Late-Life Depression

- Depression is **NOT A NORMAL CONSEQUENCE OF AGING**
    - Sadness, grief, normal responses to bereavement etc. which are more common in late life than early life
    - Occasionally is a prodrome for other illness like stroke, DM, cancer, hypoTH, CAD
- Often unrecognized
    - More likely to go unrecognized in Black, Hispanic patients, male patients
    - Difficult to dx in patients with other psychiatric comorbidities
        - Depression & Anxiety: pts get a lot of anxiolytic, hypnotic and pain meds, depression can be attributed to medication side effects…
    - Even when diagnosed it often goes untreated
- Late life depression tends to be recurrent and persistent
- Prevalence of depression in adults > 65 y/o is 2-10%
    - Varies depending upon the study, cultural context, method of diagnosis, etc
- Prevalence of depression in hospitalized adults >65 is roughly 30-40%
    - 40% for patients with stroke, MI, cancer
- Prevalence of depression up to 50% of nursing home residents are depressed
- Scope of depression in the oldest old (85+ y/o) likely underestimated –not enough studies in that population

Late-Life Depression Impacts Medical Morbidity and Mortality

- Post-MI: four-fold increase in death
- Post-stroke: 3.4 times more likely to die within 10 years
- Depression at time of admission to nursing home ↑ one-year mortality (does not quantify)
- Depressed patients have increased rates of in hospital death (odds ratio of 7.8 after controlling for severity of illness)

- Late-life depression is associated with increased number of ED and office visits, drug use, cost of prescription and OTC meds, increased incidence of substance use disorder, increased overall cost of medical care
- **Increased risk of suicide!**
    - **Older adults make up 13% entire US population but account for 24% of completed suicides**
    - They attempt less often than younger pts, but are more successful at completion
    - Older adult men have highest rate: 28.9/100,000
    - White men 85+ have highest rate of completed suicides (55/100,000)
    - **Most older adult suicide victims were in their first episode of depression and had seen a physician within the last month of life***
        - **Risk factors for this:** clinical sx of hopelessness, insomnia, agitation, restlessness, impaired concentration, active psychosis, SUD, untreated chronic pain
        - **Terminal or worsening illness**
        - **Chronic disease comorbidities**
        - **Widowhood, social isolation**
        - **Personality disorders**
        - **Prior attempt and family history**

Risk Factors for Developing Late-Life Depression

- Female
    - May be due to how we examine for depression
    - Men tend to present with anger, irritability, anhedonia, withdrawal, and substance use disorders related to depression—more likely to present this way
- Isolated
- Not married (widowed, divorced, separated, etc,)
- Lower socioeconomic status
- Chronic conditions
    - Physical illness
        - Recent onset
        - Greater severity of illness
        - Functional impairment and mobility impairment
        - Pain related to the illness
        - Number of illnesses
- Chronic Pain (poorly treated)
- Insomnia
    - Sleep disorders are associated with remission of previously controlled depression in late life
- Functional impairment
- Cognitive impairment
    - Chicken or egg? (Re: "association with dementia")
- Even if pt has "reactive depression"—response to adverse events, we should still treat as MDD be reactive depression is responsive to treatment

Late-Life Depression, Cognitive Impairment, and Dementia

- LLD Increases risk of developing dementia
    - Metanalysis of 23 prospective community based observational studies, 49,000 pts, no dementia at baseline, followed for 5 years
    - Risk of all cause dementia is greater in patients with late life depression than non-depressed controls
    - Specifically seems to be Alzheimer's type, vascular (vascular > AZ)
    - Another retrospective study of >13,500 medical records reviewed, pts without dementia at baseline over 6 years risk of developing dementia was 70% higher in patients with late life depressive sx
- **Unclear whether this is a prodrome or acts as an independent risk factor**
- Hypothesized pathogenesis
    - Damage specifically to **frontal subcortical circuitry**
        - Striatopallido-thalamo-cortical pathways
        - Left prefrontal cortex
    - **Neurodegeneration**
        - Cerebrovascular disease
            - **Depression is often subclinical ("minor depression")**
            - Microvascular lesions, chronic ischemic changes, generalized atrophy
            - Increased ventricular to volume ratios), especially periventricular lesions

Late Life Depression Syndromes

Important to note that many older adults may have clinically significant of depression, but so not fit the DSM-5 criteria for major depressive disorder (Minor depression re: below)

- **Major depression**
  - DSM 5 Criteria: identical for older and younger patients

