MedStar Health

Identification and Management of Clinical Depression in Adults 18 years or Older
Clinical Practice Guideline
MedStar Health

"These guidelines are provided to assist physicians and other clinicians in making decisions regarding the care of their patients. They are not a substitute for individual judgment brought to each clinical situation by the patient's primary care provider in collaboration with the patient. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication but should be used with the clear understanding that continued research may result in new knowledge and recommendations".

General Principles: The purpose of this guideline is to assist the primary care practitioner in detecting, diagnosing, and adequately treating clinical depression in patients 18 years of age and older. Depression is extremely common in primary care medicine. It is thought to be more prevalent than hypertension (6-17% compared to 5.8%). A recent Data Brief from the CDC/National Center for Health Statistics estimates that 8.1% of Americans age 20 and over will have had depression in a given 2-week period, and 1 in 6 Americans will experience depression in their lifetimes. Rates are higher in women than in men and increase as family income decreases. The WHO considers depression to be a major cause of disability worldwide.

Nearly three quarters of depressed patients will at some point present to their primary care practitioner, often with somatic complaints, but only 50% of these cases are diagnosed. Primary Care Providers should be skilled at evaluating and diagnosing this common disorder.

Clinical depression is a highly treatable illness. A fair to full response to therapy can be expected in 66% to 80% of patients with major depression. Unfortunately, of those diagnosed, only 10% get adequate treatment.

The "costs" of depression extend beyond absenteeism, loss of productivity and include unnecessary suffering for patients and their families, and suicide.

Disease Definition: Clinical depression can occur in many situations. In DSM-5, the depressive disorders that can be diagnosed include:

- Unipolar major depression (major depressive disorder)
- Persistent depressive disorder (dysthymia)
- Disruptive mood dysregulation disorder
- Premenstrual dysphoric disorder
- Substance/medication induced depressive disorder
- Depressive disorder due to another medical condition
- Other specified depressive disorder (eg, minor depression)
- Unspecified depressive disorder

A. Major Depression: A major depressive episode can be characterized by a period of at least 2 weeks in which five or more of the following symptoms have been present and represent a change from prior functioning. At least one of the symptoms must be either depressed mood or loss of interest or pleasure in nearly all activities (anhedonia).

- Depressed mood most of the day, nearly every day, as self-reported or observed by others
- Diminished interest or pleasure in all or almost all activities most of the day, nearly every day
- Significant weight loss when not dieting, weight gain, or decrease or increase in appetite nearly every day
- Insomnia or hypersomnia nearly every day
- Psychomotor agitation or retardation nearly every day
- Fatigue or loss of energy nearly every day
- Feelings of worthlessness or excessive or inappropriate guilt nearly every day
- Diminished ability to think or concentrate nearly every day
- Recurrent thoughts of death, recurrent suicidal ideation without a specific plan

In addition, the symptoms cause significant distress or psychosocial impairment and are not the direct result of a substance or general medical condition. Bereavement does not exclude the diagnosis of a major depressive episode.

Depression can be characterized as mild (few symptoms, minor functional impairment), moderate, or severe (many more symptoms than required for diagnosis with significant functional impairment).

Seasonal affective disorder is a subtype of major depression with seasonal onset and remission.

B. Persistent Depressive Disorder [Dysthymia]: Depressed mood for most of the day, for more days than not, for at least two consecutive years without a period of greater than two months of absence of symptoms. In addition, at least two of the following must be present:
- Poor appetite or overeating
- Insomnia or hypersomnia
- Low energy or fatigue
- Low self-esteem
- Poor concentration or difficulty making decisions
- Feelings of hopelessness

C. Premenstrual Dysphoric Disorder—Mood disorder present in most menstrual cycles in the prior year associated with significant distress and impairment of functioning. Symptoms must be present during the week prior to menses and resolve within a few days of onset of the menstrual period.

One or more of the following must be present:
- Mood swings, sudden sadness, increased sensitivity to rejection
- Anger or irritability
- Hopelessness, depressed mood, self-critical thought
- Tension, anxiety, feeling on edge

One or more of the following symptoms must also be present (to total five when combined with symptoms above)
- Difficulty concentrating
- Change in appetite, overeating, food craving
- Diminished interest in usual activities
- Low energy, fatigue
- Feeling overwhelmed or out of control
- Insomnia or hypersomnia
- Breast tenderness, weight gain, bloating, joint or muscle aches

D. Other Depressive Disorders: This category encompasses depressive disorders related to substance abuse, medication side effects, medical conditions (see High Risk Groups below) or other specified or unspecified reasons. Patients with depression and substance abuse disorder are candidates for referral to a behavioral health specialist.

Disease Detection and Screening:

A. Screening: The USPSTF recommends screening for depression in the general adult population, including pregnant and postpartum women. Screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up.

Detection of depression can be enhanced using a screening tool such as a questionnaire that identifies patients who are at risk of depression. The Patient Health Questionnaire-2 (PHQ-2) and Patient Health Questionnaire-9 (PHQ-9) are two item and nine item tools, respectively, for assisting primary care clinicians in screening and diagnosing depression as well as selecting and monitoring treatment. Screening tools for special populations (Edinburgh Postnatal Depression Scale for pregnant and postpartum patients and Geriatric Depression Scale for elderly patients) also exist but are not clearly preferable to the PHQ-9. In general, sensitivity of the various screening tools is 80-90% and specificity is 70-85%. Patients who screen positive with any tool should be further evaluated to confirm the diagnosis, evaluate for other causes, and assess the presence of co-existing psychiatric illness. (Tools attached end of guideline)

B. High Risk Groups:

1. The primary risk factors for depression are the following:

Prior episodes of depression	Prior suicide attempts
Family history of depression	Female gender
Age of onset under 40	Postpartum period
Medical co-morbidity	Lack of social support
Stressful life events	Current alcohol or substance abuse

