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Diagnosis, Assessment and Treatment of Late-life Depression in Primary Care
Disclosures

- Muriel Harris Chair of Geriatric Psychiatry
- Funding
  - NIMH: (R01 (parent and suppl), MPI: Espinoza, Narr) Biomarkers of ECT Response in MDD; (K24; Narr, PI) Biomarkers of Ketamine Response in TRD; (U01, MPİs Narr, Espinoza, Wang) Brain Connectomes of Rapidly Acting Antidepressant Interventions: ECT, Ketamine and Sleep Deprivation
  - NIH/NCATS UCLA CTSI Grant KL2TR000122 (PI:Congdon) and UCLA CTSI Grant UL1TR000124: Gene Expression and Cytokine Markers of Treatment Response
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  - Intramural: (PI) Ketamine Infusion Therapy for TRD and Biomarkers of Response to Rapidly Acting Antidepressant Interventions (UCLA Depression Grand Challenge)
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- Conflicts of interest: none
Agenda – Late-life Depression (LLD)

- Spectrum of depressive disorders
- Challenges to diagnosis
- Complications
- Differential diagnosis
- Screening
- Work-up
- Treatment
Spectrum of Late-life Depression
Case Examples

- Ms. D is 78 yo, has OSA, DM2, HTN, dyslipidemia, and is brought in by her daughter as she complains of frequent HA and fatigue. Not a “happy personality,” her mood is always low and she feels like a burden to her family.
- Ms. S is 88 yo and in generally good health. She was recently tragically widowed and c/o insomnia, lack of appetite, and inability to focus on reading or watching TV. She readily cries and wonders if life is worth living.
- Mr. M is 91 yo and diagnosed with late-onset dementia. He is s/p MI x2 and has CHF and COPD. His wife reports constant calling for her, neediness, and general irritability with caregivers. He no longer asks about their dog or cat.
Presentations of Late-life Depression

Mood Symptoms

- Major Depression
- Persistent Depressive Disorder
- Subsyndromal States
- Mood Disorder due to AMC
- Other

Psychological
- Sadness
- Guilt
- Rumination
- Self-esteem
- Suicidal ideation

Cognitive
- Poor attention/concentration
- Memory deficits
- Slowed processing

Behavioral
- Crying
- Irritability
- Social withdrawal

Physical
- Sleep disturbances
- Appetite/weight changes
- Fatigue or energy complaints
- Pain
Spectrum of Depressive Disorders

- Adjustment Disorder with depressed mood (most common subtype)
- Unipolar Depression
  - Subsyndromal Depression
  - Persistent Depressive Disorder (PDD)
    - Chronic, unremitting depression
    - Dysthymia ("low grade depression")
  - Major Depression
    - Bereavement exclusion removed
  - Substance-induced Mood Disorder
  - Mood Disorder due to Another Medical Condition
- Bipolar Depression
  - History of prior manic or hypomaniac episode
  - De novo presentation in elderly is rare
  - Usually a difficult form of depression to treat

Source: DSM5, American Psychiatric Association (May 2013)
Patient has **clinically significant** depressive symptoms but **does not** meet either time duration or symptom quantity or severity criteria for DSM5 Major Depression

- Minor depression
- Brief, recurrent depression
- Non-dysphoric depression
- PDD or Dysthymia (depressed mood for $\geq 2$ years)

 Except for PDD (aka Dysthymia), criteria for others are not well-delineated, including in older adults.

 However, these types may be more prevalent in older populations, more difficult to detect or **more commonly misdiagnosed as MDD**.