DSM-5 diagnostic criteria for a major depressive episode

A. 5 (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least 1 of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
NOTE: Do not include symptoms that are clearly attributable to another medical condition.
1) Depressed mood most of the day, nearly every day, as indicated by either subjective report (eg, feels sad, empty, hopeless) or observations made by others (eg, appears tearful). (NOTE: In children and adolescents, can be irritable mood.)
2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
3) Significant weight loss when not dieting or weight gain (eg, a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (NOTE: In children, consider failure to make expected weight gain.)
4) Insomnia or hypersomnia nearly every day.
5) Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6) Fatigue or loss of energy nearly every day.
7) Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8) Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by their subjective account or as observed by others).
9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
C. The episode is not attributable to the direct physiological effects of a substance or to another medical condition.
NOTE: Criteria A through C represent a major depressive episode.
NOTE: Responses to a significant loss (eg, bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgement based on the individual's history and the cultural norms for the expression of distress in the context of loss.
D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
E. There has never been a manic or hypomanic episode.
NOTE: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.
Specify:
With anxious distress
With mixed features
With melancholic features
With atypical features
With psychotic features
With catatonia
With peripartum onset
With seasonal pattern

  - Tends to be more chronic and relapse more in late life patients, and risk of relapse is higher in pts with lots of comorbidities

- **Dementia Syndrome of Depression**
    - Cognitive impairment that manifests within the context of depression dx
    - Previously named “Pseudodementia”
        - Conventionally defined as a depression syndrome with cognitive impairment symptoms, in which the patient’s cognitive impairment and depression resolve with antidepressant use
        - New evidence indicates that despite improvement in these symptoms with conventional depression treatment, patients who present with cognitive impairment and depressed mood late in life are at higher risk for major neurocognitive disorder
            - **A large percentage of patients with “reversible depression” will progress to irreversible cognitive impairment within 2-3 years of disease onset**
        - Patients who do not respond to initial trial of SSRI (specifically Lexepro) are at higher risk to develop major neurocognitive disorder
    - Regardless, patients with cognitive impairment SECONDARY TO MAJOR DEPRESSION MAY BE AT HIGHER RISK OF CONVERTING TO AN IRREVERSIBLE DEMENTIA SYNDROME

- **Vascular Depression**
    - Cerebrovascular disease increases risk of late life depression
    - **Post Stroke Depression: occurs after a CVA**
        - Patients with left prefrontal cortex lesions tend to have increased frequency and severity of post stroke depression
        - Highest risk is within the first 2 years from CVA
        - Peak incidence occurs within first 3-6 mos
    - **Vascular Depression: occurs in tandem with chronic ischemic changes in the brain**
        - Newer recognized disease process
            - Positive MRI findings correlated with older age of depression onset, vascular comorbidity, greater psychomotor slowing or parkinsonism, anhedonia, functional impairment, less psychosis
            - Patients with late onset depression who also have CVD factors had more cognitive impairment disability, psychomotor retardation, less insight into their illness than those without cerebrovascular disease
        - Nuanced Treatment
            - May respond to TCAs, older antidepressants, combination therapies, ECT more so than traditional treatment

- **Persistent depressive disorder (dysthymia):**
  - DSM 5 criteria same for all age adults

DSM-5 diagnostic criteria for persistent depressive disorder (dysthymia)

A. Depressed mood for most of the day, for more days than not, as indicated either by subjective account or observation by others, for at least two years.
NOTE: In children and adolescents, mood can be irritable and duration must be at least one year.
B. Presence, while depressed, of two (or more) of the following:
1) Poor appetite or overeating.
2) Insomnia or hypersomnia.
3) Low energy or fatigue.
4) Low self-esteem.
5) Poor concentration or difficulty making decisions.
6) Feelings of hopelessness.
C. During the two-year period (one year for children or adolescents) of the disturbance, the individual has never been without the symptoms in Criteria A and B for more than two months at a time.
D. Criteria for a major depressive disorder may be continuously present for two years.
E. There has never been a manic episode or a hypomanic episode, and criteria have never been met for cyclothymic disorder.
F. The disturbance is not better explained by a persistent schizoaffective disorder, schizophrenia, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder.
G. The symptoms are not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication) or another medical condition (eg, hypothyroidism).
H. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
NOTE: Because the criteria for a major depressive episode include four symptoms that are absent from the symptom list for persistent depressive disorder (dysthymia), a very limited number of individuals will have depressive symptoms that have persisted longer than two years but will not meet criteria for persistent depressive disorder. If full criteria for a major depressive episode have been met at some point during the current episode of illness, they should be given a diagnosis of major depressive disorder. Otherwise, a diagnosis of other specified depressive disorder or unspecified depressive disorder is warranted.
Specify if:
With anxious distress
With mixed features
With melancholic features
With atypical features
With mood-congruent psychotic features
With mood-incongruent psychotic features
With peripartum onset
Specify if:
In partial remission
In full remission
Specify if:
Early onset: If onset is before 21 years.
Late onset: If onset is at age 21 years or older.
Specify if (for most recent two years of persistant depressive disorder):
With pure dysthymic syndrome: Full criteria for a major depressive episode have not been met in at least the preceding two years.
With persistent major depressive episode: Full criteria for a major depressive episode have been met throughout the preceding two-year period.
With intermittent major depressive episodes, with current episode: Full criteria for a major depressive episode are currently met, but there have been periods of at least eight weeks in at least the preceding two years with symptoms below the threshold for a full major depressive episode.
With intermittent major depressive episodes, without current episode: Full criteria for a major depressive episode are not currently met, but there has been one or more major depressive episodes in at least the preceding two years.
Specify current severity:
Mild
Moderate
Severe

