Assessment and Management of Depression in Later-life

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Agenda

• Review of epidemiology of Late-life Depression (LLD)
• Review of diagnosis of LLD
  – Phenomenology
  – Time of onset
  – Complications
• Screening tools
• Treatment options
Epidemiology of Late-life Depression I

- A major public health problem
  - 2nd only to heart disease in disability
- Remains under-diagnosed and under-treated in the elderly
  - Most will receive treatment in 1º care settings
  - However, rates of treatment are very low

Epidemiology of Late-life Depression II

• Consequences
  – Amplifies disability and lessens Quality of Life
  – Increases morbidity and mortality
    • Medical: pain, heart disease
    • Psychiatric: suicide
  – Increases rates of healthcare utilization
  – Increases drug use and costs
  – Increases cost of care

NIH Consensus 1992; Frasure-Smith 1993, 1995; Unutzer 1999; Beekman 1999; Charney 2003
Epidemiology of Late-life Depression III

Prevalence rates vary across different sites and with different conditions.

* Range depends on the study
Phenomenology of Late-life Depression

• There are different types of depressive disorders.
  – Major Depression (and subtypes)
  – Subsyndromal depression (and subtypes)
• Not all require or respond to pharmacotherapy:
  – Know which type of clinical depression is being diagnosed as treatment selection may vary.
  – Some types and some patients may preferentially respond to psychotherapy (individual, group, family, or day program)
• Most types contribute to functional impairment and increased healthcare utilization.
• All types place patients at risk of complications or poorer outcomes.

NIH Consensus 1992; Consensus Update 1997; Jeste 1999
Phenomenology of Late-life Depression

- **Subsyndromal Depression**: patient has clinically significant depressive symptoms but does not meet either time duration, quantity or severity criteria for DSM-IV Major Depression
  - Minor depression
  - Brief, recurrent depression
  - Non-dysphoric depression
  - Dysthymia (depressed mood for \( \geq 2 \) years)
- Except for Dysthymia, criteria are not well-delineated.
- However, these types may be more prevalent in older populations and difficult to detect.
- Pharmacological treatments may not be needed initially and adjunctive use of psychotherapies may lead to better outcomes.

Hermens 2004; Kumar and Lavretsky 2002
DSM-IV criteria for Major Depression

- Diagnosis requires 5 of 9 symptoms present for at least 2 weeks, nearly every day or more days than not
- To use the mnemonic - one symptom must be
  - depressed mood OR
  - decrease in interest/pleasure

- S: suicidal thoughts
- I: interest decrease
- G: guilt; worthlessness
- E: energy decrease
- C: cognitive problems
- A: appetite / weight change
- P: psychomotor changes
- S: sleep disturbance

American Psychiatric Association 1994
Major Depression: Symptom Clusters and Possible Sub-typing

Symptom Presentation
≥ 5 of 9 symptoms
≥ 2 weeks duration

Major Depressive Episode

Insomnia, weight loss → Classic Depression
Anxiety, rumination → Mixed Anxiety-Depressive Episode
Onset, remission during particular time of year → Seasonal Affective Disorder (SAD)
Mood reactivity, overeating, oversleeping → Atypical Depression
Hallucinations, delusions, paranoia, nihilism → Psychotic Depression
Unreactive mood, a.m. worsening, agitation/retardation → Melancholic Depression
Current or past mania → Bipolar Depression
Concurrent medical disorder or problems → Mood Disorder due to General Medical Condition
Subtypes of particular relevance in Late-life Depression

- Cerebrovascular disease
  - Post-stroke depression: location and time effects
  - Vascular depression
    - DWM ischemic changes
    - Disruption of frontal-subcortical circuitry
    - Differing presentation: apathy, slowing, executive dysfunction, less insight; later age of onset; less psychosis?