 Notwithstanding, subsyndromal states: 1) are risk factor for subsequent conversion to MDD 2) may be a harbinger of neurodegenerative illness 3) are associated with disability and illness burden and 3) can include suicidal ideation or behaviors
Persistent Depressive Disorder

- New in DSM5: combined Dysthymia and Chronic Depression
- If patient meets MDD criteria x 2 years, then gets diagnosis of both MDD and PDD

  - Depressed mood
    - Occurs most of the day
    - For more days than not
    - For at least 2 years
  - Cannot ever have had manic, mixed, or hypomanic symptoms
  - *Never without symptoms for > 2 mos*

  - During periods of depressed mood, must have 2 of 6 symptoms
    - Poor appetite or overeating
    - Insomnia or hypersomnia
    - Low energy or fatigue
    - Low self-esteem
    - Poor concentration or indecisiveness
    - Feelings of hopelessness
Mood Disorder due to AMC

- Neurodegenerative illness
  - Alzheimer
  - Parkinson
  - Huntington
  - Vascular dementia
- Cerebrovascular Disease
  - Vascular Depression
  - Post-stroke Depression
- Post-MI Depression
- Endocrinopathies
  - Diabetes
  - Thyroid
  - Parathyroid
- Inflammatory illness
  - GCA
  - PMR
- Immunologic illness
- Cancer
Look for psychological and behavioral components of depression, not just neurovegetative symptoms.

Physical symptoms predating mood symptoms usually implies a reaction to illness.

However, if mood symptoms predate or co-vary with physical symptoms, think depressive disorder.
Comorbid Medical Illness: Clues to Depression in Medically Ill

- Depressed patients:
  - Cannot point to other reasonable causes for symptoms
  - Symptoms appear out of proportion to what is expected for level of illness
  - May reject help or treatment
    - No PT, OT
    - No visits with or pleasure from family
    - No laughter or response to humor
  - Fail usual medical treatments
Mr. T is 78 yo and newly diagnosed with pancreatic cancer. Although his doctor says he is doing well, he adds “I don’t always feel it.”

He continues “…I am used to dealing with pain, (b)ut what I am not used to dealing with is these surges that come on suddenly of deep, deep sadness. And it brings tears to my eyes.”

He often feels depressed the day after chemotherapy:
- “It is no big deal. I go in and I sit down, I joke with the nurses and I am there for an hour and a half while they inject all this stuff into me.
- Then I go home and I have a good day. Then the next day for no reason that I can fathom, it turns south on me.”
Criteria are not modified for older age
Still requires 5 of 9 symptoms

- A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
  - Depressed mood most of the day, nearly every day
  - Markedly diminished interest or pleasure in all or almost all activities most of the day, nearly every day
  - Weight loss or gain; or increase or decrease in appetite
  - Insomnia or hypersomnia
  - Psychomotor agitation or retardation
  - Fatigue or loss of energy
  - Feelings of worthlessness or excessive, inappropriate guilt
  - Diminished ability to think or concentrate, or indecisiveness
  - Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a plan, suicide attempt, or suicidal ideation with specific plan

Source: DSM5, American Psychiatric Association (May 2013)
B. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

C. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

Modifiers added:
- With anxious distress
- With mixed, melancholic, psychotic, catatonic, atypical, or seasonal features
- Rate severity: mild, moderate or severe
- Rate current episode or in partial or full remission

Bereavement exclusion removed

Source: DSM5, American Psychiatric Association (May 2013)
Challenges to diagnosis of LLD
Challenges to Diagnosis of LLD

- **Age or cohort effects**
  - Less psychological openness
  - Viewed as characterological flaw or weakness
- **Sex effects**
  - Men: non-dysphoric or angry states
  - Women: more somatic focus
- **Culture effects**
  - Degree of acculturation may influence presentation
  - Somatic expression of psychological distress
  - Less accepting of psychological care
- **Providers and family**
  - Therapeutic nihilism
  - Belief that reasons to be depressed are valid – FALSE!
  - Nursing homes are depressing for them
Challenges to Diagnosis of Depression: Concomitant Medications

- Polypharmacy
- Pharmacodynamics
  - Fatigue
  - Insomnia
  - Loss of appetite
  - Constipation
  - Anxiety or restlessness
  - Mental clouding
Complications in Late-life Depression
Medical complications of LLD

- Dehydration
- Malnutrition
- Inanition
- Other
  - Deconditioning
  - Pressure sores
  - DVT, PE
  - Contractures
**Complications of LLD: Suicide**

