Managing Late Life Depression

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Disclosures

- None relevant to this presentation

- Some off-label use of medications for augmentation will be mentioned.
Objectives

• Describe effective strategies for screening, diagnosing and treating depressive disorders in elderly adults.
Geriatric Depression

• Prevalence
• Diagnosis
• Treatment
  • Medications
  • Neurostimulation
  • Psychotherapy
• Suicide Risk Assessment
Prevalence of geriatric depression

- Public health problem
- Prevalence: 1-20%, increase with age
  - 10-12% of medical inpatients
  - 12-14% of nursing home
- Variants more common than major depression
  - Minor depression
  - Subsyndromal depression
  - Subclinical depression
  - Subthreshold depression
Depression prevalence by age and gender

Figure 1. Percentage of persons aged 12 and over with depression, by age and sex: United States, 2009–2012

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>5.61</td>
<td>5.72</td>
<td>9.5</td>
</tr>
<tr>
<td>12–17</td>
<td>4.01–3</td>
<td>5.7</td>
<td>7.42</td>
</tr>
<tr>
<td>18–39</td>
<td>7.424</td>
<td>7.44</td>
<td>9.324</td>
</tr>
<tr>
<td>40–59</td>
<td>9.84</td>
<td>9.84</td>
<td>12.34</td>
</tr>
<tr>
<td>60 and over</td>
<td>3.41</td>
<td>5.4</td>
<td>7.1</td>
</tr>
</tbody>
</table>

*1Males have significantly lower rates than females overall and in every age group.
2Significantly different from 40–59.
3Significantly different from 18–39.
4Significantly different from 60 and over.

NOTES: Depression is defined as having moderate to severe depressive symptoms. Access data table for Figure 1 at: http://www.cdc.gov/nchs/data/databriefs/db172_table.pdf#1.

Update on Diagnosis

• DSM-5 released in May 2014
  • No major differences

• Major depressive episode
  • A change in baseline functioning
  • At least 2 weeks of symptoms
  • At least either (1) depressed mood or (2) anhedonia
  • At least 5 of the following:
    - Depressed mood
    - Anhedonia
    - Weight change
    - Sleep disturbance
    - Psychomotor change
    - Fatigue/low energy
    - Worthlessness/Guilt
    - Poor concentration
    - Suicidal thoughts
Late-life onset depression

• Medical comorbidities
• Cognitive impairment
• Cerebrovascular abnormalities
• More common symptoms in elderly:
  • somatic complaints
  • anorexia and weight loss
  • psychomotor abnormalities
  • anxiety
  • suicidal behavior
  • psychosis
Depression and cognitive impairment

• Clinical manifestations differ from early-life depression
  • Executive dysfunction
    • tends to persist after depression remits
    • reduced interest in activities
    • more profound psychomotor retardation
    • poor and unstable response to antidepressants

Alexopoulos GS, Kelly RE. World Psychiatry 2009;8:140-149
Depression and vascular disease

- Clinical manifestations similar to that of depression and executive dysfunction
  - Greater frontal function impairment
  - Poorer insight
  - More psychomotor retardation
  - Less agitation and guilt
  - More disability
  - ?Poorer response to antidepressants

Alexopoulos GS, Kelly RE. World Psychiatry 2009;8:140-149
Screening tools for depression

- Patient Health Questionnaire (PHQ-9)
  - 5 – mild
  - 10 – moderate
  - 15 – moderately severe
  - 20 – severe

- Geriatric Depression Scale (GDS)

- Beck Depression Inventory (BDI)
  - Self rate, cut off score 10
<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Not At all</th>
<th>Several Days</th>
<th>More Than Half the Days</th>
<th>Nearly Every Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2.</td>
<td>Feeling down, depressed or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3.</td>
<td>Trouble falling asleep, staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4.</td>
<td>Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5.</td>
<td>Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6.</td>
<td>Feeling bad about yourself - or that you’re a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7.</td>
<td>Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8.</td>
<td>Moving or speaking so slowly that other people could have noticed. Or, the opposite - being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9.</td>
<td>Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
Screening Tool: Geriatric Depression Scale

