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 aged 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 World Health Organization ranks unipolar major depression as the 11th greatest cause of disability and mortality in the world. In the United States, major depression ranks second among all diseases and injuries as a cause of disability, and persistent depressive disorder (dysthymia) ranks 20th. The WHO considers depression to be a major cause of disability worldwide. (14).

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. (14)

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.
In addition, major depression is highly recurrent. Following recovery from one episode, the estimated rate of recurrence over two years is greater than 40 percent; after two episodes, the risk of recurrence within five years is approximately 75 percent.

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)
- Bipolar Major Depression
- Persistent depressive disorder (dysthymia)
- Disruptive mood dysregulation disorder
- Premenstrual dysphoric disorder
- Substance/medication induced depressive disorder

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●Depressive disorder due to another medical condition
●Other specified depressive disorder (e.g., minor depression)
●Unspecified depressive disorder

A. Unipolar Major Depression: This is characterized by one or more major depressive episodes and no episodes of mania or hypomania. These episodes occur for 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
- Decrease or increase in appetite nearly every day +/-weight loss when not dieting, or weight gain
- 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.

Depressive episode subtypes (specifiers) — DSM-5 specifies several subtypes of depressive episodes. However, it is not clear whether most of these subtypes are useful for choosing a specific treatment.
The diagnostic criteria for depressive episode subtypes are as follows:

●**Anxious distress** – Anxious distress is characterized by the presence of two or more of the following symptoms during most days of the depressive episode:
•Tension
•Restlessness
•Impaired concentration due to worry
•Fear that something awful may happen
•Fear of losing self-control
●**Atypical features** – Atypical features are characterized by at least three of the following symptoms during the depressive episode; at least one of the symptoms is mood reactivity to pleasurable stimuli:
•Reactive to pleasurable stimuli (i.e., feels better in response to positive events).
•Increased appetite or weight gain.
•Hypersomnia (e.g., sleeping at least 10 hours per day, or at least two hours more than usual when not depressed).
•Heavy or leaden feelings in limbs.
•Longstanding pattern of interpersonal rejection sensitivity (i.e., feeling deep anxiety, humiliation, or anger at the slightest rebuff from others), which is not limited to mood episodes, and which causes social or occupational

conflicts.
●**Catatonia** – Catatonic features are characterized by prominent psychomotor disturbances (either increased or decreased activity), which occur during most of the depressive episode
●**Melancholic features** – Melancholic features are characterized by at least four of the following symptoms during a depressive episode; at least one of the symptoms is either loss of pleasure or lack of reactivity to pleasurable stimuli [8]:
•Loss of pleasure in most activities
•Unreactive to usually pleasurable stimuli (i.e., does not feel better in response to positive events)
•Depressed mood marked by profound despondency, despair, or gloominess
•Early morning awakening (e.g., two hours before usual hour of awakening)
•Psychomotor retardation or agitation
•Anorexia or weight loss
•Excessive guilt

B. Bipolar Major depression: Bipolar disorder is a mood disorder that is characterized by periods of pathologic mood elevation (mania or hypomania). Patients with bipolar I disorder experience manic episodes and nearly always experience both hypomanic episodes and major depressive episodes. Bipolar II disorder is characterized by at least one episode of hypomania and one or more major depressive episodes. In addition, psychotic features such as delusions and hallucinations frequently accompany bipolar depressive episodes, particularly in patients with bipolar I disorder.

C. 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

D. 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

Other Depressive Disorders:

E. Substance/medication induced depressive disorder — Substance/medication-induced depressive disorder consists of a mood disturbance that is characterized by a persistently depressed or irritable mood, or diminished interest or pleasure in most activities. The mood disturbance develops during or soon after using substances for recreational purposes or using prescribed medications; the substances/medications are judged to be capable of causing the mood disturbance. In addition, the disturbance causes significant distress or impairs psychosocial functioning.