- **Prevalence**
  - In 2013, CDC reported 41,149 deaths by suicide (10th leading cause)
  - Highest rates in older adults
    - Attempts decrease but success increases due to means used, medical sequelae
    - 1st episode of Late-life depression is particularly lethal time for many
    - White males accounted for 70% of all suicides in 2013
  - Psychological autopsy: LLD is poorly identified or not diagnosed; suicidal depression is under or inappropriately treated in primary care

**Suicide Methods (2013)**

- 51.8% Firearms
- 24.5% Suffocation
- 8.0% Poisoning
- 16.1% Other

**Suicide Rate Per 100K**

- White Male
- Black Male
- White Female
- Black Female

**Age (Years)**

Suicide Assessment in Primary Care

## Complications of LLD: Suicide – Risk Factors

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active symptoms</td>
<td></td>
</tr>
<tr>
<td>• Suicidal ideation</td>
<td>Social isolation</td>
</tr>
<tr>
<td>• Hopelessness</td>
<td>Financial strain</td>
</tr>
<tr>
<td>• Impulsivity</td>
<td>Past psychiatric history (mood, schizophrenic, substance abuse, or personality disorder)</td>
</tr>
<tr>
<td>• Insomnia or sleep disturbance</td>
<td>Past history of suicide attempt</td>
</tr>
<tr>
<td>• Restlessness or agitation</td>
<td>Family history of suicide</td>
</tr>
<tr>
<td>• Anxiety, fear or panic</td>
<td>Past use of opioid analgesics, CNS depressants, or benzodiazepines</td>
</tr>
<tr>
<td>• Psychosis</td>
<td>Poorer physical functioning or impairment</td>
</tr>
<tr>
<td>• Intoxication</td>
<td>Chronic or multiple medical illness</td>
</tr>
<tr>
<td>• Poorly controlled pain</td>
<td>Chronic pain</td>
</tr>
<tr>
<td>• Delirium</td>
<td>Prior brain injury</td>
</tr>
<tr>
<td>Organized or lethal plan</td>
<td>Metastatic or advanced oncologic disease</td>
</tr>
<tr>
<td>Recent loss or widowhood</td>
<td></td>
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<tr>
<td>Recurrence of cancer</td>
<td></td>
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<tr>
<td>Failure of cancer treatment</td>
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</tbody>
</table>
Complications in LLD: Psychosis

- Not unique to older adults but very quickly can become serious and dangerous, so requires immediate assessment and treatment, often in an IP setting (psychiatric or medical)
  - 4% prevalence in community-dwelling samples
  - 20 to 45% prevalence in IP psychiatric settings
- Delusional or psychotic themes vary:
  - Extreme guilt
  - Pervasive negativism to nihilism
  - Somatization
  - Paranoia
  - Jealousy
- However, hallucinations (A > V) are less prominent
- Medical complications of depression are more frequent
- Psychotic depressions tend to recur
- Risk of suicide is not necessarily higher than in non-psychotic depression, but extreme and frequent fluctuations in thinking may provoke unpredictable or impulsive acts
Complications in LLD: Cognitive Impairment

- Neuropsychologic presentation and deficits in LLD
  - Subjective complaints usually > objective findings
  - Cognitive complaints **linked temporally** to LLD
  - Common: slowed information processing, long latency to response, poor effort or motivation, impaired attention, memory retrieval deficit (learning and recall preserved), performance on tasks tends to be uneven
    - Higher cortical functions are preserved
- Dementia of Depression (formerly Pseudodementia)
  - Prodrome of dementia
  - Risk factor for dementia
Differential Diagnosis in Late-life Depression
<table>
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<tr>
<th>Medical</th>
<th>Medications</th>
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<tbody>
<tr>
<td>Metabolic</td>
<td>Antihypertensives</td>
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<tr>
<td>Endocrinologic</td>
<td>Analgesics (opiates)</td>
</tr>
<tr>
<td>Cardiopulmonary</td>
<td>CNS depressants</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Chemotherapeutics</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>Hematologic</td>
<td>Adjustment disorder</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Anxiety disorder</td>
</tr>
<tr>
<td>Cancer</td>
<td>Substance-induced</td>
</tr>
<tr>
<td>Neurological</td>
<td>Substance Abuse or</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>dependence</td>
</tr>
<tr>
<td>Primary or metastatic</td>
<td>Life circumstances</td>
</tr>
<tr>
<td>Basal ganglia disease</td>
<td>Normal grief and</td>
</tr>
<tr>
<td>Dementia</td>
<td>bereavement</td>
</tr>
<tr>
<td>Delirium</td>
<td>Social isolation/loneliness</td>
</tr>
<tr>
<td></td>
<td>Poverty or financial hardship</td>
</tr>
</tbody>
</table>
Complicated Grief and Bereavement

