PsychoCare for Older Patients with Depression

Susan W. Lehmann, M.D.
Associate Professor and Clinical Director
Division of Geriatric Psychiatry and Neuropsychiatry
Johns Hopkins University School of Medicine

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Disclosures

• None

Objectives

1) Heterogeneity of depression in older adults and its impact on function

2) Recent work to determine best practices for treatment

3) Assessment and management of suicidal ideation in older adults
How common is depression in later life?

### Prevalence of depression

<table>
<thead>
<tr>
<th></th>
<th>Major Depression</th>
<th>Subsyndromal Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-dwelling</td>
<td>1-2%</td>
<td>13-27%</td>
</tr>
<tr>
<td>Primary care</td>
<td>10-12%</td>
<td>20%</td>
</tr>
<tr>
<td>Acute hospital</td>
<td>10-15%</td>
<td>20-25%</td>
</tr>
<tr>
<td>Inpatients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nursing homes</td>
<td>12-16%</td>
<td>30-40%</td>
</tr>
</tbody>
</table>
What is “subsyndromal depression”?

- Other names: minor depression, non-major depression, subthreshold depression
- Low mood and/or loss of interest (anhedonia)
- At least 2 additional symptoms:
  - Change in weight, sleep, motor activity, energy, concentration
  - Feelings of worthlessness
  - Thoughts of death

About subsyndromal depression

- The most common mood disorder in the older adults
- May not spontaneously remit
- 25% → Major Depression within 2 years
- Significantly impacts function, quality of life
- Reversible with similar treatment as for Major Depression
  - Meeks et al, J Affective Disorders 2011;129: 126-142

Stepped-care approach for preventive intervention

- Method
  - Randomized control trial, 33 primary care practices in the Netherlands
  - 170 adults, age 70+ with subthreshold depression received preventive intervention or usual care
- Findings: 50% reduction in incidence of new cases of major depression
TABLE 3. Uptake of interventions in the stepped-care program

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Control (n=70)</th>
<th>Experimental (n=100)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-help booklet</td>
<td>30 (43%)</td>
<td>52 (52%)</td>
<td>22 (9, 45)</td>
</tr>
<tr>
<td>Structured Telephone Follow-up</td>
<td>25 (36%)</td>
<td>52 (52%)</td>
<td>27 (9, 44)</td>
</tr>
<tr>
<td>Health education</td>
<td>10 (14%)</td>
<td>28 (28%)</td>
<td>18 (6, 31)</td>
</tr>
</tbody>
</table>

Consequences of depression for medically ill patients

- Slower recovery from hip fracture, MI’s
- Longer hospital stays, more residual symptoms after discharge from hospital
- Poorer treatment adherence
- Higher rates of healthcare utilization and more outpatient medical visits

- Pickett et al., Am J Geriatr Psychiatry 2013
Depression and mortality in older patients

- **Method:**
  - 498 subjects age 50+
  - Prospective, naturalistic, 12 year F/U
  - 36% cognitively intact, 31% cognitively impaired, 33% dementia

  » Lavretsky et. al., Am J Psych 2010; 167:589-597

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Depression and risk of dementia

- **Framingham Heart Study:**
  - 949 subjects, mean age 79
  - Depressive symptoms assessed 1990-1994
  - 17 year follow-up

- **Findings:**
  - 21.6% of subjects who were depressed at baseline developed dementia compared with 16.6% of non-depressed subjects

  » Saczynski et. al, Neurology 2010;75:35-41
Recognizing depression: Why it is so difficult in older patients

- Medical co-morbidity
  - Harder to recognize symptoms of depression
  - “Vegetative symptoms” may have multiple etiologies

- Somatic complaints often prominent
  - May not complain of low mood

- Executive dysfunction mimics dementia
  - Impairs daily functioning, causes disability

Distinguishing depression from dementia

<table>
<thead>
<tr>
<th></th>
<th>Depression</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interests</td>
<td>Anhedonia, loss of pleasure</td>
<td>Apathy, loss of interest</td>
</tr>
<tr>
<td>Self-attitude</td>
<td>Diminished</td>
<td>Diminished or intact</td>
</tr>
<tr>
<td>Cognitive testing</td>
<td>Give up, won’t try to answer some questions</td>
<td>Wrong answers</td>
</tr>
<tr>
<td>Cognition</td>
<td>Executive dysfunction: impaired planning, organizing, prioritizing</td>
<td>Memory impairment prominent</td>
</tr>
<tr>
<td>Onset of symptoms</td>
<td>Can be abrupt or gradual</td>
<td>Gradual, progressive</td>
</tr>
<tr>
<td>Symptoms variability</td>
<td>Diurnal variation: better in the evening</td>
<td>“Sundowning”: worse cognition in the evening</td>
</tr>
</tbody>
</table>

Psychotic Depression

- Delusions: fixed, idiosyncratic, false beliefs. Can seem plausible

- Patients with somatic (bodily) delusions often visit multiple specialists

- Must take a thorough history
Depression after stroke

• Other Findings:
  – Patients with prior depression or severe stroke at highest risk for depression
  – Increased all-cause mortality
  – Stroke is independent risk factor for mortality
  – Gaps remain about most effective treatment

Best treatment approaches:
What do we know?

