>9.27</td>
<td>8.41, 10.13</td>
</tr>
<tr>
<td>ziprasidone</td>
<td>4,107</td>
<td>0.59</td>
<td>0.38, 0.80</td>
</tr>
<tr>
<td>aripiprazole</td>
<td>6,162</td>
<td>0.89</td>
<td>0.62, 1.16</td>
</tr>
<tr>
<td>Typical</td>
<td>12,123</td>
<td>1.75</td>
<td>1.37, 2.13</td>
</tr>
<tr>
<td>haloperidol</td>
<td>8,044</td>
<td>1.16</td>
<td>0.86, 1.47</td>
</tr>
<tr>
<td>others</td>
<td>4,230</td>
<td>0.61</td>
<td>0.36, 0.89</td>
</tr>
</tbody>
</table>

Kamble, Chen, Sherer & Aparasu 2009

Elders in Nursing Homes: US Rate
- 1 of 3 elderly LTC residents with dementia used antipsychotic agents, mainly atypical
- Olanzapine,
- Risperidone and
- Quetiapine highest use

Kamble, Chen, Sherer & Aparasu 2009
US Rate (cont)

- Psychiatric disorders such as anxiety were associated with use of atypical agents with dementia.
- Predisposing factors 1. male, 2 bed capacity
- Need factors 1. decision-making 2. depression 3. behavioral symptoms, 4. ADLs, and 5. bed mobility

Kamble, Chen, Sherer & Aparasu, 2009

US rates (cont.)

- 8.2% were put on antipsychotics, 14.8% were given hypnotics and 7.8% were prescribed anxiolytic
- Six months after admission to a care home, 30.2% of all new residents had received at least one prescription for an antipsychotic, 37.1% for a hypnotic and 24.5% for an anxiolytic.

Kamble, Chen, Sherer & Aparasu, 2009

Myths: Setting the Stage for Pharmacological Misuse

- Older adults complain.
- Older adults are negative
- Older adults have rigid personalities
- Dementia is normal for aging
- Any cognitive impairment is Alzheimer’s,

Kennedy, 2003

Myths (cont.)

- Genetics determine illness and disability;
- Disability is inevitable
- Loss of social ties leaves elders alone and isolated;
- Most elderly are depressed, demented, or dependent;

Kennedy, 2003

Myths (cont.)

- All Elders have a chronic illness,
- Aging eliminates individual needs\potential — physiologic and social homogeneity
- Pharmacology is the most important factor to reduce dependency;
- The older the patient, the greater the cost.

Kennedy, 2003

Neurochemistry Myths

- Adult age- Adult Psychopharmacology
- Psychiatric meds control behaviors
- Psychiatric meds only affect the brain
- Learning capacity declines
Traditional Geropsychopharmacology

- Anxiolytics
- Antidepressants
- Antipsychotics
- Antiepileptic Medications
- Off Label Use –FDA Designation

Traditional Wisdom is... Use one third the normal adult dose to adjust for metabolism.

Anxiolytic use

<table>
<thead>
<tr>
<th>Generic (Brand) Name</th>
<th>Initial Dosage</th>
<th>Maximum Daily Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam (Xanax®)</td>
<td>0.125 mg to 0.25 mg BID</td>
<td>0.25 mg to 2 mg BID</td>
</tr>
<tr>
<td>Lorazepam (Ativan®)</td>
<td>0.25 mg to 0.5 mg BID</td>
<td>0.5 mg to 4 mg BID</td>
</tr>
<tr>
<td>Oxazepam (Serax®)</td>
<td>10 mg BID</td>
<td>10 mg to 30 mg BID</td>
</tr>
<tr>
<td>Temazepam (Restoril®)</td>
<td>7.5 mg Q HS</td>
<td>7.5 mg to 25 mg Q HS</td>
</tr>
<tr>
<td>Zolpidem (Ambien®)</td>
<td>5 mg Q HS</td>
<td>5 mg to 10 mg Q HS</td>
</tr>
</tbody>
</table>