Complicated Grief and Bereavement

Mourning Process

Loss → Initial acute grief

Integrated Grief (health, normal)

Complicated Grief

Possible Consequences of Loss and Grief

- Mood Disorders
- Anxiety Disorders
- PTSD
- Substance Abuse/misuse
- Medical morbidity/mortality

Prevalence: 7 – 10%

Risk Factors for CG:
- Past/current Mood or Anxiety
- Multiple losses
- Lack of perceived social support
- Loss by suicide
- Sudden/violent death
- Insecure attachments (childhood)
- Enmeshed caregiving
- Concomitant life stressors

### Differential Diagnosis of Normal Acute Grief, Complicated Grief, BR-Major Depression, and PTSD

<table>
<thead>
<tr>
<th></th>
<th>Acute Grief</th>
<th>Complicated Grief</th>
<th>Major Depression</th>
<th>PTSD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Affect</strong></td>
<td>Pining, yearning, sad</td>
<td>Pining and yearning</td>
<td>Sadness and anhedonia</td>
<td>Fear of personal danger; anxiety</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>Triggered by reminders</td>
<td>↓ over time but persistent</td>
<td>Constant and chronic</td>
<td>Triggered</td>
</tr>
<tr>
<td><strong>Self-esteem</strong></td>
<td>Preserved</td>
<td>Preserved</td>
<td>Low to self-loathing</td>
<td>Preserved</td>
</tr>
<tr>
<td><strong>Associations</strong></td>
<td>Intrusive: guilt, self-blame around death</td>
<td>Thoughts/ reminders of deceased</td>
<td>Self-critical, global blaming, failure</td>
<td>Centered on event or consequences</td>
</tr>
<tr>
<td><strong>Thought Content</strong></td>
<td>Loss of meaning or purpose</td>
<td>Not integrating back to living</td>
<td>Pessimistic and ruminative</td>
<td>Avoidance</td>
</tr>
<tr>
<td><strong>Thoughts of death and dying</strong></td>
<td>Possible joining with deceased</td>
<td>Joining with deceased</td>
<td>Feels unworthy of life; unable to cope; hopeless</td>
<td>Usually absent</td>
</tr>
</tbody>
</table>
Screening in Late-life Depression
Although the USPSTF will recommend screening for depression in the general adult population, evidence of direct benefit in the general older adult population is mixed. (Grade: B)

Importantly, evidence of harm from screening was small to none.

Further, screening if implemented should be with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up.

Thus, the above suggests that targeted screening of high at-risk older adult populations could be considered in:

- Chronic medically ill
- High vascular disease and burden
- Chronic pain
- Cancer
- Direct caregivers with high stress
- Long-term care settings

US Preventive Services Task Force (2015);
Screening in LLD: When

- According to the USPSTF, the optimum interval for screening for depression in primary care is unknown; more evidence for all populations is needed to identify ideal screening intervals.
- However, for older adults, initial screening in high at-risk populations could be considered:
  - Within 2 weeks of admission to SNF
  - Within 6 months following acute MI or acute CVA
  - When evaluating for a cognitive disorder
  - When evaluating for a substance disorder or misuse
  - When evaluating new or persistent insomnia