Substance/medication-induced depressive disorder is not diagnosed in the following situations:

●The mood disturbance precedes onset of substance intoxication or withdrawal, or exposure to medications
●The disturbance persists for a long period of time (e.g., one month) after cessation of acute intoxication or withdrawal
●There is a prior history of recurrent depressive episodes
●The disturbance occurs solely during an episode of delirium

Depressive syndromes may be caused by intoxication or withdrawal from a wide range of substances that are encountered in substance-related and addictive disorders, including alcohol, amphetamines, cannabis, cocaine, and stimulants.

Substance/medication-induced depressive disorder is often referred to as "secondary depression."

F. Depressive disorder due to another medical condition — Depressive disorder due to another medical condition consists of a mood disturbance that is characterized by a persistently depressed or irritable mood, or diminished interest or pleasure in most activities. Findings from the history, physical examination, or laboratory tests indicate that the disturbance is caused by another medical condition (e.g., adrenal insufficiency, Huntington disease, hypercortisolism, hypothyroidism, mononucleosis, multiple sclerosis, obstructive sleep apnea, Parkinson disease, stroke, systemic lupus erythematosus, traumatic brain injury, or vitamin B12 insufficiency). In addition, the disturbance results in significant distress or impairs psychosocial functioning. Onset of the mood disturbance generally occurs during the first month of the onset of the other medical condition. In some cases, depressive syndromes represent a prodrome or early manifestation of the other medical condition. Depression that results from the treatment of chronic illnesses, such as corticosteroids or interferon, is diagnosed as substance/medication-induced depressive disorder. While clinicians should always remain vigilant for the presence of other medical illnesses causing or contributing to a depressive episode, the following circumstances raise the possibility of an otherwise clinically occult medical condition contributing to the depressive presentation.

●Severe new-onset depression, including melancholia and psychotic depression
●New-onset depression in an older adult, or in a younger adult with significant chronic or acute medical conditions
●New-onset or recurrent depression that is not readily understood in the context of the patient's psychosocial stressors and circumstances
●Depression that has not responded to treatment attempts
● Depressive disorder due to another medical condition is not diagnosed if the mood disturbance clearly precedes onset of the medical condition or occurs solely during an episode of delirium
● Depression with significant coexisting anxiety or neurocognitive impairment.

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. (Grade B recommendation).

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) (Appendix C) and Patient Health Questionnaire-9 (PHQ-9) (Appendix D) 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. (Sensitivity 88%, specificity85%) (28) 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

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. **Medical Co-morbidities***: Patients with the following medical comorbidities (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 the left basal ganglia or left dorsal lateral frontal cortex. (29-31)
   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%. (32-34)
   e) Cancer - Major depression occurs in approximately 25% of this population
   f) Fibromyalgia (35)
   g) HIV/AIDS

3. **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. (Integrated into MedConnect)

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 and tricyclic antidepressants may trigger manic episodes in patients with bipolar disorder. A family history of Bipolar Disorder increases the risk that a depressive episode may be of the bipolar type as well.
   - **Alcohol dependence/drug dependence** – Substance-induced depression is a well-established etiology of various substances and is likely to resolve after 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
- Most importantly, while the symptoms are indistinguishable, a pattern of gradual improvement from week to week is strongly supportive of a normal grief response

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 or comorbid schizophrenia
- hopelessness
- general medical illnesses
- living alone with little social support
- prior suicide attempts.
- borderline personality disorder
- Bipolar Depression is also associated with higher risk

Questions about plans and means should be asked. In patients with major depression, previous suicide attempts are the best predictor of completed suicide. More than 50% of men who complete suicide do so with a firearm. Asking about and reducing access to lethal means (especially firearms) can reduce suicide risk

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 "Scales and Assessments" in provider workflow, or "Ad Hoc Charting" or then opening the folder called "Additional Assessments" and selecting "Suicide-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. (Appendix F)

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

Clinical Management:

A. Goals

1. Remission- Resolution of the depressive syndrome, which can be operationalized by a depression rating scale score less than or equal to a specific cutoff that defines the normal range. E.g., The Patient Health Questionnaire (PHQ-9) uses remission as a score < 5
2. Restore occupational and psychosocial functioning.
3. Reduce the likelihood of relapse and recurrence.