Anxiolytic use Linday, 2009

Antidepressants Elders

<table>
<thead>
<tr>
<th>Generic (Brand) Name</th>
<th>Starting Dosage</th>
<th>Daily Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram (Celexa®)</td>
<td>10 mg to 20 mg per day</td>
<td>10 mg to 40 mg per day</td>
</tr>
<tr>
<td>Escitalopram (Lexapro®)</td>
<td>10 mg per day</td>
<td>5 mg to 20 mg per day</td>
</tr>
<tr>
<td>Fluoxetine (Prozac®)</td>
<td>10 mg per day</td>
<td>5 mg to 40 mg per day</td>
</tr>
<tr>
<td>Paroxetine (Paxil®, Paxil CR®)</td>
<td>10 mg per day</td>
<td>5 mg to 40 mg per day</td>
</tr>
<tr>
<td>Sertaline (Zoloft®)</td>
<td>25 mg to 200 mg per day</td>
<td>25 mg to 200 mg per day</td>
</tr>
<tr>
<td>Buproprion (Wellbutrin®, Wellbutrin XL®)</td>
<td>150 mg to 240 mg per day</td>
<td>150 mg to 240 mg per day</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta®)</td>
<td>20 mg per day</td>
<td>20 mg to 60 mg per day</td>
</tr>
<tr>
<td>Mirtazapine (Remeron®, Remeron SR®)</td>
<td>7.5 mg at bedtime</td>
<td>7.5 mg to 45 mg at bedtime</td>
</tr>
<tr>
<td>Venlafaxine (Effexor®)</td>
<td>25 mg twice per day</td>
<td>37.5 mg to 150 mg per day</td>
</tr>
<tr>
<td>Desipramine (Norpramin®)</td>
<td>25 mg per day</td>
<td>100 mg per day</td>
</tr>
<tr>
<td>Nortriptyline (Pamelor®)</td>
<td>10 mg to 25 mg per day</td>
<td>50 mg per day</td>
</tr>
</tbody>
</table>

Antidepressants Elders Linday, 2009

Antipsychotic Use

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Starting Dosage</th>
<th>Daily Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol (Haldol®)</td>
<td>0.25 mg to 0.5 mg per day</td>
<td>0.25 mg to 4 mg per day</td>
</tr>
<tr>
<td>Aripiprazole (Abilify®)</td>
<td>5 mg per day</td>
<td>2.5 mg to 15 mg per day</td>
</tr>
<tr>
<td>Olanzapine (Zyprexa®)</td>
<td>2.5 mg per day</td>
<td>2.5 mg to 15 mg per day</td>
</tr>
<tr>
<td>Quetiapine (Seroquel®)</td>
<td>25 mg at bedtime</td>
<td>50 mg to 400 mg at bedtime</td>
</tr>
<tr>
<td>Desipramine (Norpramin®)</td>
<td>0.25 mg to 0.5 mg at bedtime</td>
<td>0.25 mg to 2 mg at bedtime</td>
</tr>
<tr>
<td>Ziprasidone (Geodon®)</td>
<td>20 mg twice per day with food</td>
<td>20 mg to 80 mg twice per day with food</td>
</tr>
</tbody>
</table>

Antipsychotic Use Linday, 2009

Risks of Falls with Drug Classes

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedatives and hypnotics</td>
<td>1.47 (1.30 - 1.64)</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>1.41 (1.26 - 1.71)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>1.36 (1.13 - 1.64)</td>
</tr>
</tbody>
</table>

Risks of Falls with Drug Classes Wollcott et al 2009

Adverse Events with Psychotropics

- 1,889 (8.8%) had a serious event – (1,044 women, 7.6%; 845 men, 10.9%),
- 718 (3.3%) died – (363 women, 2.6%; 355 men, 4.6%),
- 1,467 (6.8%) had a hospital admission – (812 women, 5.9%; 655 men, 8.4%) within 30 days.
- Men were 47% more likely than women to have a serious event Rochon et.al 2013
Black BOX: FDA Warning !!!!!!!!!!!

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS
See full prescribing information for complete boxed warning.
- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.
- RISPERDAL is not approved for use in patients with dementia-related psychosis. (5.1)

The Evidence
- Anxiolytics
- Antidepressants
- Antipsychotics
- Off Label Use – FDA Designation

Aging Neurochemistry Reality
- Neurophysiologic capacity
- Physiological capacity
- Metabolic capacity

Natural Volumetric Loss

Dopamine
- Age-related changes in
  - Dopamine synthesis,
  - Dopamine binding sites,
  - Decrease in D1 and D2 receptors
  - Significant declines in dopamine receptors, D2 and D3

Dopamine Receptor Modulation

Figure 1. Schematic illustration demonstrates subcortical and cortical dopamine modulation. The modulation of the cortical system is more prominent than that of the subcortical system, which peaks in adolescence.
Serotonin
- Decreasing levels of different serotonin receptors and
- Serotonin transporter, 5-HTT

Yamamoto et al. 2001

Serotonin Receptor Density Decline
Frontal view
Occipital view
Right hemisphere
Left hemisphere

Tauscher Et al 2002

Blood Brain Barrier Aging
- Different changes in development and aging, leading to an optimal amino acid transport
- Minimum penetration of lipophilic agents in the adult brain, reducing transport and increasing the penetration of lipophilic compounds

Anyanwu, E. 2007

Neurochemical Aging
- Levels of neurotransmitters (Acetylcholine (ACh), serotonin (5-HT) and dopamine) levels are all decreased
- Metabolic enzyme activities such as choline acetyltransferase and choline esterase increase.