US Preventive Services Task Force (2015);
Screening in LLD: How

- Validated and brief screening instruments are available for use in primary care
  - Remember, screening is not diagnosis.
  - Confirmatory interview is still needed.
- Instruments can be patient (self-report)/caregiver- or clinician-administered:
  - **Self-report**
    - Beck Depression Inventory-II
    - CESD-revised
    - IDS-SR
    - **PHQ-9**
    - GDS-30 (and others)
  - **Clinician-administered**
    - HAMD-17
    - IDS-C
    - MADRS
    - Cornell Scale Depression in Dementia (CSDD)
- Special considerations in older adults:
  - Validated across settings: OP / home / IP / LTC or SNF
  - Operating characteristics across levels of disability and illness severity
  - Validated across levels of cognitive impairment
  - Language or cultural sensitivity characteristics

### Screening Instruments for Depression in Older Adults

<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>
<th>Responsiveness to change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or 2 PHQ</td>
<td>97%</td>
<td>67%</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Limited</td>
</tr>
<tr>
<td>15 or 30 GDS</td>
<td>94%</td>
<td>81%</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Variable</td>
<td>Good</td>
</tr>
<tr>
<td>CSDD</td>
<td>90%</td>
<td>75%</td>
<td>Yes</td>
<td>Yes</td>
<td>Unknown</td>
<td>Yes</td>
<td>Good</td>
</tr>
<tr>
<td>CESD-R</td>
<td>93%</td>
<td>73%</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Good</td>
</tr>
<tr>
<td>9-item PHQ</td>
<td>88%</td>
<td>88%</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Unknown</td>
<td>Very Good</td>
</tr>
</tbody>
</table>

Abbreviations – CESD-R: Center for Epidemiologic Studies in Depression-Revised; CSDD: Cornell Scale for Depression in Dementia; GDS: Geriatric Depression Scale; PHQ: Patient Health Questionnaire

Key Points

**Screening Tool**
- Easy to use and acceptable to patients
- Self-administered
- Must still be confirmed by clinical interview

**Diagnosis of Major Depression**
- Requires item 1 and/or 2 checked
- Must be associated with social, occupational or other functional impairment
- DDX – exclude other psychiatric or medical conditions or effects of medications

**How to use effectively**
- Set treatment goals
- Determine degree of response
- Guide treatment interventions
- Use at regular intervals, e.g. q2weeks

**Scoring**
- 1-4: Minimal to no depression
- 5-9: Mild depression
- 10-14: Moderate depression
- 15-19: Moderately severe depression
- 20-27: Severe depression
Psychiatric Diagnostic Interview for Late-Life Depression
Psychiatric Interview for LLD

- Confirm symptoms:
  - Severity, time course, impact of function
  - **Specifically ask about and quantify suicidal ideation and psychosis**
- Past Medical Hx:
  - New vs. old problems
  - Stability vs. progression
- Medication and OTC review: number, new ones, side-effects
- Past Psychiatric hx:
  - Episode (**new/first onset**, relapse, recurrent)
  - Prior treatments (what tried; what worked/failed)
  - Prior complications (IP mgmt; SI; psychosis; social/functional)
- Family Psychiatric hx:
  - 1\textsuperscript{st} degree relatives (parents, siblings, children, grandchildren)
  - Type(s) of psychiatric illness
  - **Complications: suicide**
Psychiatric Interview for LLD

- Social hx:
  - Current relationships: spouse/SO; children; friends
  - Social network and spirituality (if applicable)
  - Nutritional status
  - Functional status: IADLs and BADLs
  - Screen for drug and alcohol use/abuse (changes)
  - Screen for access to firearms

- ROS: constitutional changes, weight, sleep, anxiety, pain, and cognitive problems
In the US, persons ≥ 65 years are now most likely of all to own a gun/firearm.

Although controversial, gun safety is now considered a matter of public health concern.

Older adults and guns:
- Grandparents as head of household
- Prevalence of cognitive impairment, depressive illness and substance misuse/abuse

Gun safety assessment: 5 L’s
- Locked?
- Loaded?
- Little children?
- Feeling Low?
- Learned owner?