2. Patients with the following chronic medical illnesses (not an exhaustive list) are at significantly higher risk for chronic depression. It has been shown that undetected depression in these groups can worsen the course of their medical illness.

   a) Stroke - Subgroups of post-CVA patients have depression that appears to be causally related to the injury, especially if the insult is located in the left basal ganglia or left dorsal lateral frontal cortex.
   b) Dementia - Depression is often seen in patients with or antecedent to primary dementia. Thirty to forty percent of Alzheimer's disease patients demonstrate depressive mood symptoms sometime during their illness.
   c) Diabetes - Major depressive syndrome is three times more common in this population.
   d) Cardiac disease - Ischemic heart disease, heart failure and cardiomyopathy. The prevalence of various forms of depression is estimated at 40 - 65%.
   e) Cancer - Major depression occurs in approximately 25% of this population
   f) Fibromyalgia
   g) HIV/AIDS

Special Case: Postpartum Depression: Major depressive episodes, as distinct from "baby blues" – a mild self-limited episode of depressive symptoms - is reported to have a prevalence of about 9% of American women in the 12 months following delivery. While referred to as postpartum depression, symptoms can and do begin prior to delivery in some women with roughly 50% of women reporting symptoms before or during the pregnancy. For women whose symptoms begin after delivery, onset is most frequent in the first months after delivery with over 90% occurring within 4 months.

All practitioners who care for women should be aware of postpartum depression, screen and treat it when it is diagnosed.

Other possible risk factors associated with postpartum depression in addition to those listed above:

- Depression before or during the pregnancy
- Young age
- Poor perinatal physical health (gestational diabetes, hypertension, complications post-delivery)
- Single
- Multiparity
- Family history of postpartum depression or psychiatric illness
- Unintended pregnancy/negative attitude about pregnancy
- Adverse pregnancy outcome or difficult infant or trouble breast feeding
- Intimate partner violence

The clinical features are basically the same as any other major depressive episode with lack of interest in herself and the child. Evaluation should include evaluation for suicidality, homicidal tendencies and psychosis and if present, referral to a mental health professional or an emergency department is indicated. Suicidal ideation is reported to occur in 3% of postpartum women but the rate of actual suicide is about half the rate of the general population. Other adverse outcomes, including negative impacts to the infant, are possible including poor bonding, cognitive and psychopathology in the child, and lack of healthcare/vaccinations.

Screening is recommended by USPTF and ACOG for all postpartum women. The Edinburgh Postnatal Depression Scale (Appendix E) or the PHQ-9 (Appendix D) are the tools commonly used. The PHQ-9 can also be used to diagnose depression, assess the severity of the condition and follow the response to treatment.

C. Differential Diagnosis:

1. Psychiatric: Differentiation from other psychiatric and substance use disorders can be difficult. Consider:
   - **Bipolar disorder** – if there have been features of mania/hypomania. Diagnosis can be challenging since depression can be the initial manifestation of bipolar disease, and hypomania may not be perceived by the patient as "disease". Note that SSRI's may trigger manic episodes in patients with bipolar disorder.
   - **Alcohol dependence/drug dependence** – organic depression often accompanies substance abuse and resolves in 4-8 week of abstinence
   - **Personality disorders**

2. Bereavement: Distinguishing normal grief from depression can be challenging since the response to death of a loved one varies between individuals and has a significant cultural overlay. Features favoring grief rather than major depression include the following:
   - Waves or pangs of grief or sadness rather than pervasive depressed mood

- Preservation of self-esteem
- Hope that the future will be better rather than a sense of hopelessness

3. Medical: A variety of medical conditions and medications can cause a depressive-like syndrome. These causes should be treated first. If the syndrome persists, a diagnosis of clinical depression can be made and treated accordingly. Medical conditions may include hypothyroidism, Addison's disease, vitamin B12 deficiency, parathyroid conditions, brain tumors, cocaine withdrawal, amphetamine withdrawal, etc.