- Original: 30 yes/no questions
- Short version: 15 yes/no questions
- Does it provide more sensitivity than PHQ-9?
  - No head-to-head comparison
  - GDS more sensitive than PHQ-9 in Parkinson’s patients (Williams JR Neurology. 2012 Mar 27; 78(13): 998–1006)
  - PHQ-9 becoming standard in major health systems, in EHR, and for reimbursement

http://www.stanford.edu/~yesavage/GDS.html
Persistent depressive disorder

• Previously known as dysthymia or chronic major depression

• 2 years or more of depressed mood, without any improvement for longer than 2 months, in which at least 2 of the following occur:
  • Poor appetite or overeating
  • Insomnia or hypersomnia
  • Low energy or fatigue
  • Low self-esteem
  • Poor concentration or indecisiveness
  • Feelings of hopelessness
“Bipolar depression”

- The diagnoses of “Major depressive disorder” and “Bipolar disorder” are mutually exclusive
  - Bipolar patients have “major depressive episodes”
- Unusual to have new diagnosis of bipolar disorder in geriatric patients
- Look for underlying causes
- If it really is bipolar disorder, we use mood stabilizers/antipsychotics more than antidepressants
What is “Treatment-Resistant Depression”?

• Many definitions
• Failure of several adequate dose and duration antidepressants in the current episode of depression
• Some definitions include failure of electroconvulsive therapy
• Estimated to be about 30-50% of patients
• In 792 primary care geriatric patients with major depression, only 29% achieved remission (stricter outcome than response)

Before diagnosing depression, consider…

- Common geriatric differential
  - Dementia
  - Delirium
- Polypharmacy
  - Drug-drug interactions
  - Avoid anticholinergic medications
    - Beer’s list
    - Caveat: cannot completely avoid these medications
Before diagnosing depression, consider...

- Medical conditions
  - Thyroid abnormalities
  - Obstructive sleep apnea
  - Others

- Other psychiatric conditions
  - Substance use disorder
    - Alcohol
    - Sedatives
  - Other psychiatric conditions
Depression Treatment
Psychiatrist’s definitions

- **Response**
  - ≥50% improvement from initial symptoms

- **Remission**
  - Resolution of depressive symptoms

- **Goal of treatment is REMISSION**
Approaches to Depression Treatment

- Biological
- Social
- Spiritual
- Psych
PSYCHOPHARMACOLOGY

Start low, go slow
Medications: What’s old

- **Monoamine oxidase inhibitors (MAOIs)**
  - Tranylcypromine (Parnate)
  - Phenelzine (Nardil)
  - Dietary restrictions, drug-drug interactions

- **Tricyclic antidepressants (TCAs)**
  - Amitriptyline → nortriptyline
  - Imipramine → desipramine
  - More side effects than newer meds
  - Anticholinergic
  - Advantage: measure blood levels
## Medications: What’s current -- SSRIs

<table>
<thead>
<tr>
<th>Medication</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine (______)</td>
<td>Long half-life&lt;br&gt;Inhibits CYP450 2D6&lt;br&gt;Possibly weight neutral</td>
</tr>
<tr>
<td>Sertraline (______)</td>
<td>Typically fewer drug-drug interactions</td>
</tr>
<tr>
<td>Fluvoxamine (______)</td>
<td>Inhibits CYP450 2C9</td>
</tr>
<tr>
<td>Paroxetine (______)</td>
<td>Inhibits CYP450 2D6&lt;br&gt;Weight gain&lt;br&gt;Short half-life leads to withdrawal symptoms</td>
</tr>
</tbody>
</table>
| Citalopram (______) / Escitalopram (______) | Metabolized by CYP450 2C19  
New max dose citalopram 40 mg/day due to QTc concerns  
Typically fewer drug-drug interactions |

All of these are generic.
Medications: What’s current -- SNRIs

Serotonin-norepinephrine reuptake inhibitors

<table>
<thead>
<tr>
<th>Medication</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine (______)</td>
<td>Short half-life leads to withdrawal symptoms</td>
</tr>
<tr>
<td>Duloxetine (______)</td>
<td>FDA indication for pain</td>
</tr>
<tr>
<td>Desvenlafaxine (______)</td>
<td>No generic available</td>
</tr>
<tr>
<td></td>
<td>Is basically venlafaxine except does not get metabolized by 2D6</td>
</tr>
<tr>
<td>Milnacipran (______)</td>
<td>Not FDA approved for depression; FDA approved for fibromyalgia</td>
</tr>
</tbody>
</table>