Anyanwu, E. 2007

Neurotransmitters with Aging
- Metabolic enzyme activities of choline acetyltransferase and choline esterase activities increase.
- Tryptophan hydroxylase activity is not affected.
- Monoamine oxidase-A increases

Anyanwu, E. 2007

Pharmacokinetics Principles in Aging
- Rate of Absorption
- Rate of Excretion
- Rate of Elimination
Liver function

• Changes in the hepatic sinusoid have been identified that contribute to the substantial age-related changes in liver function.
• Reduction in capacity to metabolize

La Couteur DG, et. al. 2008

Renal Aging

• A progressive linear decline in clearance from 140 ml/min/1.73m2 at age 30 to 97 at age 80 
Rowe et. al.
• 254 "normal" subjects, the mean decrease in creatinine clearance was 0.75 ml/min/year.

Lindeman RD, Tobin J, Shuck WW 1985
• Decline in renal function is associated with co-existing cardiovascular diseases and risk factors.

Baggio B, et.al 2005

Respiratory Capacity and PO2 Exchange

McCullough DJ, et. al. 2011

Evidence For Geropsychopharmacology

• Based on systematic reviews
• Evidence Based Practices

Anxiolytics in use

• Buspirone
• Chloridiazepoxide
• Diazepam,
• Lorazepam
• Hydroxyzine

Anxiolytics Evidence Based

• No controlled trials support use of benzodiazepines in the treatment of non-alcohol withdrawal related delirium and
• At this time benzodiazepines cannot be recommended for the control of agitation in dementia/ delirium.

Lonergan, Luxenberg, Sastre. 2009
Depression in Dementia

• Depression affects up to 50% of persons with dementia
• Commonly treated with Antidepressants

Schwarz Froelich & Burns 2012

Typical Elder Antidepressants

• Tricyclic antidepressants
• SSRI’s
• SNRI’s
• Atypical Antipsychotics

All TCAs versus SSRIs, Outcome

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>All TCAs</th>
<th>SSRIs</th>
<th>Risk ratio (95% CI)</th>
<th>Weight</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Rubeis 1991</td>
<td>14.5</td>
<td>8.6</td>
<td>1.7 (1.3, 2.1)</td>
<td>0.35</td>
<td>2.9 (2.0, 4.2)</td>
</tr>
<tr>
<td>O’Connor 1994</td>
<td>13.5</td>
<td>8.7</td>
<td>1.5 (1.2, 1.9)</td>
<td>0.45</td>
<td>1.3 (1.0, 1.7)</td>
</tr>
<tr>
<td>Hughes 1993</td>
<td>14.5</td>
<td>8.6</td>
<td>1.7 (1.3, 2.1)</td>
<td>0.35</td>
<td>2.9 (2.0, 4.2)</td>
</tr>
<tr>
<td>Gellinge 1995</td>
<td>14.5</td>
<td>8.6</td>
<td>1.7 (1.3, 2.1)</td>
<td>0.35</td>
<td>2.9 (2.0, 4.2)</td>
</tr>
<tr>
<td>Hulihan 1996</td>
<td>14.5</td>
<td>8.6</td>
<td>1.7 (1.3, 2.1)</td>
<td>0.35</td>
<td>2.9 (2.0, 4.2)</td>
</tr>
<tr>
<td>Fox &amp; Meeks 1995</td>
<td>14.5</td>
<td>8.6</td>
<td>1.7 (1.3, 2.1)</td>
<td>0.35</td>
<td>2.9 (2.0, 4.2)</td>
</tr>
<tr>
<td>Fox &amp; Meeks 1996</td>
<td>14.5</td>
<td>8.6</td>
<td>1.7 (1.3, 2.1)</td>
<td>0.35</td>
<td>2.9 (2.0, 4.2)</td>
</tr>
<tr>
<td>Nellis 2001</td>
<td>14.5</td>
<td>8.6</td>
<td>1.7 (1.3, 2.1)</td>
<td>0.35</td>
<td>2.9 (2.0, 4.2)</td>
</tr>
<tr>
<td>total 89% CI</td>
<td>52</td>
<td>55</td>
<td>1.89 (1.65, 2.12)</td>
<td>0.35</td>
<td>2.9 (2.0, 4.2)</td>
</tr>
</tbody>
</table>