D. Assessing the Patient for Suicide Potential

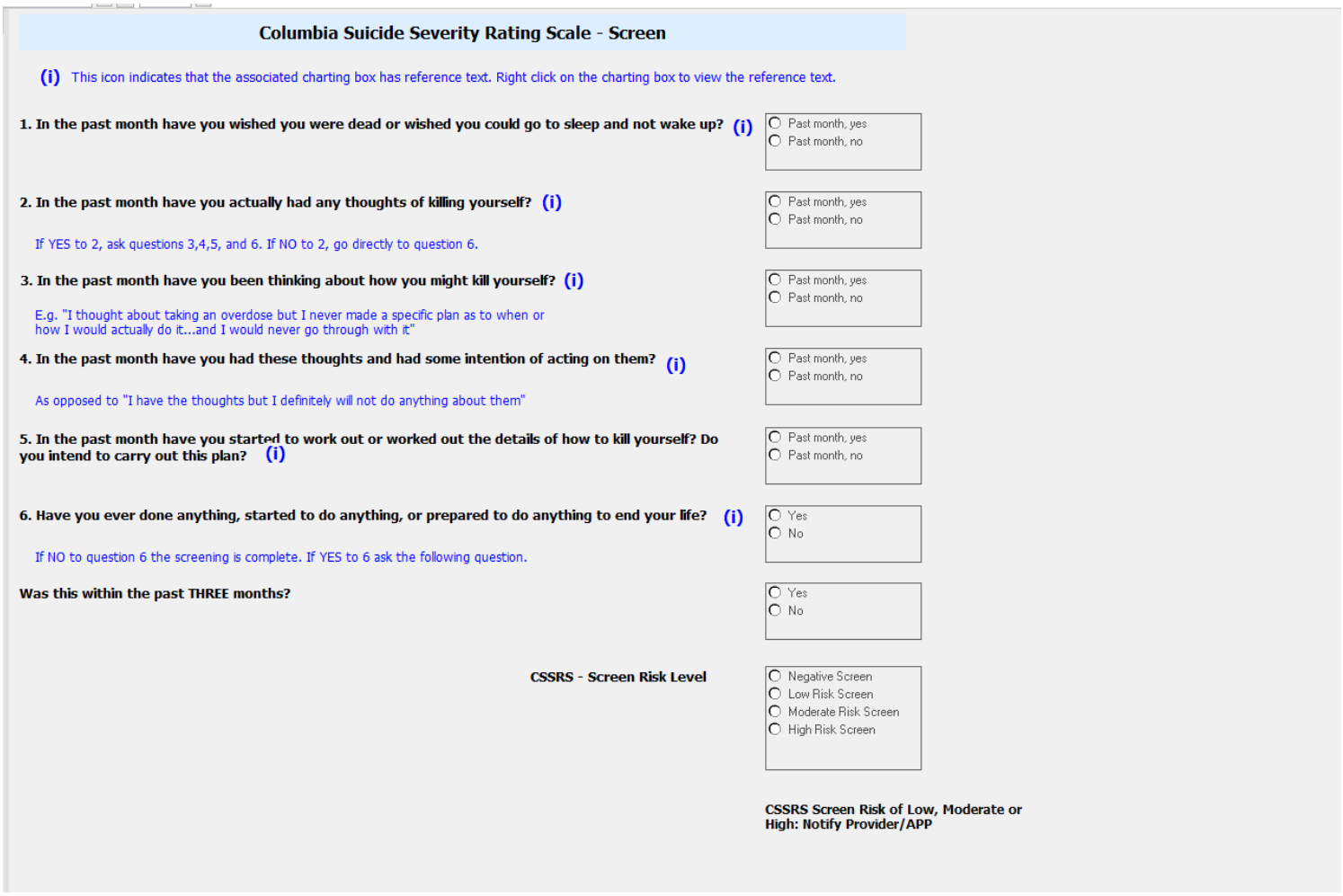
All depressed patients should have an initial evaluation for suicide potential. Risk factors for suicide include:

- male sex
- family history of suicide
- psychotic symptoms
- hopelessness
- general medical illnesses
- living alone with little social support
- prior suicide attempts.
- borderline personality disorder

Questions about plans and means should be asked. If the evaluation reveals any degree of suicidal risk, an immediate call should be made for a psychiatric assessment.

The Columbia- Suicide Severity Rating Scale (CSSRS) is a structured tool that can be used to assess suicidality. The CSSRS-short version is embedded in MedConnect and is suitable for use in an office setting. Patients who score 5 or above on the PHQ-9 or answer "Yes" to "Thoughts Better off Dead or Hurting Self" should have a suicide screen done using CSSRS. It can be found by going to "Ad Hoc Charting" or "Scales and Assessments" in provider workflow, then opening the folder called "Additional Assessments" and selecting "CSSRS Short Version". The tool will calculate the screen risk level as negative, low, moderate or high based on the answers entered. Providers should be notified of the results. What action to take is determined by entity policy.

Providers who do not use MedConnect can access the tool at
https://cssrs.columbia.edu/wp-content/uploads/Community-Card-Patients-2020.pdf



Columbia Suicide Severity Rating Scale - Screen

(i) This icon indicates that the associated charting box has reference text. Right click on the charting box to view the reference text.

1. In the past month have you wished you were dead or wished you could go to sleep and not wake up? (i)
- Past month, yes
- Past month, no

2. In the past month have you actually had any thoughts of killing yourself? (i)
- Past month, yes
- Past month, no

If YES to 2, ask questions 3,4,5, and 6. If NO to 2, go directly to question 6.

3. In the past month have you been thinking about how you might kill yourself? (i)
- Past month, yes
- Past month, no

E.g. "I thought about taking an overdose but I never made a specific plan as to when or how I would actually do it...and I would never go through with it"

4. In the past month have you had these thoughts and had some intention of acting on them? (i)
- Past month, yes
- Past month, no

As opposed to "I have the thoughts but I definitely will not do anything about them"

5. In the past month have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan? (i)
- Past month, yes
- Past month, no

6. Have you ever done anything, started to do anything, or prepared to do anything to end your life? (i)
- Yes
- No

If NO to question 6 the screening is complete. If YES to 6 ask the following question.

Was this within the past THREE months?
- Yes
- No

CSSRS - Screen Risk Level
- Negative Screen
- Low Risk Screen
- Moderate Risk Screen
- High Risk Screen

CSSRS Screen Risk of Low, Moderate or High: Notify Provider/APP

MEDICATIONS REPORTEDLY ASSOCIATED WITH DEPRESSION

Cardiovascular Drugs	Hormones	CNS Active	Anti-Cancer Agents	Anti- Infectives	Miscellaneous
Classes					
angiotensin converting enzyme inhibitors	Anabolic steroids	Tricyclic antidepressants (TCA)*		Fluoroquinolone antibiotics	H2 Antihistamines
	Estrogen containing Oral Contraceptives	Antiepileptics*		Sulfonamides	
	Glucocorticoids	Monoamine oxidase inhibitors*			
	GnRH agonists?	Selective serotonin reuptake inhibitors (SSRIs) *			
		Benzodiazepines			

Initial Approval Date and Reviews:	Most Recent Revision and Approval Date: April 2021	Next Scheduled Review Date:
April 2013, April 2015, April 2017, April 2019, April 2021		April 2023 Ambulatory Best Practice

Individual Drugs				
	Atomoxetine*	Asparaginase		Acetazolamide
Disopyramide	Baclofen	Cycloserine*	Abacavir*	Acitretin
Alpha-methyldopa	Duloxetine*		Acyclovir	Alpha* &
Clonidine	Duloxetine*	Tamoxifen	Amantadine*	Beta Interferons
Digitalis	Gabapentin*	Vinblastine	Dapsone	Isotretinoin*
Guanethidine	Gabapentin*	Vincristine	Efavirenz	Metoclopramide
Reserpine	Levodopa		Ethambutol	Varenicline*
Thiazides	Metoclopramide		mefloquine	
	Metoclopramide		metronidazole	
	Modafinil*		Nevirapine	
	Modafinil*		Oseltamivir*	
	Pregabalin*		Trimethoprim-sulfamethoxazole	
	Pregabalin*		valganciclovir	
	Ramelteon*			
	Sibutramine			
	Sodium oxybate			
	Venlafaxine*			
	Venlafaxine*			
	Zaleplon			
	Zaleplon			

* These drugs are also associated with suicidal thoughts or suicidality

Clinical Management:

A. Goals

1. Reduce, if not remove, all signs and symptoms of the disease.
2. Restore occupational and psychosocial functioning
3. Reduce the likelihood of relapse and recurrence.