  - Older patients who present with late onset dysthymia have more CVD
  - Higher risk of “double depression” (MDD) and tend to be treatment resistant

- **Minor Depression**
  - Pts do not meet diagnostic criteria for MDD, PDD, but have significant pathology (not enough sx, not enough duration)

Diagnostic criteria for minor depression

We suggest diagnosing minor depressive episodes according to all of the following criteria (A through F).
A. Two to four of the following symptoms have been present during the same two-week period:
1. Dysphoria – Depressed mood most of the day, nearly every day 2. Anhedonia – Markedly diminished interest or pleasure most of the day, nearly every day 3. Significant appetite or weight change 4. Insomnia or hypersomnia nearly every day 5. Psychomotor agitation or retardation (observable by others) 6. Anergia – Fatigue nearly every day 7. Thoughts of worthlessness or inappropriate guilt nearly every day 8. Impaired concentration or memory nearly every day 9. Recurrent thoughts of death or suicide, or suicide attempt
B. At least one of the symptoms includes dysphoria or anhedonia
C. The symptoms cause clinically significant distress of psychosocial impairment
D. The symptoms are not due to the physiologic effects of a substance, medication, or general medical condition
E. Persistent depressive disorder (dysthymia) and cyclothymic disorder are not present
F. The mood disturbance does not occur exclusively during a psychotic disorder

These criteria for minor depression are similar to the criteria that are used in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) for the diagnosis, "Other specified depressive disorder, depressive episode with insufficient symptoms" (ie, the depressive episode is characterized by an insufficient number of symptoms to meet criteria for major depression).

Reference:

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), American Psychiatric Association, Arlington 2013.

  - Can progress to MDD
  - Older adults more likely to have minor than major depression
  - Important because older pts with minor depression develop suicidality at comparable rates to those with MDD
  - Burden upon medical morbidity and mortality is comparable to that of MDD in older adults as well

- **Depression in AZD**
    - Specific diagnostic DSM-5 criteria (table below)

Depression in Alzheimer-type dementia

A. Three or more of the following symptoms, present during the same two-week period, and representing a change from a previous level of functioning. Either item one or item two must be included:
1. Clinically significant depressed mood
2. Decreased positive affect or pleasure in response to social contacts and usual activities
3. Social isolation or withdrawal
4. Disturbed appetite
5. Disturbed sleep
6. Psychomotor retardation or agitation
7. Irritability
8. Fatigue or loss of energy
9. Feelings of worthlessness, hopelessness, or inappropriate guilt
10. Recurrent thoughts of death or suicidal ideation, plan, or any attempt
B. Meets criteria for Alzheimer-type dementia
C. Depressive symptoms cause clinically significant distress or disruption in function
D. Symptoms do not occur exclusively during an episode of delirium
E. Symptoms are not due to a direct physiologic effect from a substance (medication or drug of abuse)
F. Symptoms are not better accounted for by another condition
Specify if:
Co-occurring onset: onset antedates or co-occurs with AD symptoms
Post-AD onset: onset occurs after AD diagnosis
Specify if:
With psychosis of AD
With other significant behavioral signs or symptoms
With past history of mood disorder

AD: Alzheimer disease.