- Post-MI depression

- Dementia complicated by depression
  - Alzheimer’s disease
  - Parkinson’s disease

Complications of relevance in Late-life Depression

• Dementia of depression or “pseudodementia”
  – Subcortical neuropsychological impairment is typical
  – Frontal executive dysfunction may also be seen
  – Higher cortical dysfunction may predict AD conversion

• Psychotic depression
  – psychosis may be subtle, not endorsed. Must ask.
  – more lethal, usually requires hospitalization
  – combined pharmacotherapy
  – ECT
  • Indicated sooner
  • May be treatment of choice

Birkenhager 2003; Karim 2003; Kessing 2003; Petrides 2001; Schwartz 2004
Late-life Depression:  
Time of Onset Variable

Early-onset: Teen/young adult years

Late-onset: after age 60

<table>
<thead>
<tr>
<th></th>
<th>50</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;=&quot;</td>
<td>Episode</td>
</tr>
</tbody>
</table>
Epidemiology of Late-life Depression IV
Early-onset Depression (EOD)

• Early onset
  – Develops earlier in life: teens or twenties
  – Higher biological or familial risk
    • Mood disorders
    • Substance abuse
    • Suicide

• Clinical history
  – How many episodes? Duration? Symptoms?
  – What treatments worked?
  – If family history, what worked for them?

Lebowitz 1997; Reynolds 2001; Alexopoulos 2003
Epidemiology of Late-life Depression V
Late-onset cases

- Late-onset: 1st episode vs. recurrent
  - 1st episode: no prior history, no family history, may have higher suicide risk, more medical comorbidity
  - Remission rates similar to EOD but . . .
  - Recurrence rates higher: prior episodes, positive family history, degree of residual symptoms
  - Cognitive deterioration: may reflect patient at higher risk of subsequently developing dementia (AD, VaD, or Mixed dementia) or may be prodrome of dementia

Lebowitz 1997; Reynolds 2001; Alexopoulos 2003; Mitchell 2005
Complications in Late-life Depression: Suicide

• In geriatrics: 10th leading cause of death
  – More specifically related to late-onset, 1st episode depression
  – Higher or acute risk if suicidal ideation is present with
    • hopelessness
    • restlessness
    • comorbid anxiety or psychosis
    • insomnia
    • chronically, seriously ill or suffering condition
    • social isolation: recently bereaved or widowed
    • concurrent of alcoholism or substance abuse
  – Attempts in later-life decrease BUT successful completion of suicide increases

Mosciki 1997; Fawcett 1993; Rich 1986; Gliatto 1999
Challenges in Assessing Depression in Late-life

• Gender differences
  – Males: anger, apathy, anhedonia but not sadness
  – Females: somatic symptoms, dysphoria

• Over-expression of somatic complaints

• Minimization of psychological problems

• Presence of medical comorbidity
  – Symptoms: fatigue, anorexia, insomnia, psychomotor slowing, pain
  – Cognitive impairment: detection and expression
  – Medication side-effects
  – Competing time demands

• Presence of psychiatric comorbidity

• Rationalization: by patient, family and/or provider
  – “reasons to be depressed . . .”
  – Nihilism
Differential Diagnosis of Depression in Late-life

- **Medical**
  - Endocrinopathies
  - Metabolic derangement
  - Infections
  - Cardiopulmonary disease
  - GI disturbances / cancer
  - Inflammatory processes
  - Hematological conditions
  - Musculoskeletal problems
  - Delirium

- **Neurological**
  - Cerebrovascular disease
  - Primary or metastatic tumor
  - Basal ganglia disease
  - Dementia

- **Medications**
  - Antihypertensives
  - Analgesics (opiates)
  - CNS depressants
  - Others

- **Psychiatric**
  - Adjustment disorder
  - Anxiety disorder
  - Substance-induced disorder (Alcoholism)

- **Life circumstances**
  - Grief and bereavement
  - Social isolation / loneliness
  - Poverty
Diagnosis of Depression in Physically Ill Elderly

- Features of Physical illness
  - recent onset
  - greater severity
  - functional disability
  - poorly treated pain
  - higher number of illnesses

- Functional impairment, not physical illness per se, appears to be the greater risk factor for depression in the elderly:
  - Abrupt change
  - Lower level of function

- Variation with caregiver stress level
Other Risk Factors for Depression inPhysically Ill Elderly