B. Types of Treatment:

1. Medication - Patients with moderate to severe clinical depression are appropriate candidates to be treated with medication, whether or not formal psychotherapy is also used.
2. Psychotherapy - Patients with mild to moderate clinical depression (usually dysthymia or depressive disorder NOS) may be managed with psychotherapy alone if the patient prefers. If symptoms do not improve within 2-3 months, then medication should be strongly considered.
3. Medication and psychotherapy - This may be advantageous for complicated, chronic depression and for patients with only a partial response to either treatment alone.
4. Electroconvulsive therapy (ECT) - This is only for certain patients after psychiatric consultation.

C. Medication Selection and Management

1. **Selective Serotonin Re-uptake Inhibitors (SSRI)** should be the first choice unless the patient has a history of or risk of intolerable side effects, is taking other medications that put them at risk for drug interaction, or has a personal or family history of a positive response to another class of anti-depressants.

2. **Advantages to using SSRI's** include: ease of dosing, lack of histaminic, muscarinic and adrenergic

antagonism, the potential for co-treating other psychiatric conditions (e.g. panic disorder, ADHD, bulimia, obsessive-compulsive disorder, alcoholism, self-injurious behaviors and premenstrual syndrome), and effectiveness for treating concurrent medical conditions (e.g. headaches, chronic pain, Raynaud's and some sexual disorders). Limitations of all SSRI's can include agitation, akathisia, nausea, diarrhea, serotonin syndrome, Parkinson like tremor and possible sexual side effects.

3. Early signs of positive clinical response can occasionally be seen as early as one week into therapy, though usually 4-6 weeks is required. Adequate treatment for 6-8 weeks is necessary before concluding a patient is not responding to a particular medication. If side effects are tolerable, then titration of the dosage upward is a first adjustment strategy to consider. Occasionally, titration of the dosage downward is a first adjustment strategy if it is concluded that the depressive symptoms are responding but side effects are interfering. According to the Star-D study, about one third of people on an SSRI will reach remission and an additional 10-15% will have a response. In this same trial, people who did not respond to an SSRI were switched to an alternative SSRI, an SNRI (serotonin-norepinephrine reuptake inhibitor) or buproprion (active on noradrenergic and dopaminergic neurotransmission). Among the people who switched, an additional 25% responded and each option worked equally. Thus, the data suggest that either a switch within the class or a switch to a new class is an acceptable strategy.

4. Additional medication options include combining anti-depressants or adding augmentation medications. Combining anti-depressants and adding augmentation medications is best managed by a psychiatrist.

5. The use of pharmacogenomics, particularly CYP2C19 and CYP2D6 phenotypes, while not yet mainstream, represent an emerging technology to guide antidepressant dose and choice. If results are available, refer to evidence-based clinical practice guidelines from the Clinical Pharmacogenetics Implementation Consortium (CPIC; cpicpgx.org) or consult the MedStar pharmacogenomics team. To obtain a consult with the MedStar pharmacogenomics team, place an order in MedConnect for *Consult to Pharmacogenomics and Pharmacogenetics*. These consults can also advise on whether testing could be beneficial and how to order testing if desired.

D. **Expectations of Treatment:** Active treatment should yield a response. As noted above, a response may be evident in as little as a week or treatment may need to be continued for as long as 8 weeks before it is deemed a failure and an alternate strategy adopted. Remission, or full response to treatment, may take longer. Response and remission are not the same. No matter what the treatment modality that induced the response, it should be continued to keep the patient in remission, i.e., prevent relapse. Only after the patient has been in full remission for 4-6 months should an attempt to taper the dosage of medication be entertained. Relapse is common and close follow up will be needed. Approximately 50% of patients will go on to have a relapse. Given a second episode of depression, the relapse rate is 70%, with a 3rd episode, it is >80% and after a 4th episode, it is >90%. For patients with a history of recurrent disease, prolonged, or even lifelong therapy, may be needed. And even long-term medication is not fool proof; relapses have been reported.

   If the decision is made to try to discontinue the selected medication, it should be tapered to prevent withdrawal symptoms. Patients, and their families, should be warned about early signs of recurrence of the depression.

   Patients should be seen 2-4 weeks after starting therapy to assess medication tolerability, suicide risk and early response. There should be 3 contacts within the first 12 weeks. Patients on stable, long-term medication should be seen in the office every 3-6 months for re-evaluation of the treatment plan and efficacy.

E. **Evaluating Response to Treatment**: Serial scores on the PHQ-9 can be used to evaluate a response to treatment. A drop of 5 or more points is considered an adequate response with no change in treatment regimen. A drop of 2-4 points is a partial response. A score below 5 is considered a remission. Additional details may be found at www.phqscreeners.com.

F. **Continuation of Treatment:** If this is a first episode of clinical depression in a patient with a good premorbid mood history and without a significant family history of depression, then effective medication should be continued at least for 6-12 months before considering discontinuation. Some patients are candidates for indefinite medication maintenance. These patients should be re-evaluated every 3-6 months. If medicines are tapered or discontinued, patients should be warned about early signs of recurrence.