Anything with norepinephrine helps with pain.
Medications: What’s current -- other

<table>
<thead>
<tr>
<th>Medication</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion (______)</td>
<td>Can cause increase in anxiety Contraindicated in seizure disorders and eating disorders</td>
</tr>
<tr>
<td>Mirtazapine (______)</td>
<td>Weight gain (helps with decreased appetite) Sedation (helps with insomnia) Metabolized by kidney (adjust in renal impairment)</td>
</tr>
</tbody>
</table>
Medications: What’s current -- augmentation

<table>
<thead>
<tr>
<th>Medication</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>Not just for bipolar disorder</td>
</tr>
<tr>
<td>Liothyronine (_______)</td>
<td>Thyroid hormone</td>
</tr>
<tr>
<td>Atypical antipsychotics:</td>
<td></td>
</tr>
<tr>
<td>Olanzapine (_______)</td>
<td>Several atypical antipsychotics are FDA-approved for augmentation to antidepressant for major depression</td>
</tr>
<tr>
<td>Quetiapine (______)</td>
<td>Beware of metabolic syndrome</td>
</tr>
<tr>
<td>Aripiprazole (______)</td>
<td>Weight gain frequent, even with Abilify</td>
</tr>
<tr>
<td>Brexpiprazole (_______)</td>
<td><strong>Rexulti is not generic – expensive!</strong></td>
</tr>
</tbody>
</table>

Black box warning for antipsychotics in dementia
Augmentation with Aripiprazole

- Age > 60, not remitted with venlafaxine 150-300 mg, had aripiprazole 10-15 mg or placebo added

NNT=6.6

Lenze EJ. *The Lancet* 2015;386:2404-2412
Methylphenidate Augmentation of Citalopram

Average age = 69.7 yrs
Mean citalopram dose about 35 mg/day
Mean methylphenidate dose about 16 mg/day

- Methylphenidate + Placebo, n=48
- Citalopram + Placebo, n=48
- Citalopram + Methylphenidate, n=47

Medications: What’s new

<table>
<thead>
<tr>
<th>Medication</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selegiline (______) patch</td>
<td>MAOI, no need for dietary modification unless higher dosages</td>
</tr>
<tr>
<td>Vilazodone (______)</td>
<td>Supposed to have fewer sexual side effects, but likely not</td>
</tr>
<tr>
<td>Vortioxetine (______)</td>
<td>Dose reduction if poor 2D6 metabolizer; formerly known as Brintellix</td>
</tr>
<tr>
<td>Levomilnacipran (______)</td>
<td>The levo- part of milnacipran (Savella), and FDA approved for depression</td>
</tr>
</tbody>
</table>

Do they work any better than existing antidepressants? Probably not.

None of these are generic, thus can be quite expensive.
Pharmacotherapy Algorithm for Late-Life Depression

<table>
<thead>
<tr>
<th>Step</th>
<th>Majority consensus and minority alternative</th>
</tr>
</thead>
</table>
| Step 1                                    | Escitalopram  
|                                           | Alternatives: sertraline, duloxetine                                                                        |
| Step 2 for minimal or non-response)       | Switch to duloxetine  
|                                           | Alternatives: venlafaxine, desvenlafaxine                                                                  |
| Step 3 for minimal or non-response        | Switch to nortriptyline  
|                                           | Alternative: bupropion                                                                                     |
| Step 2-3 for partial response             | Augment antidepressant with lithium or an atypical antipsychotic  
|                                           | Alternatives: combine SSRI or SNRI with mirtazapine or bupropion                                            |
| Duration of each step                     | 6 weeks  
|                                           | Alternatives: 4 weeks; 8 weeks                                                                             |

SSRI: selective-serotonin reuptake inhibitor; SNRI: serotonin-norepinephrine reuptake inhibitor