Lonergan 2009

TCA vs SSRI Pooled studies

<table>
<thead>
<tr>
<th>Outcome or subgroup</th>
<th>No. of studies</th>
<th>No. of patients</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatally to suicide</td>
<td>9</td>
<td>1000</td>
<td>Rand (M-H, Random)</td>
<td>1.07 (0.9, 1.22)</td>
</tr>
<tr>
<td>2Depression severity (MADRS)</td>
<td>2</td>
<td>96</td>
<td>Mdn Difference (M-H, Random)</td>
<td>2.41 (1.08, 4.85)</td>
</tr>
<tr>
<td>3Withdrawl due to side effects</td>
<td>12</td>
<td>1207</td>
<td>Rand (M-H, Random)</td>
<td>1.13 (0.93, 1.37)</td>
</tr>
<tr>
<td>4Total withdrawal rate</td>
<td>14</td>
<td>1320</td>
<td>Rand (M-H, Random)</td>
<td>1.23 (1.05, 1.43)</td>
</tr>
</tbody>
</table>

Lonergan 2009

SNRI

• Limited data
• Dual-action agents (either TCAs or SNRIs) do not use any additional benefits in efficacy over SSRI’S for the elderly.

Mukai & Tampi 2009

SNRI Evidence

<table>
<thead>
<tr>
<th>Authors</th>
<th>Population</th>
<th>Dose</th>
<th>Sample</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allard et al 1979</td>
<td>Outpatients</td>
<td>Venlafaxine ER 75-225 mg/d (titrated) Clomipramine 20-30 mg/d (titrated)</td>
<td>76</td>
<td>6 mo</td>
</tr>
<tr>
<td>de Guevara 1983</td>
<td>Outpatients with mild to moderate depression</td>
<td>Venlafaxine ER 75-150 mg/d (titrated)</td>
<td>14</td>
<td>6 wk</td>
</tr>
<tr>
<td>Cumha et al 1985</td>
<td>Outpatients</td>
<td>Placebo</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Cisilin et al 1979</td>
<td>Outpatients</td>
<td>Venlafaxine IR 100 mg/d (titrated)</td>
<td>27</td>
<td>10 wk</td>
</tr>
<tr>
<td>Schulteberg &amp; coworkers 1985</td>
<td>Outpatients</td>
<td>Venlafaxine ER 75-150 mg/d (titrated)</td>
<td>28</td>
<td>6 wk</td>
</tr>
<tr>
<td>Guelin et al 1982</td>
<td>Inpatients and outpatients</td>
<td>Venlafaxine ER 150-225 mg/d (titrated)</td>
<td>44</td>
<td>6 mo</td>
</tr>
<tr>
<td>Raskin et al 2001</td>
<td>Outpatients</td>
<td>Duloxetine 60 mg/d (fixed dose)</td>
<td>207</td>
<td>8 wk</td>
</tr>
</tbody>
</table>

Mukai & Tampi 2009
SNRI Effectiveness

- Dual action agents, such as TCAs and SNRIs do confer any additional efficacy benefits over SSRI’s for treatment of depression in the elderly.

Mukai & Tampi 2009

Atypicals For Depression

<table>
<thead>
<tr>
<th>Study</th>
<th>TCAs</th>
<th>Atypicals</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol 60 mg</td>
<td>146</td>
<td>137</td>
<td>0.6 (0.4, 0.9)</td>
</tr>
<tr>
<td>Haloperidol 20 mg</td>
<td>209</td>
<td>206</td>
<td>0.9 (0.6, 1.3)</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>36</td>
<td>37</td>
<td>0.8 (0.6, 1.1)</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>42</td>
<td>43</td>
<td>1.1 (0.8, 1.5)</td>
</tr>
</tbody>
</table>

Total patients: 744

Lonergan 2009

Augmentation with Antipsychotics

- No therapeutic effects were found for haloperidol compared to placebo and trazodone & compared to risperidone and placebo
- RCTs with risperidone, olanzapine, and aripiprazole have shown modest efficacy for reducing aggression and overall agitation in AD

Kales et al 2012

SSRI’s Harmless?

- Increased Risk of falls
- Deplete sodium through renal excretion
- Prolong QTC (citalopram)

Schwarz Froelich & Burns 2012

There is currently no firm evidence supporting use of antidepressants in patients with depression and dementia.

- Treatment of psychosis and agitation in patients with dementia remains a clinical challenge.
- Antipsychotics are associated with increased mortality

Schawrts Lefrec and Burns 2013

Antidepressants are associated with a substantial risk for adverse effects, and
- Efficacy is not proven.

Schwartz Froelich & Burns 2012
Atypical Antipsychotics

- Serotonin Dopamine Agonists
- Multiple variable receptor activities
  - Histamine
  - Muscarinic
  - 5Ht1-7
  - D1-5
  - Alpha adrenergic.