G. **Psychiatric Referral:** Referral for mental health consultation, treatment and/or psychotherapy can occur at any time at the PCP's discretion and/or the patient's choice.

Immediate referral is recommended for*:*

- *significant evidence of danger to self and/or others*
- *presence of psychotic symptoms*

Referral is **strongly** recommended for*:*

- *depression with co-morbid psychiatric or substance abuse*
- *suspicion of bipolar disorder*
- *depression during pregnancy and the postpartum*
- *treatment-resistant depression*
- *childhood depression*
- *depression with dementia*

Patient Education:

A. Clinician counseling:

1. Natural history of the disease: Depression isn't just a brief blue mood or a passing sadness that lifts in a few hours or even a few days. Clinical Depression occurs when a person experiences physiologic symptom such as changes in sleep, appetite, sexual function, feeling of sadness and difficulty in the ability to function normally. These symptoms last for several weeks or more.

2. Treatment Plan:
   - *Medication* - Patients with moderate to severe clinical depression are appropriate candidates for medication. Compliance with antidepressants can be a problem. Discuss with patients that usually 4-6 weeks of medication is required for a full response. Explain and discuss common side effects of medications such as sexual dysfunction, restlessness, anticholinergic effects, orthostatic hypotension, and GI symptoms. Medication guides regarding the risk of suicidal thoughts and actions with antidepressants will be provided by the pharmacy when medications are dispensed.
   - *Psychotherapy* - Can be successful for patients with mild to moderate clinical depression. If symptoms do not significantly improve within 2-3 months, then medication should be considered.
   - *Medication and Psychotherapy* - This combination can be beneficial for complicated, chronic depression or with individuals who have experienced only partial response to either treatment alone.

3. Self-help Strategies:
   - Identify activities that make you feel better and try to focus on them. Do things for yourself. Take up hobbies. Listen to music. Participate in activities even when you may not want to.
     Do not withdraw from others. Join a support group and talk to your friends. Call on your support group or therapist for help when you need it. Ask for assistance at home and work if the load is too great to handle.
   - Eat nutritious, well-balanced meals. Avoid drinking alcohol and coffee. Exercise on a regular basis, several times a week
   - Get adequate rest and keep your sleep cycle as regular as possible.
   - Concentrate on good grooming and cleanliness.
   - Perform progressive relaxation exercises daily and diaphragmatic breathing exercises during times of high stress.
   - Perform frequent mental imaging of good life experiences. Develop and maintain an attitude that things will work out.
   - Learn new, positive problem-solving techniques.
   - Call your provider or therapist if you feel suicidal.

B . Resources for patients:

- National Institute Mental Health: 866-615-6464 or http://www.nimh.nih.gov/health/publications/index.shtml
- Center for Disease Control: https://www.cdc.gov/reproductivehealth/depression/resources.htm
- National Alliance on Mental Health (NAMI) https://www.nami.org/#
- National Suicide Prevention Lifeline: 1-800-273-TALK or 1-800-273-8255
- American Psychiatric Association: http://www.psychiatry.org/mental-health
- Mental Health America: http://www.nmha.org/mental-health-information
- https://www.nimh.nih.gov/health/topics/depression/index.shtml
- https://www.cdc.gov/learnmorefeelbetter/programs/depression.htm
- https://www.cdc.gov/tobacco/campaign/tips/diseases/depression-anxiety.html

Selected Formulary for Medical Management of Depression

I. Selective Serotonin Reuptake Inhibitors (SSRI's)

Drug name	Initial Dose	Dosing Range	Positives	Limitations
citalopram *Celexa*® ($82)	20mg daily	20-40mg daily max dose 20 mg for age >60	Minimal drug interactions compared with other SSRIs Generic available Lower incidence of sexual dysfunction	Do not use doses >40 mg due to risk of QT prolongation

escitalopram *Lexapro®* ($148)	10mg daily	10-20mg daily	Minimal drug interactions compared with other SSRIs Possible quicker onset in resolving panic- related symptoms	
fluoxetine *Prozac®* ($167)	10-20mg daily (Elderly dose 10mg/day)	20-80mg daily	Energizing feeling Lower cost of care	• Longer half life • More agitation
paroxetine *Paxil®* ($90)	10-20mg daily (CrCl <30mL/min dose 10mg/day)	20-50mg daily Maximum dose 40 mg if CrCl <30mL/min	Better for agitation Usually has better pricing	• More problems with withdrawal • More anticholinergic side effects
paroxetine *Paxil® CR* ($180)	25 mg daily	25-62.5 mg daily Maximum dose 50mg if CrCl <30mL/min		
sertraline *Zoloft®* ($88)	25-50mg daily	25-200mg daily	More helpful in Parkinson's patients	Usually needs higher doses to be effective • More titration
vilazodone *Viibryd®* ($360 – brand only)	10 mg daily	20-40 mg daily	May have low sexual side effects May lead to less weight gain	
vortioxetine *Trintellix®* ($508 – brand only)	5-10 mg daily	20 mg daily	May be alternative to partial or non-responders to SSRIs due to mulit-modal mechanism; minimal effect on weight and sexual function	

Potential side effects of all SSRI's include agitation, nausea, diarrhea, sexual side effects, akathisia and serotonin syndrome (hyperthermia, rigidity, myoclonus, autonomic instability, and potentially delirium and coma)

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II. Norepinephrine Dopamine Reuptake Inhibitors (NDRI's)

Drug name	Initial Dose	Dosing Range	Positives	Limitations
bupropion *Wellbutrin*® ($120)	100mg bid	200-450mg daily in 3- 4 divided doses Max single dose=150mg	• Low sexual side effects May help with nicotine addiction Increases total REM time Effective in many SSRI non-responders	• Seizures 0.4% (dose dependent, more common with immediate release) • GI upset • Tinnitus • Agitation • Tremor **Contraindicated if history of seizures or eating disorders**
Wellbutrin SR® ($230)	150mg q am	Max 400mg in divided doses Max single dose=200mg		
Wellbutrin XL® ($502) 100mg bid	150 mg q am	150-450mg daily		