UpToDate®

    - Of note, depression is a common complication in most dementias

Diagnosing Late-Life Depression

- Can be hard to do
    - Concurrent medical illnesses with overlapping sx can muddy the waters
        - Consider when mood or somatic sx out of proportion to expected
        - Poor response to treatment
        - Poor motivation to participate in treatment
        - Lack of engagement with care team
    - Medication side effects (polypharmacy)
    - Impaired communication
    - Multiple somatic complaints
    - Not enough time in the exam room to address given multiple chronic diseases requiring attention
    - Therapeutic nihilism (skeptical of therapeutic agents being able to help)
    - Pt perceived stigma, reluctant to admit there is a problem
- Diagnosis in frail, Oldest-Old (age 85+ years)
    - Limited studies in this age group
        - Think about this when change in mood or interest 2+ weeks
        - Non-physical sx
        - Physical sx that follow onset of depressed mood and are out of proportion to what would be expected with known comorbidities
        - Social regression or incapacity
        - Reassuring against depression: pt continue to respond to affection from family and caregivers, keeps sense of humor, looks forward to visitors, accepts assistance in care

Screening instruments

- Self vs. Interviewer reports
- **PHQ2** is 100% sensitive in adults >65 (77% specific)
    - Specificity increased with age, male gender, varied amongst races and ethnic groups
- **Geriatric depression scale** (2/5 is considered positive)
- **PHQ9** covers all DSM5 criteria and has been shown to be a reliable measure in large population study of older adults
    - Studies suggest this is particularly good for monitoring response to treatment in primary care setting
- **Cornell Depression Scale for Dementia**
    - Observer and informant-based information
    - Helpful in cognitively impaired older adults
- **Center for Epidemiologic Studies Depression scale**
    - Commonly used in community studies and primary care settings

Screening instruments for late-life depression for use in primary care

	Sensitivity percent	Specificity percent	Inpatient	Outpatient	Physically ill	Cognitively impaired
Two-question screen	97	67	Unknown	Yes	Unknown	No
Geriatric Depression Scale (5-item)	94	81	Yes	Yes	Yes	Unknown
Patient Health Questionnaire-9 (9-item)	88	88	Unknown	Yes	Yes	Unknown
Cornell Scale for Depression in Dementia (19-item)	90	75	Yes	Yes	Unknown	Yes
Center for Epidemiologic Studies - Depression Scale (20-item)	93	73	No	Yes	Unknown	No

PHQ-2, 9

Over the last 2 weeks, how often have you been bothered by any of the following problems?	**Not at all**	**Several Days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. 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	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3

Total Score: 1-4 Minimal depression; 5-9 Mild depression; 10-14 Moderate depression; 15-19 Moderately severe depression; 20-27 Severe depression

Geriatric Depression Scale

Geriatric Depression Scale (Long Form)

Patient's Name:_____ Date:_____

Instructions: Choose the best answer for how you felt over the past week.

No.	Question	Answer	Score
1.	Are you basically satisfied with your life?	YES / NO	
2.	Have you dropped many of your activities and interests?	YES / NO	
3.	Do you feel that your life is empty?	YES / NO	
4.	Do you often get bored?	YES / NO	
5.	Are you hopeful about the future?	YES / NO	
6.	Are you bothered by thoughts you can t get out of your head?	YES / NO	
7.	Are you in good spirits most of the time?	YES / NO	
8.	Are you afraid that something bad is going to happen to you?	YES / NO	
9.	Do you feel happy most of the time?	YES / NO	
10.	Do you often feel helpless?	YES / NO	
11.	Do you often get restless and fidgety?	YES / NO	
12.	Do you prefer to stay at home, rather than going out and doing new things?	YES / NO	
13.	Do you frequently worry about the future?	YES / NO	
14.	Do you feel you have more problems with memory than most?	YES / NO	
15.	Do you think it is wonderful to be alive now?	YES / NO	
16.	Do you often feel downhearted and blue?	YES / NO	
17.	Do you feel pretty worthless the way you are now?	YES / NO	
18.	Do you worry a lot about the past?	YES / NO	
19.	Do you find life very exciting?	YES / NO	
20.	Is it hard for you to get started on new projects?	YES / NO	
21.	Do you feel full of energy?	YES / NO	
22.	Do you feel that your situation is hopeless?	YES / NO	
23.	Do you think that most people are better off than you are?	YES / NO	
24.	Do you frequently get upset over little things?	YES / NO	
25.	Do you frequently feel like crying?	YES / NO	
26.	Do you have trouble concentrating?	YES / NO	
27.	Do you enjoy getting up in the morning?	YES / NO	
28.	Do you prefer to avoid social gatherings?	YES / NO	
29.	Is it easy for you to make decisions?	YES / NO	
30.	Is your mind as clear as it used to be?	YES / NO	
		TOTAL	

This is the original scoring for the scale: One point for each of these answers.
Cutoff: normal-0-9; mild depressives-10-19; severe depressives-20-30.

1. NO	6. YES	11. YES	16. YES	21. NO	26. YES
2. YES	7. NO	12. YES	17. YES	22. YES	27. NO
3. YES	8. YES	13. YES	18. YES	23. YES	28. YES
4. YES	9. NO	14. YES	19. NO	24. YES	29. NO
5. NO	10. YES	15. NO	20. YES	25. YES	30. NO

Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res* 1983; 17:37-49.