• Past history of depression
• Cognitive impairment
• Age over 75 years
• Impaired social support
• Alcohol abuse
• Poor education
Exclusion of Depression in Physically Ill Elderly

Look for “positive” or joining behaviors. Unlikely to be depressed if:

• Appreciates humour (laughs and smiles broadly)
• Responds warmly to affection
• Shows an interest in life, pleasurable activities
• Looks forward to family visits
• Accepts help
• Participates in treatment (PT, OT, etc)
• Points to reasonable causes for physical symptoms
**Diagnosing Major Depression In Physically Ill Elderly**

- Depression criteria should emphasize:
  - change of mood or interest with at least 2 weeks duration
  - non-physical symptoms
  - social regression or incapacity
- Anorexia, sleep disturbances, fatigue and motor retardation:
  - These should only be considered if they accompany the above depressive symptoms and cannot be explained by physical illness or its treatment
  - If present at the outset, these symptoms get worse with mood and are out of proportion to symptoms expected from medical illness
Screening for Late-life Depression

- Two-question screen
- Geriatric Depression Scale
- Cornell Scale for Depression in Dementia
- PHQ-9

- Caveat on screening: should not be sole basis for diagnosis.
- Gold standard: clinical interview
Screening Tools for Assessment of Late-life Depression

- Two-question screen
  - during the past month have you often been bothered by feeling down, depressed, or hopeless? And,
  - during the past month have you often been bothered by little interest or pleasure in doing things?
- Validated in primary outpatient care settings and in older patients
- Not validated in cognitively impaired patients or in inpatient or LTC settings
- Cannot be used to follow response to treatment
Screening Tools for Assessment of Late-life Depression II

- Geriatric Depression Scale
  - 30-item, 15-item, 10-item, and 5-item
  - Validated across outpatient and inpatient settings; available in several languages
  - Emphasizes psychological components of depression
  - May be limited in greater than mildly cognitively impaired individuals (MMSE < 17)
  - May not be sensitive to change

Brink and Yesavage 1982, 1987; Montorio 1996; Rinaldi 2003
Screening Tools for Assessment of Late-life Depression III

- Cornell Scale for Depression in Dementia
  - Observational and informant based
    - 19-item scale
    - 38 maximum; ≥ 12 indicates depression
  - Validated in mild to moderately impaired groups, but
  - Not yet validated across all cultural or ethnic groups
  - Can be used to follow change to treatment

Alexopoulos 1988
Screening Tools for Depression in Late-life IV: PHQ - 9

Spitzer, Williams, Kroenke, et al. 1999

Scores:
- 5-9 = mild
- 10-14 = moderate
- $\geq 10$: likely major depression
- 15-19 = moderately severe
- $\geq 20$ = severe

If you checked off any problems, how difficult have these made it for you to do your work, take care of things at home, or get along with others?
- not difficult
- somewhat difficult
- very difficult
- extremely difficult

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by any of the following problems?</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>a. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>b. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>c. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>d. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>e. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>f. Feeling bad about yourself — or that you are 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>g. 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>h. 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>i. 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 Instruments for Late-life Depression for Use in Primary Care

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Inpatient</th>
<th>Outpatient</th>
<th>Physically ill</th>
<th>Cognitively impaired</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Question Screen</td>
<td>97%</td>
<td>67%</td>
<td>No</td>
<td>Yes</td>
<td>Unknown</td>
<td>No</td>
</tr>
<tr>
<td>GDS 5-item</td>
<td>94%</td>
<td>81%</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Unknown</td>
</tr>
<tr>
<td>CSDD (19-item)</td>
<td>90%</td>
<td>75%</td>
<td>Yes</td>
<td>Yes</td>
<td>Unknown</td>
<td>Yes</td>
</tr>
<tr>
<td>CES-D (20-item)</td>
<td>93%</td>
<td>73%</td>
<td>No</td>
<td>Yes</td>
<td>Unknown</td>
<td>No</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>88%</td>
<td>88%</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Treatment Strategies for Depression in Late-life

- Psychotherapy
- Somatic therapy
  - Medications
  - Brain Stimulation: ECT and VNS (rTMS?)
- Decision on which to pursue is predicated upon
  - severity
  - persistence
  - degree of associated suffering
  - extent of related disability
  - values expressed by patient and family
Treatment Strategies for Depression in Late-life