B. Types of Treatment:

1. **Pharmacotherapy** - Patients with moderate to severe clinical depression are appropriate candidates to be treated with medication, whether formal psychotherapy is also used. (39, 40, 41, 45-48). For patients in acute phase of mild MDD for whom CBT is not available/feasible monotherapy with SGA is a reasonable alternate approach. First-line treatment typically consists of starting a second-generation antidepressant.
   Second-generation antidepressants that are available to treat unipolar major depression include:
   ●Selective serotonin reuptake inhibitors (SSRIs)
   ●Serotonin-norepinephrine reuptake inhibitors (SNRIs)
   ●Atypical antidepressants: such as Bupropion or Mirtazapine
   ●Serotonin modulators

Older, first-generation antidepressants are less commonly used and include:
●Tricyclic antidepressants TCA
●Monoamine oxidase inhibitors (MAOIs): while MAOIs might show greater effectiveness due to less receptor specificity, this also results in higher rates of side effects).
(39-41)

2. **Psychotherapy** – Various psychotherapeutic interventions are available and are considered first-line therapy for mild to moderate depression. Psychotherapy is generally considered to be as effective as pharmacotherapy. A meta-analysis of 53 trials showed that there was no significant difference in response rate among the various types of psychotherapies. (36-38) These include:
    - Cognitive behavioral therapy (CBT) and behavioral activation: Patients identify negative thoughts and patterns and reframe and modify these in a constructive way
    - Interpersonal therapy (IPT): Patients identify and address the role those interpersonal relationships have on perpetuating depressive symptoms
    - Problem solving therapy- Patients identify strategies to solve problems in a practical manner and increase self-efficacy
    - Psychodynamic therapy-Patients identify and explore the unconscious elements that contribute to current issues. 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.
    - Behavioral Activation (during which patients identify negative thoughts and patterns and reframe and modify these in a constructive way)
    - Supportive psychotherapy
    - Family and couple's therapy

   The highest level of evidence exists for CBT and IPT. (39, 41, 42, 43, 44). The primary limitations to psychotherapy are cost, insurance coverage, and access to treatment. Telehealth-based delivery of psychotherapy has been shown to be an effective way to improve outcomes in resource-limited and time-limited settings with similar patient satisfaction as in-person interventions. (20)

3. **Medication and Psychotherapy**- This may be advantageous for complicated, chronic depression and for patients with only a partial response to either treatment alone or patients with severe depression (e.g., PHQ-9 > 20, hospitalization), recurrent depression, and patients with psychosocial difficulties that interfere with treatment adherence. (Appendix A)
4. **Electroconvulsive therapy (ECT)** - This is only for certain patients after psychiatric consultation. The primary indication for ECT is severe major depression that is life-threatening or significantly impairs functioning. Most effective and fastest acute treatment for major depression.

5. **Transcranial Magnetic Stimulation** - reserved for treatment-resistant patients. It can be efficacious and generally well-tolerated. It is contraindicated in patients with increased risk for seizures, implanted metallic hardware, cochlear implants, implanted electrical devices and unstable general medical disorders.

6. **Esketamine -** an analogue of ketamine, is a newer therapy that is FDA-approved for treatment-resistant depression in conjunction with an oral antidepressant. Esketamine is administered intra-nasally and has a rapid onset of action

C. Medication Selection and Management

A landmark meta-analysis performed by Cipriani et al. comparing 21 antidepressants from 522 trials, with respect to their effectiveness and tolerability against one another, showed the following results summarized below. Generally, all 21 agents showed a statistically significant effect compared to placebo (19)

Most effective: amitriptyline, escitalopram, mirtazapine, paroxetine, venlafaxine, and vortioxetine
Least effective: fluoxetine, fluvoxamine (SSRI), and trazodone
Better tolerated: citalopram, escitalopram, fluoxetine, sertraline, and vortioxetine
Highest dropout rate (mostly due to side effects or lack of efficacy): amitriptyline, clomipramine, duloxetine, fluvoxamine, trazodone, and venlafaxine.