Cornell Depression Scale

Depression: Cornell Scale for Depression in Dementia

Resident: _____ Room #: _____ Date: _____

Scoring system: a = unable to evaluate 0 = absent 1 = mild or intermittent 2 = severe

Mood-related Signs	a	0	1	2
Anxiety: anxious expression, ruminations, worrying	☐	☐	☐	☐
Sadness: sad expression, sad voice, tearfulness	☐	☐	☐	☐
Lack of reactivity to pleasant events	☐	☐	☐	☐
Irritability: easily annoyed, short-tempered	☐	☐	☐	☐
Behavioral Disturbance	**a**	**0**	**1**	**2**
Agitation: restlessness, hand wringing, hair pulling	☐	☐	☐	☐
Retardation: slow movement, slow speech or slow reactions	☐	☐	☐	☐
Multiple physical complaints (Score 0 if GI symptoms only.)	☐	☐	☐	☐
Loss of interest: less involved in usual activities (Score only if change occurred acutely, e.g., in less than one month.)	☐	☐	☐	☐
Physical Signs	**a**	**0**	**1**	**2**
Appetite loss: eating less than usual	☐	☐	☐	☐
Weight loss (Score 2 if greater than 5 lbs. in one month.)	☐	☐	☐	☐
Lack of energy: fatigues easily, unable to sustain activities (Score only if change occurred acutely, e.g., in less than one month.)	☐	☐	☐	☐
Cyclic Functions	**a**	**0**	**1**	**2**
Diurnal variation of mood: symptoms worse in the morning	☐	☐	☐	☐
Difficulty falling asleep: later than usual for this individual	☐	☐	☐	☐
Multiple awakenings during sleep	☐	☐	☐	☐
Early morning awakening: earlier than usual for this individual	☐	☐	☐	☐
Ideational Disturbance	**a**	**0**	**1**	**2**
Suicide: feels life is not worth living, has suicidal wishes, makes suicide attempt	☐	☐	☐	☐
Poor self-esteem: self-blame, self-depreciation, feelings of failure	☐	☐	☐	☐
Pessimism: anticipation of the worst	☐	☐	☐	☐
Mood-congruent delusions: delusions of poverty, illness or loss	☐	☐	☐	☐

Score: _____

Notes/Current medications: _____

Assessor: _____

See Reverse for Directions

PRIMARIS
Healthcare Business Solutions

Center for Epidemiologic Studies Depression Scale

Center for Epidemiologic Studies Depression Scale (CES-D)

Date: _____

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you've felt this way during the **past week**. Respond to all items.

Place a check mark (✓) in the appropriate column. **During the past week...**	**Rarely or none of the time (less than 1 day)**	**Some or a little of the time (1-2 days)**	**Occasionally or a moderate amount of time (3-4 days)**	**All of the time (5-7 days)**
1. I was bothered by things that usually don't bother me.				
2. I did not feel like eating; my appetite was poor.				
3. I felt that I could not shake off the blues even with help from my family.				
4. I felt that I was just as good as other people.				
5. I had trouble keeping my mind on what I was doing.				
6. I felt depressed.				
7. I felt that everything I did was an effort.				
8. I felt hopeful about the future.				
9. I thought my life had been a failure.				
10. I felt fearful.				
11. My sleep was restless.				
12. I was happy.				
13. I talked less than usual.				
14. I felt lonely.				
15. People were unfriendly.				
16. I enjoyed life.				
17. I had crying spells.				
18. I felt sad.				
19. I felt that people disliked me.				
20. I could not "get going."				