• Psychotherapy
  – **Type**: supportive psychotherapy, problem-solving therapy, cognitive-behavioral therapy, interpersonal psychotherapy
  – **Modality**: individual, couples, family, group
  – **Location**: office; partial hospital or day treatment; IOP; senior community centers; assisted living, residential or LTC sites
  – **Practitioners**: psychiatrists, psychologists, social workers, nurse therapists, MFTs

Arean 2002; Garner 2003; Unutzer 2003
Treatment Strategies for Depression in Late-life

• Indications for Psychotherapy
  – Patient or family preference
  – Sensitivity to medication(s) or reluctance to try
  – Polypharmacy
  – Minor depressive states: 1st choice?

• Adjunctive use
  – Collaborative care models: Project IMPACT (Unutzer 2002)
  – Stepped care models (Katon 1999)

• Obstacles
  – Limited coverage
  – Limited providers
  - Patient resistance / stigma
  - Therapist ageism
“Now have this prescription filled and take as directed. Then two nights after the first full moon, procure the left hind leg of a he-frog and a root of St. John’s-wort....”
Treatment Strategies for Depression in Late-life

• Pharmacotherapy is indicated when:
  – psychotherapy has failed, ie, symptoms persist
  – serious depressive symptoms interfere with daily functioning or impair health or safety
  – after discussion, patient prefers

• Choice of antidepressant depends on:
  – Efficacy
  – Adverse events (safety)
    • Tolerability
    • Interruption
  – Compliance
  – Cost

Mittman 1999; Solai 2001; Sommer 2003; Williams 2000
Defining an Adequate Medication Trial

- Right medication, ie, accurate diagnosis
- Right dosage
  - Underdosing is very common in primary care and among elderly patients
  - Start low, go slow, but go.
- Right duration
  - 4 to 6 weeks for *maximal* effect, but
  - May be able to see some initial improvement after 2 weeks
  - For elderly, some may take as long as 8 to 12 weeks
- In the beginning, more frequent follow-up, encouragement, checking for compliance and providing reassurance will improve effectiveness of treatment.
## Common SRI’s

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose/day</th>
<th>Therapeutic Range/day*</th>
<th>Generic</th>
<th>CYP 450 effects</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluoxetine</strong> (Prozac®)</td>
<td>5-10mg Qam</td>
<td>10-20mg</td>
<td>Y</td>
<td>+++</td>
<td>+/+++</td>
</tr>
<tr>
<td><strong>Sertraline</strong> (Zoloft®)</td>
<td>12.5-25mg Qam</td>
<td>50-150</td>
<td>Y</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td><strong>Paroxetine</strong> (Paxil®)</td>
<td>10 Qhs</td>
<td>20-30</td>
<td>Y</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td><strong>Citalopram</strong> (Celexa®)</td>
<td>10 Qhs</td>
<td>20-40</td>
<td>Y</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Escitalopram</strong> (Lexapro®)</td>
<td>5-10mg Qam</td>
<td>10-20</td>
<td>N</td>
<td>±</td>
<td>±</td>
</tr>
</tbody>
</table>

* Dosage for Major Depression

Mittman 1999; Solai 2001; Sommer 2003; Williams 2000
Adverse Effect Profiles of SRIs

SRIs: proserotonergic; variably anticholinergic, antihistaminergic or antidopaminergic

- **Common**
  - nausea
  - loose stools
  - restlessness
  - akathisia
  - insomnia
  - headache
  - sexual dysfunction

- **Uncommon (?)**
  - weight loss / gain
  - hyponatremia (SIADH)
  - sinus bradycardia
  - bleeding (anti-platelet effect)
  - Parkinsonism
  - Serotonin Syndrome
## “Dual Action” and Atypical Antidepressants

