Late Life Major Depression: Treatment Options

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Disclosure

• Funded by HRSA Geriatric Workforce Enhancement Program (GWEP)
  – Mid-Atlantic Geriatric Workforce Education Program (PI: Schulz; HRSA U1Q HP028736)
    University of Pittsburgh
Major Depression

- Sadness / depressed mood
- Loss of pleasure (anhedonia)
- Impaired sleep
- Impaired appetite
- Low energy
- Restlessness or looking ‘slowed down’
- Poor concentration
- Feelings of worthlessness or guilt
- Thoughts of death or suicidal thoughts
Major Depression

- 2 week duration minimum
- Emotional distress or functional impairment

*Note:* Presumed causality is NOT part of the diagnostic process!
MAJOR DEPRESSION

• Treatable in Primary Care:
  – UNIPOLAR Major Depression

• Punt to Psychiatry:
  – BIPOLAR Major Depression
  – Major Depression comorbid with Substance Abuse
  – Major Depression comorbid with Schizophrenia
Case Study -- Mrs. Jones

79 yo WF widow who lives alone. Her only chronic condition is well controlled hypertension. The daughter is concerned that the patient is not her normal self. She has given up most of her recreational & social activities, such as reading and playing bridge. She is behind in paying her bills. The patient reports that everything is such an effort now. She endorses poor sleep and low energy. You note a 5 pound weight loss.
Case Study  -- Mrs. Jones

What is the highest priority in terms of ruling out a diagnosis?
(1) Dementia (Major Neurocognitive Disorder) with or without depressed mood.
(2) Mild Cognitive Impairment (Mild Neurocognitive Disorder) with or without depressed mood.
(3) Delirium with or without depressed mood.
(4) Major Depression r/o Neurocognitive D/O
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3. Delirium with or without depressed mood.
4. Major Depression r/o Neurocognitive D/O
Case Study -- Mrs. Jones

Based on your additional assessment, you determine that the patient is not delirious and demonstrates only mild impairment in memory. You are concerned that her impaired function is due to depression.
Case Study -- Mrs. Jones

The most efficient way to screen for major depression would be to:

(1) Refer to psychiatry

(2) Screen for depressed mood and anhedonia (lack of enjoyment/motivation) using the PHQ-2

(3) Screen for all symptoms of Major Depression using the PHQ-9
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PHASES OF TREATMENT

• ACUTE

• CONTINUATION

• MAINTENANCE
PHASES OF TREATMENT

ACUTE TREATMENT

• **Required Elements:**
  – Pharmacotherapy ± Adjunct Meds
  – Psycho-Education

• **Desirable but Optional elements:**
  – Psychotherapy
Pharmacotherapy

• General Principles

- Treat to **full remission** of symptoms
- All antidepressants are equally effective
- Side effects appear early & usually transient
- Choose medication based on tolerability
- Monitor side effects and risk of suicide
Pharmacotherapy

- Early frequent patient contact is needed
  - to monitor side effects
  - to monitor/encourage compliance
  - to monitor response
  - to re-assess suicide risk
- Age alone does not dictate medication dosing
- A therapeutic trial at a particular dose of medication is at least 6 weeks in duration
- Failure to achieve FULL remission of sx indicates need for addition or change in tx
RECOMMENDATIONS

- Be comfortable with 3 antidepressants
  - (e.g., dosing strategies & side effect profiles)
- Work aggressively for full remission of depressive symptoms.
- Refer to psychiatry if a patient fails to achieve a **full remission** of symptoms after 2-3 **therapeutic trials** of an antidepressant.
- Provide education about illness and treatment
- Always offer/encourage referral for therapy.
- Monitor for suicidality; have an emergency plan.
ANTIDEPRESSANTS

- Tricyclic antidepressants (TCAs)
- Monoamine oxidase inhibitors (MAOIs)
- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin-norepinephrine reuptake inhibitors (SNRIs)
- Atypical agents
# ANTIDEPRESSANTS

<table>
<thead>
<tr>
<th>SSRI</th>
<th>SNRI</th>
</tr>
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<tbody>
<tr>
<td>Prozac (fluoxetine)</td>
<td>Effexor (venlafaxine)</td>
</tr>
<tr>
<td>Luvox (fluvoxetine)</td>
<td>Pristiq (desvenlafaxine)</td>
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<tr>
<td>Paxil (paroxetine)</td>
<td>*Cymbalta (duloxetine)</td>
</tr>
<tr>
<td>Zoloft (sertraline)</td>
<td>Fetzima (levomilnacipran)</td>
</tr>
<tr>
<td>Celexa (citalopram)</td>
<td>ATYPICAL</td>
</tr>
<tr>
<td>*Lexapro (escitalpram)</td>
<td>*Remeron (mirtazapine)</td>
</tr>
<tr>
<td>Viibryd⁺ (vilazodone)</td>
<td>Wellbutrin (buprorion)</td>
</tr>
<tr>
<td>Brintellix++] (vortioxetine)</td>
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⁺ 5HT₁A partial agonist; ++5HT₃ antagonist & 5HT₁A agonist
ANTIDEPRESSANTS

Common to All: Risk of Hypomania/Mania

SSRI: nausea, diarrhea, bleeding, hyponatremia, serotonin syndrome

SNRI: nausea, diarrhea, bleeding, hyponatremia, serotonin syndrome, PLUS orthostatic BP, hypertension, closed angle glaucoma

Bupropion: activation/anxiety, tremor, seizure; least likely to cause weight gain

Mirtazapine: sedation, weight gain, increased triglycerides, low incidence hyponatremia
SCREEN FOR HX OF MANIA

• Use of an antidepressant in a patient with Bipolar D/O, without concomitant use of a mood stabilizer, can induce mania.