Useful as screen
Imperative if doing home visits
Know local gun safety laws
- Have family remove or secure
- Call police to remove

Work-up in Late-life Depression
Physical Exam in LLD

- Vital signs, weight, intake, elimination (BM)
- Guided by comorbid conditions
- Attention to
  - Temporal wasting
  - Skin exam: turgor; edema; cellulitis; neurotic excoriations, hives, or rashes; pressure sores
  - Extremities: swelling, edema, DVT
  - Neurologic exam
    - Muscle tone, motor strength
    - Reflexes
    - Gait and balance
Mental Status Exam in LLD

- Appearance and behavior
  - Groomed, kempt, dressed vs. unkempt, malodorous, sloppy
  - Calm, appropriate vs. restless, fidgety, agitated, slowed, withdrawn
- Orientation, cognition, fund of knowledge
  - Level of alertness
  - Cognitive screen: MOCA, Mini-Cog, Clock-drawing test
  - Current events: TV shows, newspapers, books, magazines, internet
- Speech: tone, rate, rhythm
  - Hypophonic, slowed
- Language
- Thought process: linear, goal-directed, coherent vs. bradyphrenic, slowed, halting, loose associations, illogical
- Thought content: SIHI, A/VH, paranoia, delusions, hypochondriasis
- Insight and judgment:
  - Acknowledges being ill? Is depression a possibility? Wants help?
  - What does person want to do? What help will be accepted?
Exam/labs/studies in LLD

- **When** to check
  - 1\textsuperscript{st} onset in an older adult without history of MDD
  - Associated medical illnesses/recurrences
  - Use of meds with narrow therapeutic index/SE
  - New, focal or localizing neurologic signs
  - Atypical presentation
  - Lack of improvement
What to check

- **Routine**
  - Labs: BMP, CBC, RUA
  - ECG: especially if starting TCA or drug with cardiac (QTc prolongation) effects or in patients with known cardiac history

- **Elective**
  - TSH with reflex consult
  - LFTs, albumin, prealbumin (severe weight loss)
  - B12 and folate
  - Sleep study

- **Neuroimaging (structural: MRI > CT; functional: PET)**
  - Late-onset, first episode
  - Atypical presentation or time course
  - Cognitive findings >> mood symptoms
  - New, focal, or localizing neurologic finding on exam
  - Treatment-refractory illness
Treatment in Late-life Depression
Treatment in Late-life Depression

- **Non-somatic**
  - Self-directed activities: internet or app-based, bibliotherapy, community resources (city or county level)
  - Sociobehavioral
    - Groups
    - **Exercise**
  - Psychotherapy: manualized (CBT, IPT, problem-solving, behavioral activation); supportive; psychodynamic

- **Somatic**
  - CAM
    - Accupuncture
    - **Tai chi, yoga, meditation**
    - Supplements
    - Nutrients
  - **Bright light therapy**
  - Pharmacotherapy
  - Neuromodulation
    - ECT
    - TMS
    - VNS
    - Others: tDCS, tACS, CES
    - Research: MST, DBS, eCS

Choosing a treatment approach

- Understand the goals of therapy from the patient and family perspective
- Set clear and realistic targets
  - Symptom measurement based
  - Functionally relevant
  - *Aim for remission, not just response*
- Decision on which approach is predicated upon
  - severity
  - persistence
  - degree of associated suffering
  - extent of related disability
  - values expressed by patient and family
## Application of Interventions according to Severity of MDD in Older Adults

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>TRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sociobehavioral</td>
<td>++</td>
<td>+</td>
<td>Adjunct</td>
<td>Adjunct</td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>+++</td>
<td>+++</td>
<td>+/+</td>
<td>Adjunct?</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>-</td>
<td>+/+</td>
<td>+++</td>
<td>Adjunct/+++</td>
</tr>
<tr>
<td>Neuromodulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ECT</td>
<td>++</td>
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<tr>
<td>• TMS</td>
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<td>+?</td>
<td>?</td>
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<tr>
<td>• VNS</td>
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</tr>
<tr>
<td>• CES</td>
<td>+?</td>
<td>?</td>
<td>-</td>
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</tr>
</tbody>
</table>

+ to +++: strength of evidence; TRD: Treatment-resistant Depression; ?: data unclear, unavailable or preliminary
Deciding between Psychotherapy and Pharmacotherapy

**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
  - Patient resistance / stigma
  - Limited providers
  - Therapist ageism

**INDICATIONS FOR PHARMACOTHERAPY**
- Psychotherapy has failed, i.e., 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

*Often, the fullest and best sustained antidepressant response is to the combination of psychosocial therapy and pharmacotherapy*
Review entire med list including all prescribed, OTCs, supplements, vitamins, etc.