1. **Selective Serotonin Re-uptake Inhibitors (SSRI)** could 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. 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, weight gain, drowsiness, insomnia, serotonin syndrome, Parkinson like tremor and sexual side effects. In elderly patients there is an increased risk of hyponatremia.
   Specific examples from this drug class include:
   - Fluoxetine: good tolerability, least amount of weight gain
   - Escitalopram: among the SSRIs with highest efficacy
   - Citalopram: better tolerability, however higher risk of QTc prolongation
   - Paroxetine: highest association with weight gain, significant sexual side effects, and discontinuation syndrome (development of withdrawal-like symptoms including headache, agitation, irritability, diaphoresis, "electric shock-like" sensations and even hallucinations following abrupt cessation or taper of antidepressant)
   - Sertraline: fewer drug-drug interactions (no specific CYP inhibition), higher bioavailability when taken with food, higher rate of GI side effects

   Special considerations:
   Older patients: sertraline, citalopram, and escitalopram are good first line choices. There is now concern with QTc prolongation with citalopram and escitalopram and the FDA has adjusted the recommended doses down., especially in women, making them a more careful choice in older women or patients with cardiac vulnerability. Avoid paroxetine and fluoxetine due to higher risk of anti-cholinergic effects and overstimulation
   ESRD: preferred agent is sertraline, as no renal dosing is required
   Breast cancer patients: concerns regarding interference of fluoxetine and paroxetine with tamoxifen (CYP2D6 interaction)

2. **Serotonin Norepinephrine Reuptake Inhibitors**: Similar side effect profile to SSRIs, including GI side effects, sexual dysfunction, headaches, but also with increased risk for hyponatremia. Specific examples include:
   - Venlafaxine: ER (extended-release) preferred over IR (immediate-release) due to

easier dosing and less nausea; most frequently studied agent
- Duloxetine: needs careful dosing in renal impairment, commonly used in conjunction with chronic neuropathic pain treatment

3.**Atypical Antidepressants**: Often used to augment effects of SSRIs but may also be used as first line treatments.

- Mirtazapine: increased appetite (also causes weight gain), improves symptoms of insomnia (but can also cause increased fatigue)
- Bupropion: A dopamine and norepinephrine reuptake inhibitor, sustained release bupropion exhibits lower rates of sexual side effects and weight gain than other second-generation anti-depressants (SGAs) but may lower seizure threshold in susceptible hosts.

4. **Serotonin Modulators**: Advances in understanding brain neurophysiology have led to the development of serotonin modulators, including:

- Nefazodone
- Trazodone
- Vilazodone
- Vortioxetine

The serotonin modulators are distinct from other classes of antidepressants that include selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, atypical antidepressants, tricyclics, and monoamine oxidase inhibitors. Serotonin modulators act as antagonists and agonists at postsynaptic serotonin receptors and inhibit reuptake of postsynaptic serotonin to varying degrees; effects upon norepinephrine reuptake are minimal.
The recently FDA-approved agents vortioxetine (serotonin modulator, similar to SSRI) and levomilnacipran (SNRI) have been classified as first-line therapy, and vilazodone (serotonin modulator) as second line by the Canadian Network for Mood and Anxiety Treatment (CANMAT) guidelines. However, no comparable U.S. guideline exists, due to the lack of generic options and because costs are typically high. (21)

Drug interactions and metabolism — Coadministration of serotonin modulators with another drug can decrease or increase the metabolism of the serotonin modulator, which may necessitate either adjusting the dose of the serotonin modulator or using a different antidepressant. Thus, prior to initiating or altering therapy with serotonin modulators, clinicians should check interactions with other medications. The drug interaction tool provides specific dose recommendations for prescribing serotonin modulators concomitantly with drugs that affect the serotonin modulator's metabolism. Serotonin modulators are metabolized by hepatic cytochrome P450 3A4 (CYP3A4) or 2D6 (CYP2D6) enzymes. Administering a serotonin modulator in conjunction with another drug that inhibits these enzymes can increase serum concentrations of the serotonin modulator, resulting in drug accumulation and toxicity. Prescribing a serotonin modulator concurrently with medications that induce the enzymes can decrease serum concentrations of the serotonin modulator and lead to therapeutic failure.