• Screening questions for Mania: Unique period (lasting 4+ days) of abnormal elevated/irritable mood, of increased energy/decreased sleep, and/or of increased activity.
RISK OF SUICIDE

• Delayed onset of treatment benefit ....patients can get worse before getting better.
• Treatment might not work for that particular patient.
• **FDA Black Box:** All antidepressants may increase risk of suicidal thoughts or behavior in children, adolescents, & young adults.

| Table 1. Drug-Placebo Difference in # Cases of Suicidality per 1000 Patients |
|--------------------------|---------------------------------|
| Age Range    | Increases Compared to Placebo     |
| <18          | 14 additional cases              |
| 18-24        | 5 additional cases               |
|              | **Decreases Compared to Placebo** |
| 25-64        | 1 fewer case                     |
| ≥65          | 6 fewer cases                    |
Case Study -- Mrs. Jones

You have diagnosed Mrs. Jones with major depression. As the presence of depression is a major risk factor for suicide, you inquire whether she has had thoughts that life is not worth living. After a delay, she response ‘yes’.
Your next step(s) is/are (choose all that apply):
(1) Ask if she has any thoughts of killing herself.
(2) Ask if she has a suicide plan.
(3) Ask if she has the means to carry through her plan.
(4) Ask if she has already tried to kill herself.
(5) All of the above.
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(5) All of the above.
Case Study  --  Mrs. Jones

Mrs. Jones endorses suicidal ideation with a plan to overdose.

She refuses to go to the ER for a psychiatric evaluation.

At this point, your best option is... (Choose ONE).
Case Study -- Mrs. Jones

(1) Discharge her home with instructions to get an appointment with a psychiatrist.

(2) Call the local crisis service to have a team come to meet with her.

(3) Discharge her to home after the daughter agrees to secure all medication.

(4) Discharge her home with a follow up with you in 3 days.

(5) Admit to local hospital for dehydration and order an inpatient psychiatric consult.
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PROGNOSIS

Major depression is a recurrent illness but full inter-episode recovery is the norm.

~ 60% of patients who have one episode of major depression will have a 2\textsuperscript{nd} episode.

~ 90% of patients who have 3 episodes of major depression will have a 4\textsuperscript{th} episode.

~ 2/3 of patients have full recovery between episodes.

~ 1/3 of patients have partial recovery between episodes and are at high risk for recurrence.
Case Study  --  Mrs. Jones

You have successfully managed Mrs. Jones’ depression. She is currently taking citalopram 20mg/d.

When you see her for a routine visit months later, she wants to stop the citalopram because she has been doing so very well for the last 4 months.
At this time, you advise the patient that, based on the available research, her best option is:

A) to stop the medication because there is no signs/symptoms of depression

B) to continue the medication for at least another 8 months, then stop.

C) to remain on the medication for the rest of her life.
At this time, you advise the patient that, based on the available research, her best option is:

A) to stop the medication because there is no signs/symptoms of depression

B) to continue the medication for at least another 8 months, then stop.

C) to remain on the medication for the rest of her life.
PHASES OF TREATMENT

**Acute Phase**: From onset of treatment to resolution of ALL symptoms.

**Continuation Phase**: 6-9 months AFTER resolution of ALL symptoms; **patients advised to remain on medications**.

**Maintenance Phase**: Prevention of relapse after 6-9+ months symptom free.

*APA Practice Guidelines for Depression 2000*
If first lifetime episode, uncomplicated -- taper &
discontinue antidepressant after completion of
continuation phase (at least 6 months of ‘wellness’).

If 3rd or more lifetime episode or at least one episode with
significant suicidality and/or functional impairment --
indefinite continuation of ‘full dose’ antidepressant
regime.

APA Practice Guidelines for Depression 2000
Continued treatment with antidepressant medication for 2 years prevented recurrence of major depression in subjects aged 70+ years regardless of single vs recurrent. (NNT=4)

However, subjects with greater medical burden received less benefit from ongoing treatment.