Treatment of Late Life Depression

- Success depends on multiple factors
- Must consider the following when choosing a venue, agent, etc.
    - Suicidality
    - Psychotic sx
    - Pt medication list: are any meds causing depressive sx? Re: BDZ, opiates, pain meds
    - SUD, especially EtOH
    - Comorbidities associated with depression: Th, DM, chronic pain
    - Hx depression or depressive episodes
    - Family Hx depression and response to treatment
- Initial Treatment: Two-Pronged Approach
    - Should be psychotherapy and/or somatic therapy
        - Meds
            - Metanalysis do not indicate difference in remission rates across medication classes
                - Though there are higher withdrawal rates from treatment with TCA due to side effects
            - Meds alone often not successful in treating patients with **more executive dysfunction**
            - **Medication rejection**: older adults sometimes concerned about psychotropic meds—fear of dependence, reject depression as medical illness, concerned meds will blunt normal emotions, hx negative experiences in the past
            - **Choosing a Medication:**
                - **SSRIs are first line**
                    - **Risks/ side effects:** parkinsonism, akathisia, anorexia, sinus bradycardia, fragility fractures (dose dependent)
                    - Increased rate of suicide in men 66+ y/o
                    - Citalopram causes increased QTc
                        - >60 y/o, do not exceed dose > 20 mg per day (or avoid altogether if starting a new agent!)
                    - Best Sertraline, Escitalopram
                        - Escitalopram not nearly as QTc prolonging as Citalopram
                        - Geriatric psychiatry chooses this often as a first agent!
                - **SNRIs are second line**
                    - Often thought to be helpful for patients with chronic pain
                        - Some studies do suggest they can be good for neuropathic pain, chronic fatigue syndrome, depression with somatic sx
                    - Can cause diastolic hypertension & GI distress
                    - Duloxetine is associated with falls
                - **Atypical Antidepressants (third-line)**
                    - **Mirtazapine**
                        - Use with comorbid insomnia, agitation, restlessness, anorexia
                        - Sometimes good for pts with PD, essential tremor, chemo related nausea
                        - Side effects: Can be sedating esp. at initiation and lower doses, ↑ appetite, dry mouth

        - **Bupropion**
            - More activating
            - **DO NOT USE IF**: seizure Hx, concurrent BDZ use, Concurrent CNS depressant use, EtOH withdrawal, bulimia nervosa
    - **TCA (for treatment failure with other agents)**
        - Cautious use for: cardiac disease, narrow angle glaucoma, BPH, urinary retention, orthostatic hypotension, dementia (more confused)
    - **Methylphenidate**
        - Data suggests that combining low dose methylphenidate with SSRI leads to faster treatment response and can be helpful with treatment resistance (methylphenidate 5mg/ Citalopram 20-40 mg per day)
            - Remember though, can't > 20 mg Citalopram in pt > 60 y/o
    - **Aripiprazole**
        - For treatment resistant late-life depression
        - Start at 2 mg per day and can up-titrate to 10 mg per day
        - Side effects: akathisia, parkinsonism
    - **ECT**
        - Very helpful in treating psychotic depression
        - Used for patients who failed medication treatment or who have depression that is severe and life threatening
        - Jury out on TMS, DBS
- **Nuances to treating Late Life Depression vs. Depression in Younger Adults**
    - **Full response to treatment may take 8-10 weeks (vs the 6 weeks we counsel younger pts)**
    - **Monotherapy** is preferred –when we need to augment agents, it is better to refer out
    - **Initiation dose should be ½ typical starting dose for younger patients** –but both young and older adults have same goal for therapeutic dosing
    - Follow up interval 2 weeks from initiation, see in person by 4 weeks
    - Duration of treatment 6-12 mos following remission
        - Pts with dysthymia may need long term treatment
        - If pt history indicates 3+ episodes before the age of 50 keep them on meds for life
        - Long term treatment may indicate need for psych referral
        - Older adults relapse more often than younger adults
- **Psychotherapy**
    - CBT, problem solving therapy, interpersonal psychotherapy
    - Method depends on severity, type, chronicity, contraindications to meds, and patient preference
        - Moderate to severe: should also get meds
        - Chronic Depression: should also get meds
    - **Problem solving therapy** is especially helpful for patients with executive dysfunction (thoroughly setting goals, planning, initiating and sequencing bx)—improves remission of depression, degree of disability, self-care, communication, and psychosocial function at 24 week follow up
        - 2-4 mos for short term treatment has been shown effective

- **Physical Exercise**
  - both CV and resistance training are helpful in treating depression 60+ yoa
  - More evidence for CV > resistance training

- **Collaborative Care Models**
  - 80% mental health treatment for older adults is delivered in **primary care setting**
    - Collaborative Care/ Integrative Care/ Care Management Programs are most effective way to do this
    - Significantly better outcomes in several studies
    - Consists of meds and or therapy + case manager follow-up
      - Focus on patient education and empowerment
      - Use physician + non-physician mental health professional (depression care manager) to integrate psychiatric and primary care
      - **IMPACT (Improving Mood-Promoting Access to Collaborative Treatment) Study**
        - 1801 primary care patients with late life MDD and or persistent depressive disorder
        - Collaborative care vs. usual care
        - Better cost effectiveness, depressive sx control, physical functioning, quality of life scores in collaborative care intervention group; less CV events in collaborative care group as well
      - Additional studies support decrease in all-cause mortality for late life depression