III. Serotonin Norepinephrine Reuptake Inhibitors (SNRI's)

Drug name	Initial Dose	Dosing Range	Positives	Limitations
duloxetine *Cymbalta*® ($235)	40-60 mg/day as single dose or as two divided doses	20-30mg bid or 60mg once daily Max 60mg/day	• Benefit in neuropathic pain	Possible urinary retention and hepatotoxicity Possible elevation in BP Use not recommended in patients with renal insufficiency (creatinine clearance<30) or end stage renal disease Use not recommended in patients with hepatic disease given potential for contributing to hepatic failure
venlafaxine *Effexor*® ($70)	37.5-75mg daily in divided doses	75-375mg daily (w/food)	Possible greater efficacy Low side effects Possible greater efficacy w/chronic pain	BP elevation Weight gain Frequent dosing Sexual side effects
Effexor XR®($476)	37.5-75mg daily	75-225mg daily (w/food)		

desvenlafaxine *Pristiq*® ($174)	50 mg daily	50 mg daily 25mg daily or 50mg every other day if CrCl < 30mL/min	Once daily administration	Doses of 50-400 mg daily have been studied; no additional benefit has been observed at doses > 50 mg Possible BP elevation Nausea/dizziness Similar side effect profile to
levomilnacipran *Fetzima*® ($520)	20 mg daily x 2 days then 40 mg daily	40-120 mg daily Max 80mg daily if CrCl <60mL/min Max 40mg daily if CrCl <30mL/min	May be more beneficial for treatment of symptoms related to norepinephrine deficiency (decreased concentration, mental and physical slowing, decreased self-care)	

Potential side effects of all SNRI's include agitation, nausea, diarrhea, sexual side effects, akathisia and serotonin syndrome (hyperthermia, rigidity, myoclonus, autonomic instability, and potentially delirium and coma).

IV. Serotonin Antagonist and Reuptake Inhibitors

Drug name	Initial Dose	Dosing Range	Positives	Limitations
trazodone ($90)	50mg bid (Depression) 25-50mg hs (Insomnia)	150-400mg daily in divided doses (w/food) Insomnia: 50-100mg hs (some may require antidepressant doses)	Sedative properties	Over-sedation and/or possible orthostasis Priapism
nefazodone *Serzone*® ($294)	100mg bid	150-600mg daily in two divided doses Max 600mg/day in divided doses	Unlikely to cause sexual dysfunction Beneficial in patients with anxiety Improves sleep Less priapism Less orthostatic hypotension	Many drug interactions (Xanax, Halcion, digoxin) Mania Early intolerance

V. Tetracyclic Antidepressants

Drug name	Initial Dose	Dosing Range	Positives	Limitations
mirtazapine *Remeron*® ($86)	15mg daily hs	15-45mg hs	Appetite stimulation Sedative properties Minimal GI side effects	Over sedation Weight gain Metabolic disorders

VI. Tricyclic Antidepressants (TCA's)

Drug name	Initial Dose	Dosing Range	Positives	Limitations
amitriptyline *Elavil*® ($57)	25-75mg hs (Elderly dose 10mg/ day)	100-300mg daily	Sedative properties Efficacy in neuropathic pain Well known therapeutic and toxic levels	Weight gain Cardiac arrhythmia Orthostatic hypotension Anticholinergic Not recommended for elderly
nortriptyline *Pamelor*® ($127)	25-50mg hs	150 mg/day as single or divided doses	Well known therapeutic and toxic levels Less anticholinergic	Cardiac arrhythmias
amoxapine ($238)	25-50mg daily 1-3 times daily	100-400mg daily Doses >300mg/day should be divided Max dose 300mg in older adults	Potential benefit in depression with psychosis	EPS or tardive dyskinesia (avoid in Parkinson's) Sedation Orthostasis
desipramine *Norpramin*® ($379)	25-50mg daily	100-200mg daily Max 300mg/day	Sedative properties	Weight gain Cardiac complications
doxepin *Sinequan*® ($54)	25-50mg hs	75-300mg daily one dose hs or in divided doses Max single dose 150mg	Sedative properties Patients with neurodermatitis	Over sedation Weight gain Cardiac complications
imipramine ($262)	25-50mg hs	50-300mg Once daily or in divided doses	Minimal drug Interactions Patients with insomnia Patients with enuresis	Contraindicated in post MI patients Dose 30-100mg/day recommended in elderly and peds
protriptyline ($540)	10-20mg in 3-4 doses	20-60mg/day in 3-4 doses	Good for withdrawn or anergic patients	Multiple daily dosing Cardiac complications Weight gain
trimipramine ($283)	25-50 mg hs or in divided doses	50-300mg hs	Patients with insomnia or anxiety	Weight gain Sedation

VII. Monoamine Oxidase Inhibitors (MAOIs)

Drug Name	Initial Dose	Dosing Range	Positives	Limitations
isocarboxazid *Marplan*® ($682 – brand only)	10mg bid	40-60mg/day divided bid-qid	Patients with resistant or atypical depression or anxiety	Dietary restrictions Drug interactions Hypertensive crisis Avoid in patients with HTN or cardiac conditions
phenelzine *Nardil*® ($101)	15mg tid	60-90mg/day divided tid	As above	As above
selegiline transdermal patch *Emsam*® ($2214)	6mg/24 hours	6-12mg/24 hours	As above Less weight gain Less sexual dysfunction	Caution in Parkinson's As above
tranylcypromine *Parnate*® ($324)	10-30mg daily in divided doses	30-60 mg/day in divided doses	As above	As above