Adjunct Medications

- ANXIETY
- INSOMNIA
DEPRESSION + ANXIETY

Co-morbid anxiety common:
28% with current GAD
9% with Panic Disorder

Co-morbid anxiety associated with
more severe somatic symptoms
increased suicidal ideation
increased suicide rate
worse short term treatment response

Lenze 2000 Am J Psych; DeLuca 2005 Int J of Geriatric Psych
DEPRESSION + ANXIETY

At risk of agitation on SSRI/SNRI—start low
Short term use of Benzodiazepines may be needed
  Avoid long acting formulations (e.g., valium, clonazepam) $\rightarrow$ ↑↑ risk of sedation and falls.
  Avoid quick onset formulations (e.g., alprazolam) $\rightarrow$ ↑ addiction potential.
Typically, use lorazepam (due to ‘ease’ of metabolism and relatively short half life) e.g., 0.25-1mg qday-t.i.d.
DEPRESSION WITH INSOMNIA

Sleep as both biology and behavior

Educated/promote good sleep hygiene
Consistent bed and wake up times
Limited naps (< one x 30 min nap)
Exercise in the mornings
Limited caffeine
Decrease light exposure in the evening
Out of bed if not sleeping (‘dark activities’) 
Bedroom for sex and sleep
DEPRESSION WITH INSOMNIA

Sleeping pills: intended for short term use
Side effects
• Motor impairment
• Cognitive impairment
• Complex sleep behaviors e.g., sleep driving
• Dependency
• Withdrawal
Generally for sleep initiation.
Except for zolpidem CR, eszopiclone, suvorexant which are helpful for sleep maintenance.
DEPRESSION WITH INSOMNIA

- Benzodiazepines: lorazepam 0.25-1mg, temazepam
  SE: confusion, falls
- Trazodone: 25-100mg
  SE: orthostatic BP, falls, priapism
- Zolpidem (Ambien, Ambien CR):
  ↓ in females 5mg or 6.25mg CR
DEPRESSION WITH INSOMNIA

- **Eszopiclone (Lunesta):** 1mg initial dose. 2mg max dose in elderly, severe hepatic impairment, or with CYP3A4 inhibitor (ketoconazole, diltiazem)
  - SE: unpleasant taste, dry mouth, respiratory infection, headache

- **Ramelteon (Rozerem):** 8mg
  - Appropriate for long-term use, decreased addiction risk
  - Levels ↑ by CYP3A4 inhibitor (Ketoconazole), CYP2C9 inhibitor (Fluconazole), Donepezil & Doxepin
  - SE: nausea (1%), insomnia (1%), ↓ testosterone, ↑ prolactin
DEPRESSION WITH INSOMNIA

- Zaleplon (Sonata): 5mg max dose for elderly and underweight

- Suvorexant (Belsomra) [orexin receptor antagonist, regulates the sleep-wake cycle]
  
  - 5mg initial dose; may increase to 10mg
  
  - ↑ levels with obesity and in women

  - 5mg max dose with moderate CYP3A inhibitors (Diltiazem)

  - Do not use in severe hepatic impairment or with strong CYP3A inhibitors

  - May affect digoxin concentrations
Psycho-Education

Key points

– Depression as medical illness (patient in sick role)
– Patient is not to blame
– Affects medical health & ability to function
– Risk of suicide: transmission through generations
– People can and do get better: Treatment works!
– Management of side effects
– Three stages of treatment
– Role of psychotherapy
– Importance of behavioral activation
PSYCHOTHERAPY

Appropriate as monotherapy for mild depression and as an adjunct to medication in moderate to severe cases.

Structured, brief psychotherapies are preferred and more likely to be reimbursed by insurance companies.

APA Practice Guidelines for Depression 2000; Bradbury 2008
**Cognitive Therapy (CBT):** Identify and correct core beliefs that lead to and/or reinforce depression; alter behaviors that lead to and/or reinforce depression.

**Problem Solving Therapy (PST):** Reduce learned helplessness by teaching an explicit process of solving problems. Includes 6 problem solving steps plus behavioral activation.

**Interpersonal Therapy (IPT):** Focus on 1 of 4 ‘depressogenic’ areas: grief, role transitions, role disputes, interpersonal deficits that lead to isolation.
ECT

• Still the most effective treatment for depression
• ECT Is Not A “Last Ditch Effort”…Primary Indications for ECT Referrals

• ECT Treats More than Depression..... Multiple Diagnostic Indications

• No Absolute Contraindications to ECT.... Only Relative Contraindications

• ECT is Safe and Effective in Many Populations.... Sometimes First Line Treatment
TMS

• Non-invasive
• No anesthesia or sedation
• Outpatient procedure easily performed in psychiatrists’ offices
• 37-minute daily procedure (3000 pulses)
• 4-6 week treatment course
• Antidepressant medication monotherapy may be used for maintenance
• Cost $6000-8000
TMS - Safety

• Less then 5% discontinuation rate due to adverse events in clinical studies
• Most common adverse event related to TMS is localized pain or discomfort at or near the treatment area during active TMS
• No systemic side effects
• No adverse effect on cognition
• Post marketing experience confirms a rare risk of seizure with TMS treatment
• No seizures reported during NeuroStar clinical studies (10,000 treatments)
• <0.003% per treatment, <0.1% per patient
  – Approximately 420,000 treatments to date in post-marketing experience
• Long-term safety demonstrated in 6 months follow-up
• For TMS Referral 412-246-5063
Summary

• Treatment of late-life depression should be to remission
• Remember Acute, Continuation and Maintenance Phases of treatment
• Assess for suicide all along particularly during the early phase of treatment