Off-Label Atypical Use with Dementia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Strength of evidence</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavioral problems in dementia</td>
<td>Moderate for</td>
<td>Meta-analysis found a small benefit for risperidone and aripiprazole on agitation and psychotic outcomes.</td>
</tr>
<tr>
<td></td>
<td>risperidone,</td>
<td>Meta-analysis shows a possible trend toward effectiveness of olanzapine for psychotic but results did not reach statistical significance.</td>
</tr>
<tr>
<td></td>
<td>olanzapine, and</td>
<td>There are 3 studies of quetiapine; were too dissimilar in their design and outcomes to pool.</td>
</tr>
<tr>
<td></td>
<td>quetiapine;</td>
<td>Result in the (Clinical Antipsychotic Trials of Intervention Effectiveness-Alzheimer’s Disease; CATIE-AD) showed no differences in time to discontinuation of medication between risperidone, olanzapine, quetiapine, and placebo.</td>
</tr>
<tr>
<td></td>
<td>Low for aripiprazole.</td>
<td></td>
</tr>
</tbody>
</table>

- Association between mortality and antipsychotics is understood and may be due to a direct medication effect
  - Kales et al 2012

Typical Vs Atypical Mortality Risks

- Haloperidol (RR=1.54, 95% CI =1.38-1.73)
- Risperidone (reference risk),
- Olanzapine (RR =0.99, 95%CI=0.89-1.10),
- Quetiapine (RR=0.73, 95% CI=0.67-0.80).
  - Kales et al 2012

Anticonvulsants in use

- Valproic acid
- Carbamazepine
- Levetiracetam,
- Ox carbazepine,
- Topiramate and
- Zonisamide’s
  - Holroyd & Overdyke 2012

Stable Findings

- Valproic acid
  - 83% develop hyperamonia
  - Induced encephalopathy
- Carbamazepine
  - Three RCT’s indicate management of aggression and hostility
  - Yeh, Chuang 2012

Dolder & Neely 2012
Anticonvulsants Evidence Review

- Data are relatively limited.
- Levetiracetam, ox carbazepine, topiramate and zonisamide’s – not recommended as behavioral treatment with dementia.

Dolder and Neely 2012

Pretreatment Screening

- Take a good drug and alcohol history –
- Polypharmacy accounts for majority of iatrogenic morbidity.
- Antidepressant trial in older patients should last at least 6-8 weeks.
  - Continuation treatment is 12 months.
- Lithium dose ranges are lower in the elderly – 0.4-0.6 mmol/1.

BURNS 1994

Lifestyle & Pharma Aids

- 1. Eliminate Caffeine - including hidden forms,
  - Educate on caffeine effects - last > 24 hours and affects sleep even if taken in the morning.
- 2. Attempt to eliminate alcohol. In patients with dementia, remove and/or limiting amount.
- 3. If reflux (causing arousals; silent or with cough): avoid food and fluids 2-3 hours before HS, raising head of bed, & consider trial of antacid).

Roth 2012

- 4. For allergic rhinitis (causes snoring/apnea, postnasal drip, and coughing): Try nasal steroid spray at HS, if persistent, add daytime antihistamine.
- 5. If suspected pain, use mattress foam topper
  - Ensure firm bed (with or without mattress topper) for back pain.
- 6. Schedule acetaminophen;
- 7. Avoid opiates.

Roth 2012

- 8. Circadian rhythm factors:
  - Avoid or time daytime naps using hard-back chair for TV - no recliners
  - Offer stimulating activities during the sleepy times
  - Ensure bright light in day,
  - Lower lights in evening and night.
- 9. Consider nighttime melatonin with morning light and strict wake time.
- 10. Ensure that patient does not have other primary sleep conditions that affect sleep, like RLS

Roth 2012

- 11. Dose medication with sleep-disrupting effects earlier in the AM
  - (β-blockers, cholinesterase inhib., SSRIs, venlafaxine, bupropion).
  - Donepezil (Aricept) causes sleep disruption more than other cholinesterase agents.
- 12. Use non activating antidepressants.
- 13. Consider trial of switching to alternative galantamine or rivastigmine.

Roth 2012
- 14. Dose cholinesterase inhibitor in the AM.
- 15. Nocturia: eliminate all access to fluids in 3 hours before bedtime.
- 16. Ensure that patient does not have other primary sleep conditions that affect sleep, like RLS.
- 17. Nocturia: eliminate all access to fluids in 3 hours before bedtime.
- 18. Consider taking twice daily medications at dinner rather than before bed to reduce fluid load.

**Traditional Psychotherapy**

- Intentional interpersonal relationship used by trained psychotherapists to aid a client in solving problems.