Ask specifically about alcohol, opiates, THC

Address polypharmacy
  - Stop (taper where needed)
  - Consolidate

Detox and observe when possible, safe

Reassess when there are fewer confounds
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

Espinoza R, Unutzer J, Fan M. The Effectiveness of Usual Care for Late-life Depression. Findings from Project IMPACT. 2005 Annual Meeting of the American Association for Geriatric Psychiatry, San Diego, CA
Ensuring an Adequate Medication Trial

- Discuss commonly experienced side-effects
- Be sensitive to patient concerns, e.g. weight gain, lethargy or dulling, sedation, sexual dysfunction
- Know how to intervene
  - Reduce medication dosage and slow titration
  - Change timing
- Ask the patient to repeat back what they have heard
- Bring the patient back in 1-2 weeks for a medication and symptom review
  - Ask patient to keep a log of symptoms and side-effects
  - Specifically query about suicidal ideation
  - Use a mood scale, e.g. PHQ-9 to follow response
## Commonly Available Antidepressants

<table>
<thead>
<tr>
<th>SRI Class –</th>
<th>TCA Class –</th>
<th>MAOI Class –</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>Amitriptyline</td>
<td>Isocarboxazid</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Nortriptyline</td>
<td>Phenelzine</td>
</tr>
<tr>
<td>Paroxetine (IR, CR)</td>
<td>Protriptyline</td>
<td>Tranylcypromine</td>
</tr>
<tr>
<td>Fluvoxamine (IR, CR)</td>
<td>Imipramine</td>
<td>Selegilene</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Desipramine</td>
<td></td>
</tr>
<tr>
<td>Escitalopram</td>
<td>Clomipramine</td>
<td></td>
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<tr>
<td></td>
<td>Trimipramine</td>
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</tr>
<tr>
<td></td>
<td>Maprotiline</td>
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<tr>
<td></td>
<td>Amoxapine</td>
<td></td>
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<tr>
<td></td>
<td>Doxepine</td>
<td></td>
</tr>
<tr>
<td><strong>SNRI Class –</strong></td>
<td><strong>TCA Class –</strong></td>
<td><strong>MAOI Class –</strong></td>
</tr>
<tr>
<td>Venlafaxine (IR, XR)</td>
<td>Venlafaxine (IR, XR)</td>
<td>Venlafaxine (IR, XR)</td>
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<tr>
<td>Desvenlafaxine</td>
<td>Desvenlafaxine</td>
<td>Desvenlafaxine</td>
</tr>
<tr>
<td>Duloxetine (DR)</td>
<td>Duloxetine (DR)</td>
<td>Duloxetine (DR)</td>
</tr>
<tr>
<td>Milnacipran</td>
<td>Milnacipran</td>
<td>Milnacipran</td>
</tr>
<tr>
<td>Levomilnacipran</td>
<td>Levomilnacipran</td>
<td>Levomilnacipran</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Atypical Agents –</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
</tr>
<tr>
<td>Mirtazapine</td>
</tr>
<tr>
<td>Trazodone</td>
</tr>
<tr>
<td>Nefazodone</td>
</tr>
<tr>
<td>Vilazodone</td>
</tr>
<tr>
<td>Vortioxetine</td>
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<tr>
<td>Esketamine</td>
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</tbody>
</table>

*All* are equally efficacious in LLD, though SRIs may be better tolerated in most patients.
Suggested LLD Medication Algorithm