Antidepressant considerations in geriatrics

• Use lower dosages to ensure tolerability

• Pharmacokinetics
  • Avoid fluoxetine due to long half life

• Anticholinergic side effects
  • Avoid paroxetine and TCA’s

• Cardiac conduction problems
  • Avoid TCA’s

• Hypertension
  • Avoid venlafaxine

Alamo C. Psychogeriatrics 2014;14:261-268
Antidepressant considerations in geriatrics

- Hyponatremia
  - Caution when using SSRIs and venlafaxine
- Sexual side effects
  - SSRIs in general
  - More with escitalopram, paroxetine, venlafaxine?
  - Less with bupropion, mirtazapine
- Osteoporotic fractures
  - Depression associated with lower bone density
  - Antidepressants, esp SSRIs, might worsen risk

Alamo C. Psychogeriatrics 2014;14:261-268
General antidepressant selection guidelines

• There is no one antidepressant class that is clearly better than another

• There is not an antidepressant clearly better than another for depression versus anxiety

• Factors when choosing antidepressant
  • Response including personal or family response
  • Tolerability and side effects
  • Comorbid conditions such as pain
  • Benefit for side effects such as appetite stimulation
  • Availability and cost
Do antidepressants work?

- Various negative studies of antidepressants versus placebo
- Similar findings in older patients
  - High placebo response rates
  - Negative 8 week study of citalopram in patients ≥ 75 years old
  - In the nursing home setting, 2 RCT with placebo showed no benefit while open label studies showed some benefit
- Overall conclusion: antidepressants work better in moderate to severe depression

Good first-line choices

- Escitalopram
- Sertraline
- Generic
- Fewer drug-drug interactions
What’s new: ketamine (research)

- Anesthetic agent
- Side effects: dissociation, psychosis
- Risks: addiction
- Not FDA-approved for psychiatry applications
- In psychiatry, sub-anesthetic IV dose given (0.5 mg/kg) over 40 minutes
- Improvement within a few minutes to hours, but lasts only hours to days
- Improvement lasts up to 4 weeks in some repeated infusion studies
- Little to no evidence in older patients

Bobo WV. Depr Anxiety 2016;33:698-710.
NEUROMODULATION
Electroconvulsive therapy (ECT)

• Remains the most effective treatment for depression
  • for untreated late-life depression
    • response 90%, remission 70%
  • for medication-treatment-resistant depression
    • response 70%, remission 50%

• BF and RUL both efficacious
  • response 64-68%, remission 40-50%
  • 64-79% needed between 6-12 for remission

Bjolseth TM. J Affective Disorders 2015;175:8-17
Neurostimulation: Electroconvulsive therapy (ECT)

- 6-12 treatments under anesthesia
- Usually improvement within 2-3 weeks
- Modern ECT is much more tolerable and safer
- Indications
  - Depression with neurovegetative symptoms
  - Depression with psychotic features
  - Catatonia
  - Dementia with behavioral dyscontrol (emerging evidence)
Electroconvulsive therapy (ECT)

• ECT is more effective in older patients.

• In RCT of 230 patients, remission rates for older patients (>=60) vs younger patients (<60)
  • BT: 75% vs 58%
  • RUL: 70% vs 46%

• Latest technique: right unilateral ultrabrief
  • Fewer cognitive impairments
  • Has been done safely at Mayo Clinic 5x/week (as opposed to traditional 3x/week)

Transcranial magnetic stimulation (TMS)

- FDA-approved for major depression only
- 30 daily treatments (6 weeks of Mon-Fri treatment)
- No anesthesia
- No memory impairments
- Outpatient procedure
- Main side effect: scalp pain and discomfort at treatment site
Neurostimulation: Transcranial magnetic stimulation (TMS)

- Response rate (56%) not as good as ECT, and about the same or a little better than medications
- Less data for geriatric populations: In patients between 40-90 (average age early 60’s)
  - Only 4 randomized double-blinded trials, of which 2 were positive
  - But none of these studies used a full 30 treatment sessions
- TMS should still be considered in geriatric patients

Carpenter LL *Depr Anxiety* 2012;29:587-96.
PSYCHOTHERAPY
Psychotherapy

- Efficacious in cognitively intact elderly depressed
  - Interpersonal psychotherapy (IPT) - focus on loss, grief, and role transitions
  - Problem-solving therapy (PST) - stimulate activity in the dorsolateral prefrontal cortex, well-suited for patients with depression and executive dysfunction
  - Supportive psychotherapy
  - Cognitive-behavioral therapy (CBT)

Alexopoulos GS, Kelly RE. World Psychiatry 2009;8:140-149
Psychotherapy in older patients

• Meta-analysis of 44 studies comparing psychotherapy to control groups, other therapies or pharmacotherapy showed NNT of 3, and effects were maintained at 6 months or longer post-randomization.