Other Findings:
• Patients with prior depression or severe stroke at highest risk for depression
• Increased all-cause mortality
• Stroke is independent risk factor for mortality
• Gaps remain about most effective treatment
Common treatment issues in geriatric depression

- Antidepressants not prescribed
  - "You'd be depressed, too…"

- Insufficient dosing
  - Start low, go slow, but final doses usually same as for younger patients

- Premature discontinuation
  - Mistaking symptoms for side effects

Treatment approach: Initial weeks

- Selective serotonin reuptake inhibitors are first-line
- "Start low, go slow" but final dose likely to be similar to younger patient
- Common adverse effects: GI distress, tremor (dose-related)
- Watch for SIADH

Geriatric depression and treatment adherence

- Non-adherence rates to treatment for geriatric depression may be as high as 60% (Wetherell and Unutzer, 2003)

- 241 older patients with unipolar depression (Bresworth et al, 2008)
  - 28% reported nonadherence with antidepressant medications
  - Both antidepressant medication nonadherence and perceived barriers to taking medication were significantly related to 12 month depression scores
Other challenges in late-life depression

- Heterogeneous disorder
- SSRI's considered first-line
- Full response to treatment can be delayed (8-12 weeks)
- Antidepressant response rate of 48%, remission rate of 33.7%¹

  ¹Kok et al, J Affect Disord 2012

Neural predictors of treatment response?

- 33 patients with LLD treated with venlafaxine, received serial fMRI scans paired with affective task
- Finding: Remitters on venlafaxine had decrease in emotional reactivity in middle temporal gyrus; seen in first 24 hours
- Antidepressant treatment may affect neural basis of emotional reactivity depending on illness remission

Emotion regulation as a path to remission for LLD?

- Enhancing capacity for emotion regulation may enhance antidepressant treatment response
- Psychotherapies designed to improve emotional regulation:
  - Problem-solving therapy
  - Cognitive-behavioral therapy

Executive dysfunction is predictor of poor treatment response

- Two times less likely to reach remission with pharmacotherapy¹
- Planning & organization significantly associate with antidepressant response²
- Problem-solving therapy improves depression but not executive functioning³


Can cognitive remediation improve depression?

- 11 patients (ages 60-89) who failed to remit with SSRI or SNRI for 8 weeks
- Received 30 hours of computer cognitive remediation over 4 weeks while staying on same meds
- Unblinded study
  - Morimoto et al Am J Geriatr Psych 2016;24:816-820
Implications

• LLD with executive dysfunction may be a "phenotype" of LLD
• Computerized cognitive remediation may benefit mood and executive dysfunction

Maintenance treatment with SSRI
(Reynolds et al., NEJM, 2006)

• Method: 116 patients who responded to paroxetine and psychotherapy
  – Randomly assigned to paroxetine, placebo, placebo + psychotherapy, paroxetine + psychotherapy
  – Followed for 2 years for relapse/recurrence
ECT in Late Life Depression

Systematic review of cognitive effects:
- Increased rates of interictal/postictal cognitive decline, esp in patients with dementia
- Higher rates of delirium (30% without dementia; 75% with dementia and LLD)
- No conclusive evidence for persistent cognitive deficits after 6 months
  - Kumar et al. Am J Geriatr Psych 2016; 24:547-565

Continuation/maintenance ECT +NRTP in LLD with psychosis

- Method: randomized, longitudinal, single-blind design
- Age 60+ who remitted with ECT
- Compared patients who received maintenance nortriptyline (NRTP) to patients who received maintenance ECT plus NRTP
PRIDE: Prolonging remission in depressed elderly

Method:
- Right unilateral ultrabrief pulse ECT and venlafaxine to treat LLD
- 7 academic centers

Findings:
- Among those who remitted, mean HAM-D scores decreased by 24.7 points
The graph shows baseline-adjusted least squares 24-item HAM-D mean scores from a basic mixed-effects repeated-measures model (unstructured covariance), with difference in baseline-adjusted least squares treatment means at study end (uncorrected, CI [-1.8, 1.5], p = 0.016). For the model containing baseline HAM-D score, site, and psychosis, Δ = 2.0 (95% CI [0.2, 3.8], p = 0.021). Treatment-by-site, treatment-by-psychosis, and treatment-by-baseline HAM-D score interaction terms were not significant. For the comparison of the trajectories of HAM-D mean scores over time (time as continuous) in a mixed-effects model ( Mundorff-adjusted model): treatment-by-time interaction, p = 0.084; main effect of time, p = 0.001; main effect of treatment, p = 0.12; and baseline HAM-D score, p < 0.001. For analyses by treatment: main effect of time for the ECT plus medication group, p < 0.001; no effect of time for the medication only group, p = 0.58.