VIII. N-Methyl-D-Aspartate Receptor Antagonist

Drug name	Initial Dose	Dosing Range	Positives	Limitations
esketamine *Spravato*® ($389/28mg – brand only)	56-84mg twice weekly, evaluating need for continued use after 4 weeks	56-84mg once-twice weekly (goal is least frequent dosing interval needed to maintain response)	Useful for treatment-resistant depression Not a daily PO dose - may be useful for patients with poor adherence	Abuse potential Must be administered in a certified medical office

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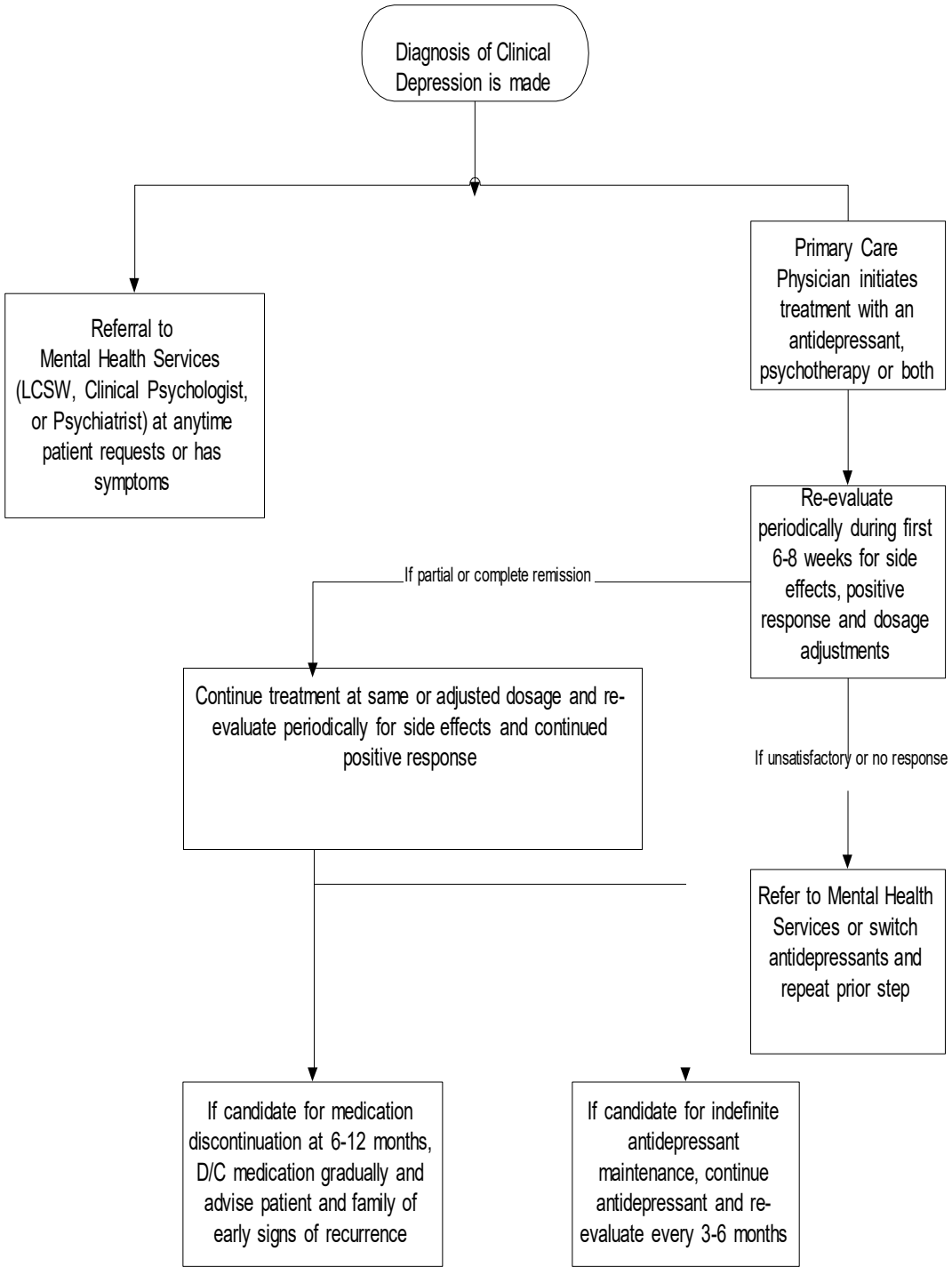
Appendix A: Clinical Depression Treatment Algorithm



Initial Approval Date and Reviews:	**Most Recent Revision and Approval Date: April 2021**	**Next Scheduled Review Date:**
April 2013, April 2015, April 2017, April 2019, April 2021		April 2023 Ambulatory Best Practice

Appendix B: Geriatric Depression Scale

Name_____PCP_____
DOB_____ Date Completed_____

Circle your answer of YES or NO for each of the following items, do not skip any items.

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 in good spirits most of the time?	YES	NO
6. Are you afraid that something bad is going to happen to you?	YES	NO
7. Do you feel happy most of the time?	YES	NO
8. Do you often get restless and fidgety?	YES	NO
9. Do you prefer to stay at home, rather than going out and doing new things?	YES	NO
10. Do you feel you have more problems with memory than most?	YES	NO
11. Do you think it is wonderful to be alive now?	YES	NO
12. Do you feel pretty worthless the way you are now?	YES	NO
13. Do you feel full of energy?	YES	NO
14. Do you feel that your situation is hopeless?	YES	NO
15. Do you think that most people are better off then you are?	YES	NO

Cut point for positive response: ≥ 6
Time to administer: 2-5 minutes
Can be used to monitor treatment response

Initial Approval Date and Reviews:	Most Recent Revision and Approval Date: April 2021	Next Scheduled Review Date:
April 2013, April 2015, April 2017, April 2019, April 2021		April 2023 Ambulatory Best Practice

Appendix C: Patient Health Questionnaire 2 (PHQ-2)

Name_____DOB_____

Date Completed_____

Over the past two 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
Little interest or pleasure in doing things.	**0**	**1**	**2**	**3**
Feeling down, depressed, or hopeless.	**0**	**1**	**2**	**3**

Total point score: _____

These questions, which can be used by practitioners as part of a general medical review of systems, can help identify which patients are exhibiting signs and symptoms of depression, and which of them may benefit from completing the PHQ-9. It can be administered by asking for responses as yes/no or rated on a scale of zero to three. Any "yes" or a score of three or more indicates possible depression and requires further evaluation.