UpToDate Medication Titration Resource

Drug properties and doses of antidepressants in older adults and medically ill

Drug	Starting dose	Suggested dose range	Precautions*	Potential advantages
Selective serotonin reuptake inhibitors (SSRIs)¶				
Escitalopram	5 mg every morning or every evening	5 to 20 mg daily	Mild discontinuation symptoms may occur absent tapering.	Applies to escitalopram and citalopram: Generally well tolerated. Non-sedating, low risk of sleep disturbance, comparatively few significant drug interactions. Good choice for initial treatment of depression in most older adults.
Citalopram	10 mg every morning or every evening	10 to 20 mg$^{\Delta}$ daily	Dose-related risk of QT prolongation$^{\P\Delta}$. Mild discontinuation symptoms may occur absent tapering.	
Sertraline	12.5 to 25 mg every morning	25 to 200 mg daily	More frequent gastrointestinal symptoms including diarrhea. Variable oral bioavailability. Oral solution contains alcohol. Discontinuation symptoms may occur absent tapering.	Non-sedating, low risk of insomnia, lacks significant cardiovascular effects. Good choice for initial treatment of depression in most older adults.
Fluoxetine	5 to 10 mg every morning	5 to 60 mg daily	Activating. Significant drug interactions. Prolonged half-life and active metabolites require weeks to reach steady state, prolonging time needed to evaluate effect of dose adjustment and complicating wash-out and withdrawal.	Activating effect may be useful for treatment of depressed patients with low energy or hypersomnia. Tapering upon discontinuation is not needed due to long half-life.
Paroxetine	10 mg every evening	10 to 40 mg every evening	Weakly anticholinergic. May cause constipation, dry mouth, or drowsiness. Associated with more severe discontinuation symptoms in absence of tapering.	Useful for patients with insomnia. Moderate half-life with no active metabolites.
Fluvoxamine	25 mg every evening	25 to 200 mg every evening	Significant drug interactions. Short half-life associated with discontinuation symptoms in absence of tapering.	May be useful for patients with insomnia.
Serotonin-norepinephrine reuptake inhibitors (SNRIs)$^{\diamond}$				
Venlafaxine (extended release)	37.5 mg once daily	75 to 225 mg once daily	Applies to venlafaxine and desvenlafaxine: Activating. May cause dose-dependent increases in blood pressure (primarily diastolic) and heart rate. Monitor blood pressure regularly. Gastrointestinal symptoms (eg, nausea) may be more prominent with immediate-release venlafaxine. Associated with discontinuation symptoms absent tapering. Taper desvenlafaxine by increasing interval between doses.	Applies to venlafaxine and desvenlafaxine: Activating effect may be useful for treatment of melancholic depressed patients with low energy or hypersomnia. Useful for patients with comorbid painful conditions such as diabetic neuropathy.
Venlafaxine (immediate release)	18.75 to 37.5 mg every morning or twice daily	75 to 150 mg twice daily		
Desvenlafaxine	50 mg every morning CrCl <30 mL/min: 50 mg every other day	50 mg every morning CrCl <30 mL/min: 50 mg every other day		
Duloxetine	10 to 20 mg daily	20 to 60 mg once daily	Significant drug interactions.	Mildly sedating. Low risk of insomnia. Useful for patients with comorbid painful conditions such as diabetic neuropathy or chronic pain.
Atypical antidepressants$^{\diamond}$				
Mirtazapine	7.5 mg every evening	15 to 60 mg every evening	Prolonged half-life and active metabolites. Risk of accumulation with renal and/or hepatic insufficiency. Dose reductions necessary. Drowsiness, weight gain. Rare reports of agranulocytosis.	Sedating. Low risk of sexual dysfunction. Appetite stimulant and antinausea effects can be noted within days. Useful for patients with insomnia or who may benefit from weight gain.
Bupropion sustained release	75 mg in morning initially then twice daily	150 mg in morning and midafternoon (twice daily)	Avoid in seizure disorders and depressed patients with agitation. Dose-dependent increase in diastolic blood pressure. May worsen insomnia.	Stimulant effect may be useful for treatment of depressed patients with low energy and apathy. Low risk of cognitive toxicity. Dopaminergic action may be advantageous for depressed patients with Parkinson disease.
Vilazodone	10 mg once daily with food for seven days or more	20 to 40 mg once daily with food	Take with food to assure bioavailability. Diarrhea, nausea, vomiting, dizziness, insomnia. Significant drug interactions via CYP 3A4 require dose adjustment.	Low incidence of weight gain or sexual dysfunction. Role in therapy for treatment of depressed older adults or adults with comorbid illness is not yet defined.
Trazodone	12.5 to 25 mg taken 30 to 60 minutes before bedtime for hypnotic effects	25 to 100 mg taken 30 to 60 minutes before bedtime for hypnotic effects; antidepressant effects require higher doses	Sedation, orthostatic hypotension, nausea. Residual daytime sedation and cognitive impairment. Reports of hyponatremia.	Used in low doses as adjunct to SSRI for treatment of insomnia.
Tricyclic antidepressants (TCAs)§				
Nortriptyline	10 mg every evening	10 to 100 mg every evening or in two divided doses	Applies to nortriptyline and desipramine: May be poorly tolerated by medically ill and older adults due to anticholinergic effects that include dry mouth, constipation, urinary retention, or altered vision (eg, avoid in prostatic disease or narrow angle glaucoma). May be fatal in overdose. Potentially cardiotoxic, can cause arrhythmia or orthostatic hypotension.	Applies to nortriptyline: Established therapeutic serum concentration 50 to 150 ng/mL. Mildly sedating. Taken at bed time for depressed patients with insomnia. May be useful for melancholic, anxious, depressed patients who have not responded to first- and second-line antidepressants.
Desipramine	10 mg every morning	25 to 150 mg every morning or in two divided doses	Significant drug interactions.	Applies to desipramine: Established therapeutic serum concentration 125 to 300 ng/mL. Mild stimulant effects may be useful for depressed patients with low energy and hypersomnia who have not responded to first- and second-line antidepressants.