**Types of Psychotherapy studied**

- Problem Solving
- Insight Oriented
- Psychodynamic
- Cognitive Behavioral Therapy
- Mindfulness
- Modular Psychotherapy

**Evidence Overview**

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<tr>
<td>Jonkers et al.</td>
<td>RCT</td>
<td>361 elders</td>
<td>Nurse managed One Group Pre Post test</td>
<td>Three months after the interventions, significantly fewer depressive symptoms.</td>
</tr>
<tr>
<td>Winkelaar et al</td>
<td>RCT</td>
<td>61 elder adults</td>
<td>Psychological enrichment community intervention</td>
<td>With psychological enrichment, significantly higher improvements in anxiety symptoms were found compared to usual care.</td>
</tr>
<tr>
<td>Silveira, et al</td>
<td>Cochrane</td>
<td>2 trials on CBT vs. usual care</td>
<td>CBT and CBT vs. usual care</td>
<td>CBT was superior to usual care and no differences between CBT and usual care.</td>
</tr>
<tr>
<td>Josten-Weyn</td>
<td>one group pre post</td>
<td>22 Elders</td>
<td>CBT</td>
<td>Positive changes after a CBT intervention on anxiety and depression.</td>
</tr>
<tr>
<td>Jonkers et al.</td>
<td>RCT</td>
<td>361 Elders</td>
<td>Nurse managed One Group Pre Post test</td>
<td>Increases in self efficacy.</td>
</tr>
<tr>
<td>Van Schaik, et al</td>
<td>RCT</td>
<td>2 groups 143 patients</td>
<td>IPT v. usual care</td>
<td>Reduced depression, improved social and mental functioning.</td>
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</table>

**Psychotherapy**

- Modular psychotherapy reduces anxiety symptoms, worry, depression and improved quality of life.
- Interpersonal therapy reduces depression, improves social and overall mental functioning.
- Interpersonal therapy increases time to remission of depression with lower cognitive functioning.
- Cognitive behavioral therapy reduces depression, worry, increases life satisfaction.
- Self-worth therapy reduces depressive symptoms two months after treatment.
- Problem-solving therapy reduces depressive symptoms and number of depressive days for up to 2 years after treatment.

**Cognitive Stimulation**

- Using stimulation of any basic cognitive function to prevent the decline of functional skills and offset depression.
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<td>31 elders</td>
<td>CBT memory</td>
<td>Significant change in functional status and depression</td>
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<tr>
<td>Upah, et al. 2010</td>
<td>RCT</td>
<td>26 elders</td>
<td>CBT memory</td>
<td>Significant change in functional status and depression</td>
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<tr>
<td>Smolen, et al. 2005</td>
<td>RCT</td>
<td>60 elders</td>
<td>CBT memory</td>
<td>Significant change in functional status and depression</td>
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<td>Kawashima, et al.2005</td>
<td>RCT</td>
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<td>CBT model of everyday memory</td>
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Cognitive Exercises Summary

- Visual Speed training (search, identify and locate visual information) can reduce depression rates at one year
- Reading and math problems help restore frontal lobe function and independence
- Virtual reality memory training can improve performance on memory and long term recall

Exercise

- Any bodily activity that enhances or maintains physical fitness and overall health.

Yoga reduces daytime dysfunction, depression, improves sleep quality, physical and mental health
Exercise improves MMSE scores
Recreational therapy reduces agitation, passivity, and clinging to caregiver
Tai Chi and Wai Tan Kung reduce sympathetic nervous system activity

Reminiscence Therapy

- Guided by a trained person to reflect on a variety of aspects relating to their lives. Reflections may be themed on one period in time or wider and reflect a guided discussion through an issue across time.

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<tr>
<td>Bi, Tomiko &amp; Kase, 2012</td>
<td>RCT 2 groups post and test</td>
<td>30 in intervention, 30 in control</td>
<td>Multidimensional exercise</td>
<td>Intervention group showed greater and significant decrease in the score of depression</td>
</tr>
<tr>
<td>Dehena et al. 2021</td>
<td>RCT 2 groups</td>
<td>Tai Chi in cognitive action</td>
<td>Motor or Cognition</td>
<td>Tai Chi group showed increased depression and cognitive function in intervention group</td>
</tr>
<tr>
<td>Dow et al. 2019</td>
<td>RCT 2 groups</td>
<td>120 adults over 60</td>
<td>Tai Chi vs control group</td>
<td>Tai Chi group showed increased depression and cognitive function</td>
</tr>
<tr>
<td>Lu &amp; Fan 2018</td>
<td>Observation</td>
<td>90 elderly people</td>
<td>Tai Chi and Wai Tan Kung</td>
<td>Tai Chi and Wai Tan Kung group showed significant reduction in depression</td>
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<tr>
<td>Abou, Sule, Duen &amp; Ume 2020</td>
<td>RCT 2 groups</td>
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<td>Wang, et al. 2007</td>
<td>RCT</td>
<td>102 elderly</td>
<td>Group reminiscence therapy</td>
<td>Improved cognition, self-esteem, reduced depression</td>
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<td>Chen, et al. 2006</td>
<td>Quasi-experimental</td>
<td>10 elderly nursing home residents</td>
<td>Reminiscence therapy</td>
<td>Improved self-esteem, behavioral changes</td>
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<tr>
<td>Redmon, 2006</td>
<td>Cross-over RCT</td>
<td>80 people with dementia</td>
<td>Individual reminiscence therapy</td>
<td>Both interventions reduced agitation behavior</td>
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<td>Wang, 2006</td>
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<td>Hsieh &amp; Wang 2003</td>
<td>Systematic Review</td>
<td>9 studies</td>
<td>Reminiscence therapy</td>
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<td>Hsieh &amp; Wang 2003</td>
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<td>80 long-term care residents</td>
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<td>Behavioral group showed reduced agitation</td>
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Reminiscence Therapy