- **Step 1:** Start with SRI or SNRI
  - Start low, go slow, but go!
  - Ensure adequate dosage and duration trial
  - Consider relevant drug-drug interactions or other medical comorbidities
- **Step 2:** In about 2-4 weeks
  - Re-evaluate, confirm adherence, and address concerns
  - Repeat symptom-based measurement scales
  - If not in therapeutic range, adjust dosage and reassess in 2 to 4 weeks
- **Step 3:** By 6 to 8 weeks
  - If not worsening, repeat step 2 and reassess in 2 to 4 weeks
  - If worsening, go to step 4
- **Step 4:**
  - If by 10-12 weeks, there is < 50% improvement, or if at step 3 there is worsening, then consider
    - A medication switch to a different class
    - An augmentation trial with psychostimulant, atypical antipsychotic, lithium, or T3/T4
    - Referral to psychotherapy
    - Referral to MH consultant (Psychologist, SW, RN, Psychiatrist) for diagnostic clarification or additional therapeutic options
Ketamine for Geriatric TRD?

- Available for use in general anesthesia since 1970
  - Off-label: pain (analgesia), agitation
  - Known to have abuse potential
  - Side-effects: neurotoxicity, cognitive dysfunction, CV (↑HR, ↑BP), psychomimetic, DI, uropathy
- IV ketamine shown to have rapid-acting antidepressant efficacy in treatment-resistant depression
  - Subanesthetic dosing: 0.5mg/kg over 40 min
  - Single or serial infusions
  - Acute response rates of 60-70%
  - Durability of response remains an open question
  - No RCTs in older adult populations; small case series or anecdotal reports
Intranasal Esketamine (Spravato®) FDA approved March 2019

- only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS)
  - Must be given in a controlled setting
  - Monitored for 2 hours post-spray
  - Cannot drive until next day “after a restful sleep”
- Not yet evaluated in older adult populations
- Used adjunctively
- Must have TRD

Table 1: Recommended Dosage for Spravato

<table>
<thead>
<tr>
<th>Phase</th>
<th>Weeks 1 to 4:</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction Phase</td>
<td>Day 1 starting dose: 56 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Administer twice per week</td>
<td>Subsequent doses: 56 mg or 84 mg</td>
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<tr>
<td>Maintenance Phase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weeks 5 to 8:</td>
<td>Administer once weekly</td>
<td>56 mg or 84 mg</td>
</tr>
<tr>
<td></td>
<td>Week 9 and after:</td>
<td>56 mg or 84 mg</td>
</tr>
<tr>
<td></td>
<td>Administer every 2 weeks or once</td>
<td></td>
</tr>
<tr>
<td></td>
<td>weekly*</td>
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</tbody>
</table>

* Dosing frequency should be individualized to the least frequent dosing to maintain remission/response.
Medication Outcomes in Medical Comorbidity

- Neurodegenerative disorders
  - Alzheimer
  - Parkinson
- Neurological disorders
- Cerebrovascular disorders
  - Vascular depression
  - Post-stroke depression
- Cardiovascular disorders
- Renal disease
- Hepatic disease
- Cancer
- Endocrinopathies
- Immunologic disorders
Neuromodulation for LLD

- ECT – Electroconvulsive Therapy
  - Gold standard for TRD including in older adults
  - PRIDE study of Venlafaxine plus Lithium
- VNS – Vagus Nerve Stimulation
- TMS – Transcranial Magnetic Stimulation
  - rTMS vs dTMS
  - iTBS vs cTBS
- CES (Cranial Electrostimulation) – tDCS, tACS
- Research: DBS, MST, eCS
Although LLD is not a normal consequence of aging, the burden of LLD is real and significant.

Timely recognition is important to avoid unnecessary suffering, worsening overall health outcomes and complications.

The spectrum of depressive disorders and challenges to diagnosis should be kept in mind when evaluating an older adult.

Screening can be used effectively and efficiently:

- Always include an assessment for suicidal ideation, psychosis and cognitive impairment.

Treatment of LLD includes an assessment of patient goals and values.

While medications are equally efficacious, systematic care is more essential to addressing the burden of depressive illness.

Psychotherapy is under utilized in LLD.

Among neuromodulation interventions, ECT remains the gold standard, especially for TRD and life-threatening LLD.