CYP: cytochrome.

* Specific interactions of antidepressants with other medications may be determined using the Lexi-Interact™ drug interactions program included with UpToDate.

¶ For additional information refer to topic on unipolar depression in adults and SSRIs.

Δ Maximum recommended daily dose of citalopram is 20 mg for patients >60 years of age, with significant hepatic insufficiency, or taking interacting medications that can increase citalopram levels.

◇ For additional information refer to topic on SNRIs and other antidepressants for treating depressed adults.

§ For additional information refer to topic on tricyclic and tetracyclic antidepressants for treating depressed adults.

Geriatric Review Syllabus Medication Titration Resource

Drug	Initial dosage	Final dosage	Comments and precautions
SSRIs			
Citalopram	10 mg qam	20 mg qam	Risk of QT_c prolongation in doses >20 mg/d, nausea, tremor, hyponatremia, serotonin syndrome
Escitalopram	10 mg qam	10–20 mg qam	Nausea, tremor, hyponatremia, serotonin syndrome; reduce dosage in renal insufficiency
Sertraline	25 mg qam	100–200 mg qam	Nausea, tremor, hyponatremia, insomnia, serotonin syndrome; few drug interactions; liquid available; FDA approved for OCD, PTSD, social anxiety disorder, panic disorder
Selective Serotonergic and Noradrenergic Reuptake Inhibitors (SSRIs/SNRIs)			
Duloxetine	20–30 mg qam	60 mg qam	Drug interactions (CYP1A2, -2D6 substrate); chronic liver disease, alcoholism, increased serum transaminase; reduce dosage in renal insufficiency; equally SSRI and SNRI; narrow dose range; activating; FDA approved for diabetic neuropathic pain, fibromyalgia, GAD
Venlafaxine XR	37.5–75 mg qam	75–225 mg qam	Can increase blood pressure; headache, nausea, vomiting; do not stop abruptly; reduce dosage in renal insufficiency; SSRI and SNRI; activating; few drug interactions; FDA approved for GAD, Parkinson disease, social anxiety disorder, neuropathic pain
Vortioxetine	5 mg qam	10-20 mg qam	Nausea; no data available on doses >5 mg in older adults
Tricyclic Antidepressants (TCAs)			
Nortriptyline	10–25 mg qhs	25–100 mg qhs	Glaucoma (avoid if closed-angle), constipation, urinary retention, diabetes; may be fatal in overdose; therapeutic window 50–150 ng/mL serum level
Others			
Aripiprazole	5 mg qam	15 mg qam	Adjunctive treatment with SSRIs and venlafaxine; prolonged half-life, may produce agitation at high dosages because of D_2 dopamine receptor agonist activity
Bupropion	75 mg q12h 150 mg qam	150–300 mg q12h 300 mg extended release qam	Agitation, insomnia, seizures, activating, not sedating
Methylphenidate	5 mg qam	20 mg q12h	Adjunctive treatment with citalopram; weight loss, insomnia, agitation, hypertension; faster onset for frail and apathetic patients
Mirtazapine	7.5 mg qhs	15–45 mg qhs	Dry mouth, weight gain, sedation (may improve sleeplessness), daytime drowsiness, potential for neutropenia; orexigenic (stimulates appetite); reduce dosage in renal insufficiency