- Reminiscence therapy improves cognitive function, self-esteem, reduces depression
- Reminiscence therapy can be effective for institutionalized people

Music Therapy

- An interpersonal process in which the therapist uses music activities to help clients to improve or maintain their health
- Activities involve improvising, re-creating, composing, listening
- After the activity clients discuss the music, reactions to music, such as thoughts, images or feelings.

- Music therapy can reduce irritability, agitation, and problem behaviors in people with depression and dementia
- Music therapy can improve language functioning in people with dementia
- Music therapy can improve sleep in depressed elders

Community Vigilance and Treatment Models

- Treatment approach designed to provide comprehensive, community-based psychiatric treatment and support to elders

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<tr>
<td>Lou, 2001</td>
<td>Systematic Review</td>
<td>7 studies</td>
<td>Music therapy and relaxation</td>
<td>In a sample of older adults, music therapy reduced agitation and improved relaxation</td>
</tr>
<tr>
<td>de Vries, van Lieshout, &amp;/versluis, 2006</td>
<td>Mixed-methods</td>
<td>38 elderly adults</td>
<td>Music therapy and relaxation</td>
<td>Music therapy reduced agitation and improved relaxation</td>
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<tr>
<td>Reppenhagen, 2001</td>
<td>Repeated measures</td>
<td>12 nursing home residents</td>
<td>Music therapy and relaxation</td>
<td>Music therapy significantly reduced agitation and improved relaxation</td>
</tr>
<tr>
<td>Gotl, Duffy, 1998</td>
<td>Review of literature</td>
<td>19 studies</td>
<td>Music therapy</td>
<td>Music therapy improved sleep and agitation in depressed elders</td>
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<tr>
<td>Suzuki, et al. 2004</td>
<td>Pre and post test</td>
<td>23 elderly</td>
<td>Music therapy</td>
<td>Music therapy improved sleep and agitation in depressed elders</td>
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<tr>
<td>Leger &amp; Baker, 2007</td>
<td>Pre and post test</td>
<td>35 people with Alzheimer’s disease</td>
<td>Music therapy</td>
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University of Nebraska Medical Center

Community Vigilance and Treatment Models

- Treatment approach designed to provide comprehensive, community-based psychiatric treatment and support to elders

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Music Therapy

- Music therapy can reduce irritability, agitation, and problem behaviors in people with depression and dementia
- Music therapy can improve language functioning in people with dementia
- Music therapy can improve sleep in depressed elders

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**Community Treatment Models**

- Gatekeeper Models
- Assertive Community Treatment Models
- Primary Care Problem Solving

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<td>Corsentino, et al 2009</td>
<td>Longitudinal Survey</td>
<td>2938 adults over 65 in North Carolina</td>
<td>NA</td>
<td>More frequent relationships and attendance associated with reduced cognitive decline</td>
</tr>
<tr>
<td>Car Colles &amp; March 2011</td>
<td>Cohort Systematic Review</td>
<td>14 studies</td>
<td>Community Psychosocial interventions</td>
<td>20 studies reported improved depressive symptoms</td>
</tr>
<tr>
<td>Rabins et al. 2010</td>
<td>Prospective RCT</td>
<td>945 adults 60 and older</td>
<td>Screening group and control</td>
<td>Screening helps to reduce psychiatric symptoms and prevent high rates of depression</td>
</tr>
</tbody>
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**Community**

- Enhanced community treatment reduces anxiety symptoms, worry, depressive symptoms, and improved mental health-related quality of life
- Mental health screening for elders helps providers to identify treatment needs and improve outcomes
- More frequent religious attendance is associated with reduced cognitive decline

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<td>Systematic Cochrane Review</td>
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<td>No evidence that folic acid with or without vitamin B12 improves cognitive function in unselected elderly people with or without dementia</td>
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<td>2 RCT</td>
<td>Vitamin E</td>
<td>No evidence of vitamin E effect</td>
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**Dietary Supplements**

- A dietary supplement, also known as food supplement or nutritional supplement, is a preparation intended to supplement the diet and provide nutrients, that may be missing or may not be consumed in sufficient quantity in a person's diet.