**rTMS in Late Life Depression?**

- Few reported successes for repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (TDC) or deep brain stimulation (DBS)
  - Galvez et al. 2015; Current Psych 17:5910
  - Milev et al.; 2009; J. ECT 25:44-49

**Combined citalopram and methylphenidate enhance treatment response** (Lavretsky et al., Am J Psy)

April 25, 2017
**Treatment-resistant depression lacks effective guidance**

**TRDOA workload as a percentage of TRD practice**

- TRD- failure to achieve remission with adequate trials of 2 or more antidepressants
- Commonly seen by clinicians
- Need for more RCT studies

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**How common is geriatric suicide?**
Geriatric suicide: increased lethality

- Among all ages: 1 completed suicide for every 25 attempts
- Among elderly: 1 completed suicide for every 4 attempts
- In 2000, 72.9% of geriatric suicide due to firearms (more than any other age group)

> Minino et al., 2000
Psychological autopsy studies

- Uses information gathered after death from relative, health care records
  - Diagnosis and intent are inferred
- 90% or more of suicide victims have diagnosable psychopathology at time of death (depression is most common diagnosis among victims age 60+)

Social factors in geriatric suicide

- Psychological autopsy studies show role of:
  - Stressful life events
    - Loss through bereavement
    - Lack of family/social support (family discord, financial problems)
  - Social connectedness
    - Lack of a confidante, living alone

Yeates et al., Psychiatr Clin N Am 2011;34:451-468

Medical illness and risk of suicide

Method:
- All Ontario residents age 66 and older who committed suicide 1992-2000 and their prescription records during previous 6 months
- Logistic regression to identify odds ratios

Juurlink et al., Arch Intern Med 2004;164:1179-1184
Number of illnesses and relative risk of suicide

Medical illness and suicide risk

Findings (1329 suicides identified):
- 9 conditions were independent predictors of increased suicide risk: bipolar disorder, depression and severe pain had the strongest associations
- DM, ischemic heart disease, Parkinson’s: no increased risk
- Cases were 2 times as likely to have seen PMD in week before death compared with controls

Continuum of suicidality in older adults

- Suicidal ideation
  - Thoughts of death: normative, reflective nonpathologic;
  - Thoughts of death: passive death wishes
  - Active thoughts: plan for self-harm

- Suicidal behavior
  - Past attempt(s) increase risk
Antidepressants reduce risk of suicide among elderly depressed patients

Method: Meta-analysis of 372 double-blind randomized placebo-controlled trials of antidepressants in adults

Outcome: suicidal ideation/behavior

Findings: Relative risk for suicidal ideation/behavior during antidepressant treatment was age-dependent:
- Higher for adults under 25; no different than placebo for ages 25-64
- Decreased for adults over 65 who received antidepressants
  ➔ Stone et al., BMJ 2009;339:b2880

Primary care is ideal setting to identify suicide risk

- More likely to see older adults with mental health concerns
- Higher rates of depression in primary care settings
- Suicidal ideation linked to poor medical outcomes
  ➔ Raue et al, Curr Psychiatry rep, 2014

Prevention of Suicide in Primary Care Elderly: Collaborative Trial (PROSPECT)

- Why focus on primary medical care?
  - Depression is often undetected or inadequately treated, especially in primary care settings
  - Up to 75% of older patients who suicide have seen PMD 1-4 weeks prior to suicide
PROSPECT Study

Method: 599 patients age 60 and older with major or minor depression, from 20 primary care practices
- Randomly assigned to intervention or usual care
- Intervention: algorithm-based recommendations given by trained care managers to physicians, and help with treatment adherence for 24 months

Alexopoulos et al., Am J Psych 2009;166:882-890

Percentage of Depressed Older Primary Care Patients Who Received Treatment for Depression

Summary: Late-Life Depression

- Impacts function, morbidity, and mortality
- Recent focus on developing interventions based on pathophysiology of late life depression
- Ongoing studies to investigate antidepressant drug combinations; more RCT’s needed
- Emerging treatment strategies support importance of psychotherapy with pharmacotherapy
- Collaborative care models improve geriatric depression outcome and reduce suicidality