• Systematic review - age>55 for acute depression showed psychotherapy compared to control was effective, although effect size was variable

• Common psychotherapies
  • Cognitive behavioral therapy
  • Problem-solving therapy
  • Supportive therapy

Huang, AX. Am J Geriatr Psychiatry 2015;23:261-273
Complementary and alternative therapies

- Cognitive: relaxation training, imagery, self-help, hypnosis, biofeedback
- Oral medication: herbal, vitamins, homeo & naturopathic
- Physical treatments: massage, chiropractics, osteopathy, acupuncture, yoga
- Other: diet, lifestyle, spiritual, energy, aroma, folk, etc.
- Perceived helpfulness similar to conventional treatments

Kessler RC. Am J Psychiatry 2001; 158: 289
Suicide in older adults
Suicide: 10th leading cause of death (U.S.), 2013

- Diseases of the heart (heart disease)
- Malignant neoplasms (cancer)
- Chronic lower respiratory diseases
- Accidents (unintentional injuries)
- Cerebrovascular diseases (stroke)
- Alzheimer’s disease
- Diabetes mellitus (diabetes)
- Influenza and pneumonia
- Nephritis, nephrotic syndrome and nephrosis (kidney disease)
- Intentional self-harm (suicide)

- Suicide: 41,149 deaths (1.6% of total deaths)
- 4.7 persons per hour

http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_02.pdf
Suicide rate per 100,000 by age group

- In 2013, highest risk ages 45-54
- In 2003, highest risk ages >85

http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_02.pdf
Suicide Facts

- Completed suicides: 78% men, 22% women
- Women more likely to have suicidal thoughts

- Most common methods
  - Among men, firearms 57%
  - Among women, poisoning/overdose 35%

- At autopsy, tested positive for
  - Alcohol – 33%
  - Antidepressants – 24%
  - Opioids – 20%

http://www.cdc.gov/ViolencePrevention/pdf/Suicide-DataSheet-a.pdf
Suicide Facts – Primary care setting

• Of completed suicides, 45% saw their primary care doctors in the last month while 20% saw mental health specialist.

• In older adults:
  • Those with mental health problems visit their primary care physicians more than mental health specialists.
  • Suicidal ideation present in up to 10%.

Suicide in older adults

- More lethal
- Attempters are more frail, more isolated, more likely to have a plan, and more determined
- Means of suicide
  - Firearms > poisoning > suffocation
- Older adults 2x as likely to use firearms than people < 60 years
Suicide Risk Factors

- Depression
- Serious suicidal ideation
- Functional impairment
- Stressful life events (e.g. death of spouse, financial)
- Substance use
- Medical illness

- Access to firearms or other lethal means
- High anxiety/agitation
- Hopelessness
- Previous suicide attempt or psychiatric hospitalization
- Family history of suicide or attempt
- Personality factors

Decreases risk of suicide

- Well developed social support network
- Strong reasons for living
- Responsibility for young children
- Religiosity
- Extraversion and optimism
- Effective coping and problem-solving

How to intervene

• Ask – “Have you had thoughts of harming yourself?” “…or others?”
• Be aware of PHQ-9 Question 9
• Distinguish between passive versus active suicidal thoughts
  • “Did you think of a plan?”
  • “Would you carry it out?”
• Document risk assessment
• Decide next steps:
  • Routine outpatient follow-up
  • Referral to mental health appointment
  • Referral to Crisis Center (usually county)
  • Send to Emergency Department
Summary

• Depression in late life is associated with cognitive decline, medical comorbidities, and greater decline in overall health.

• There are many therapeutic biological and psychosocial approaches for the treatment of late-life depression.

• Know when to refer to Psychiatry.
Thank you!

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