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**Spirituality**

- Inner path enabling a person to discover their being and the “deepest values \ meanings by which people live.
- Considered an integral aspect of religion
Evidence Overview

- No RCT’s, Difficult to do
- Observational reports and questionnaires

Religion Summary

- Religion as a factor in helping elders cope with stressful life events and medical illnesses (Koenig et al., 1992; Levin, 1995).
- Religiousness associated with less severe depressive symptoms
- More frequent religious attendance is associated with reduced cognitive decline

Remaining Interventions

- Reiki - Reduces ALZ - no tests on depression
- Pet Therapy
  - 2 studies
  - One positive and one showed no effect

Grief

- Bowlby’s (1980) on attachment and separation.
- Research has identified psychiatric syndromes has relationships to
  - Mortality,
  - Bereavement-related behaviors, and
  - Dementia (Harwood, 2001)

Grief

- Normative process of movement
- Linked with successful coping and resolution of a loss

Bereavement

- Abnormal reaction to the stress of loss and the challenges of adaption
- Correction of cognitive distortions associated with insecure attachment styles
- Predispose to complicated grief
Bereavement (cont)

• 40% meet criteria for MDD within a month of the death.
• At 12 months 15% are depressed and
• At 2 years, 7% (Hensley PL 2006)

Bereavement

• With medications, depression symptoms improve more than bereavement Hensley 2006
• Interpersonal psychotherapy

Bereavement RX

• Remission for nortriptyline plus interpersonal psychotherapy was 69%
• Nortriptyline, 56%
• Interpersonal psychotherapy, 29%

Conclusion

• A variety of non pharmacological interventions exist with demonstrated effectiveness in reducing and managing depression in the elderly.
• Many interventions focus on proactive interventions
• More complex issues of bereavement may need pharmacological support.

Non pharmacological Assistance

• A variety of non pharmacological interventions exist with demonstrated effectiveness in reducing and managing depression in the elderly.
• Many interventions focus on proactive interventions
• Several have significant impact on the magnitude of psychopharmacology used

Nursing Staff Interventions

• 1. Remove TV from the bedroom.
• 2. Ensure hands and feet are not cold at HS;
  – Suggest feet soaks, warm socks, bath.
  – Ensure that bedroom is not overly hot.
• 3. Review sleep time versus time in bed and

Paniagua & Paniagua 2012
4. Set later bedtime, and strict wake time for mild sleep restriction.
5. Make clock not visible in bedroom.
6. Ensure that environment is free of noise and is dark at night
7. Have routine in place to void immediately before bed.
8. Dose diuretics earlier in the day if possible.

EBP Summary

1. AD and other dementias require behavioral interventions first and then medications to treat moderate-to-severe disturbances
2. Nonpharmacological therapy may be inadequate in many patients
3. Pharmacological options are hindered by poor balance of efficacy and safety.

3. Better response of atypical antipsychotics for dementia patients without psychosis but adverse effects are serious
4. Meta-analysis, found that haloperidol was beneficial for dementia patients with aggression, not free of adverse events
   - but not for general agitation (i.e., wandering, verbal agitation, etc.).

5. There is no FDA-approved indication for a drug to treat psychosis or agitation in persons with dementia.
6. More RCTs in dementia patients with psychosis and/or agitation for atypical antipsychotics (aripiprazole, olanzapine, quetiapine, and risperidone) and for haloperidol

7. RCTs examining antipsychotics for agitation and/or psychosis in dementia suggest a modest effect compared to placebo.
8. Individual trials have yielded negative results.
9. CATIE-AD trial suggested side effect burdens may negate clinical effectiveness.
10. Mortality is significantly higher with atypical antipsychotics than with placebo with dementia.
11. The FDA black-box warning identifies the risks of atypical antipsychotics.
12. Risk difference is 1–2% over 8–12 weeks.
13. In addition to acute and subacute adverse effects such as excessive sedation, postural hypotension, and falls
14. Atypical antipsychotics are less likely than typicals (especially haloperidol) to cause or exacerbate EPS and tardive dyskinesia.

15. No other differences in efficacy or safety have been demonstrated.

16. Individual typical or atypical drugs may have less propensity for certain side effects and should match client needs.

Jette et al. 2012

References