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dosage (mg)</th>
<th>Range (mg)</th>
<th>Treatment Resistance</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine (IR / SR)</td>
<td>18.75-37.5 BID</td>
<td>75-150</td>
<td>Yes 150-225mg</td>
<td>Minimal</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>15-30 Qhs</td>
<td>30-45</td>
<td>Yes 60-90mg</td>
<td>Minimal</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>20mg Qam</td>
<td>20-90</td>
<td>Unknown</td>
<td>Minimal</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>50-100 BID or TID</td>
<td>300-600</td>
<td>Unknown</td>
<td>Probable</td>
</tr>
<tr>
<td>Trazodone</td>
<td>25-50 Qhs</td>
<td>300-600</td>
<td>Unknown</td>
<td>Minimal</td>
</tr>
<tr>
<td>Bupropion (IR / SR / XL)</td>
<td>50-75 BID</td>
<td>100-450</td>
<td>Possible</td>
<td>Minimal</td>
</tr>
</tbody>
</table>
Other Options for LLD

• Tricyclic antidepressants
  – Secondary amines: nortriptyline, desipramine
  – Closer monitoring: EKG, BP, drug levels
  – Side effects; lethality in OD

• MAOIs
  – Isocarboxazid, phenelzine, tranylcypromine, selegiline (transdermal patch)
  – Safer cardiac profile
  – Side effects

• Combination strategies
  – Adjunctive: antidepressant + antidepressant
  – Augmentative: antidepressant + (lithium, thyroid, psychostimulant, atypical antipsychotic, anticonvulsant, D3 agonists, other drugs and supplements (fatty 3-omega acids, SAM-E)
  – Limited data in the elderly; no DBRCTs
Brain Stimulation Therapies

- ECT
- VNS
- rTMS
- Others: DBS, MST
Electroconvulsive Therapy in Late-life Depression

• Advantages of ECT
  – Superior efficacy (80 - 90%) in severe depression compared to antidepressant medication (when used as 1st line)
  – good efficacy (50 - 60%) in medication resistant depression
  – more rapid onset of action
  – good safety profile: very low mortality and low morbidity
  – absence of medication side effects

2001 APA Task Force on ECT; Espinoza 2003
Electroconvulsive Therapy in Late-life Depression

• Disadvantages of ECT
  – Repeated general anesthesia
  – Cognitive and memory effects: acute vs. chronic
  – Minor treatment side-effects: headache, muscle ache, falls (especially in the elderly)
  – Acute relapse if a maintenance plan is not instituted
  – Cost of series

2001 APA Task Force on ECT; Espinoza 2003
Electroconvulsive Therapy in Late-life Depression

• Indications
  – Serious, life-threatening mood disorders
  – Treatment failures
  – Chronic depression with significant psychosocial, functional, cognitive impairment
  – Psychotic depression: probably treatment of choice
  – Some dementia syndromes
    • Mood or psychotic features
    • Behavioral dyscontrol
  – Possibly cases of delirium

2001 APA Task Force on ECT; Espinoza 2003
Electroconvulsive Therapy in Late-life Depression

• Treatments can be inpatient or outpatient depending on severity of illness
• If patient shows a positive acute response, a maintenance plan must be instituted:
  – Meds: probably combination (TCA + lithium); others?
  – ECT
  – ECT + meds

Vagus Nerve Stimulation

• Approved by the FDA in July 2005
  – Adjunctive use only in Treatment-Resistant Depression (TRD)
  – Failed at least 4 adequate antidepressant trials
• Not an acute treatment, may take 6 – 12 months for effect
• Does not replace medications, ECT or psychotherapy
• Oldest patient implanted was 84 years old
• Surgery takes about 1.5 to 2 hours
• Stimulator tested during implantation

• Generators are made of titanium
• Battery can last up to 7-10 years
• Limits on certain types of radiological studies and treatments

Figure 2. Use of programming wand to adjust generator stimulator parameters. Photo courtesy of Cyberonics, Inc.
Summary

- Depressive disorders are prevalent and diagnosable in older populations.
- Medical comorbidity can increase the challenges of accurate diagnosis.
- Look for psychological symptoms and signs to increase the specificity of diagnosis.
- Tools are available to assist in screening for depression across different settings and patient populations.
- Treatment strategies include psychotherapies, medications or brain stimulation approaches.