Score interpretation: Cut point for positive response ≥ 3

PHQ-2 score	*Probability of major depressive disorder (%)*	*Probability of any depressive disorder (%)*
1	15.4	36.9
2	21.1	48.3
3	38.4	75.0
4	45.5	81.2
5	56.4	84.6
6	78.6	92.9

Information from Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. Med Care 2003;41: 1284-92.

Appendix D: Patient Health Questionnaire 9 (PHQ-9)

Patient's name: _____ Date: _____

Over the past two weeks, how often have you been bothered by any of the following problems?

(For each question, circle the number that represents the best answer.)

	Not at all	Several days	More than one half of 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 asleep 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 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
Add Columns				

SUM OF ALL COLUMNS=

10. If you have had any of these problems, how difficult have they made it for you to do your work, take care of things at home, or get along with other people? (circle the best answer)

Not difficult at all **Somewhat difficult** **Very difficult** **Extremely difficult**

Initial Approval Date and Reviews:	Most Recent Revision and Approval Date: April 2021	Next Scheduled Review Date:
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Patient Health Questionnaire-9 (PHQ-9). The PHQ was developed by Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke, and colleagues. For research information, contact Dr. Spitzer at ris8@columbia.edu. PRIME-MD (Primary Care Evaluation of Medical Disorders) is a trademark of Pfizer, Inc.

Scoring PHQ-9: Confirmation of Depression and Patient Monitoring

A. Scoring instructions: The total PHQ-9 score is the sum of the scores for the responses to questions 1 through 9.
B. If there are at least 4 checks in the gray highlighted section (including Questions #1 and #2), consider a depressive disorder. Add score to determine severity.

Interpretation of Total Score
Total Score Depression Severity
1-4 Minimal depression
5-9 Mild depression
10-14 Moderate depression
15-19 Moderately severe depression
20-27 Severe depression

C. Consider Major Depressive Disorder
If there are at least 5 checks in the gray highlighted section (one of which corresponds to Question #1 or #2)

D. Consider Other Depressive Disorder
If there are 2 to 4 checks in the gray highlighted section (one of which corresponds to Question #1 or #2)
Note: Since the questionnaire relies on patient self-report, all responses should be verified by the clinician and a definitive diagnosis made on clinical grounds, taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient. Diagnoses of Major Depressive Disorder or Other Depressive Disorder also require impairment of social, occupational, or other important areas of functioning (Question #10) and ruling out normal bereavement, a history of a Manic Episode (Bipolar Disorder), and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

E. To monitor severity over time for newly diagnosed patients or patients in current treatment for depression:

Initial response after Four weeks of an Adequate Dose of an Antidepressant		
PHQ 9	Treatment Response	Treatment Plan
Drop of 5 points from baseline	Adequate	No change, follow up 4 wks
Drop of 2-4 points from baseline	Possibly Inadequate	May warrant an increase in antidepressant dose
Drop of 1 point or no change or increase	Inadequate	Increase dose; augmentation; switch medicine; psych consultation; add counseling
Initial response after Six weeks of Psychological Counseling		
PHQ 9	Treatment Response	Treatment Plan
Drop of 5 points from baseline	Adequate	No change, follow up 4 wks
Drop of 2-4 points from baseline	Possibly Inadequate	Probably no treatment change needed. Share results with psychotherapist
Drop of 1 point or no change or increase	Inadequate	If depression-specific psychological counseling (Cognitive –Behavioral Therapy, etc) discuss with therapist and consider adding antidepressant For patient satisfied with other type of counseling, consider starting antidepressant For patients dissatisfied in other psychological counseling, review treatment options and preferences

Adapted from MacArthur Depression Toolkit www.depression-primarycare.org

Appendix E: Edinburgh Postnatal Depression Scale (EPDS)

In the past 7 days:

4. I have been anxious or worried for no good reason
   - __ No, not at all 0
   - __ Hardly ever 1
   - __ Yes, sometimes 2
   - __ Yes, very often 3

5. I have felt scared or panicky for no very good reason
   - __ Yes, quite a lot 3
   - __ Yes, sometimes 2
   - __ No, not much 1
   - __ No, not at all 0

6. Things have been getting on top of me
   - __ Yes, most of the time I haven't been able to cope 3
   - __ Yes, sometimes I haven't been coping as well as usual 2
   - __ No, most of the time I have coped quite well 1
   - __ No, I have been coping as well as ever 0

7. I have been so unhappy that I have had difficulty sleeping
   - __ Yes, most of the time 3
   - __ Yes, sometimes 2
   - __ Not very often 1
   - __ No, not at all 0

8. I have felt sad or miserable
   - __ Yes, most of the time 3
   - __ Yes, quite often 2
   - __ Not very often 1
   - __ No, not at all 0

9. I have been so unhappy that I have been crying
   - __ Yes, most of the time 3
   - __ Yes, quite often 2
   - __ Only occasionally 1
   - __ No, never 0

10. The thought of harming myself has occurred to me
    - __ Yes, quite often 3
    - __ Sometimes 2
    - __ Hardly ever 1
    - __ Never 0

A score of 12 or more identifies most women with postpartum depression. Women who report depressive symptoms without suicidal ideation or major functional impairment (or score between 5 and 9 on the EPDS) should be re-evaluated within one month.

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