The hepatic metabolism of the serotonin modulators includes the following:

●Trazodone and vilazodone – Trazodone and vilazodone undergo extensive hepatic metabolism by CYP3A4 [2,3]. Strong CYP3A4 inhibitors and inducers are listed in the table (table 1).

●Vortioxetine – Vortioxetine undergoes extensive metabolism by CYP2D6 and is also metabolized by other CYP enzymes [4]. Drug-drug interactions can occur when vortioxetine is co-administered with medications that inhibit CYP2D6 metabolism, or medications that induce other CYP metabolic pathways. CYP2D6 inhibitors are listed in the table (table 2).
●Nefazodone – Although nefazodone seems to undergo extensive metabolism by CYP3A4 based upon in vitro data, this has not been well studied [5,6]. Strong CYP3A4 inhibitors and inducers are listed in the table (table 1).

Nefazodone is itself a strong inhibitor of CYP3A4 and can elevate levels of comedications that are dependent upon CYP3A4 for clearance.
Serotonin modulators can also interact with other medications that elevate serotonin in the central nervous system, potentially resulting in the serotonin syndrome with the potential serious effects of altered mental status, agitation, myoclonus, and hyperreflexia. These drug-drug interactions (e.g., with monoamine oxidase inhibitors) can be severe. Other medications with MAOI activity include the antibiotic linezolid. Very rarely serotonergic antidepressants may produce a serotonin syndrome with the concomitant use of buspirone, dextromethorphan, tramadol, or St. John's Wort. All SGA are contraindicated in patients who receive MAIOs in the previous two weeks because of drug-drug interactions that can cause serotonin syndrome and, in some cases, hypertensive crisis.

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

6. 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 which is improvement ≥50 percent but less than the threshold for remission. 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 adherence, and to monitor

emergence of mania, tolerability, suicide risk and early response. Addressing specific adverse effects is important to maintaining adherence until patients respond. 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. Some side effects are more noticeable with certain medications than others.

- **Diarrhea** occurs more often with sertraline than bupropion, citalopram, fluoxetine, fluvoxamine, mirtazapine, nefazodone, paroxetine, and venlafaxine (16 versus 8 percent of patients).
- **Nausea and vomiting** occurs more often with venlafaxine than SSRIs as a class (33 versus 22 percent).
- **Sexual dysfunction** occurs less often with bupropion than escitalopram, fluoxetine, paroxetine, and sertraline (6 versus 16 percent; paroxetine is especially problematic).
- **Somnolence** occurs more often with trazodone than bupropion, fluoxetine, mirtazapine, paroxetine, and venlafaxine (42 versus 25 percent)
- **Weight gain** is greater with mirtazapine (0.8 to 3.0 kg after six to eight weeks of treatment) than fluoxetine, paroxetine, trazodone, and venlafaxine. And is less likely with Bupropion

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. **Collaborative Care Approach:** For patients with mild to moderate major depressive disorder, consider referral to a collaborative care model, when it is locally available. This model has a care manager who meets with patients, discusses care recommendations with a psychiatrist, and coordinates medications and referrals with the primary care physician. The collaborative care team tracks this population over time, paying attention to measurement-based outcomes (such as PHQ-9) and progressively intensifying treatment until the specified outcomes are achieved

H. **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 disorders*
- *suspicion of bipolar disorder*
- *depression during pregnancy and the postpartum*
- *treatment-resistant depression*
- *childhood depression*
- *depression with dementia*

Patient Education:

Initial Approval Date and Reviews:	**Most Recent Revision and Approval Date:**	**Next Scheduled Review Date:**
April 2013, April 2015, April 2017, April 2019, April 2021, April 2023	**April 2023**	April 2025 Ambulatory Best Practice

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.
   - Exercise: While exercise, in low quality studies, was described to be comparable to CBT (23), a comparison to the use of second-generation antidepressants remained inconclusive. (20). Furthermore, it is unclear what the "dose" of exercise should be to achieve a clinical benefit. (15). However, patients, if able to exercise, should not be discouraged given that the risk of harm is low, and it provides other health benefits
   - Eat nutritious, well-balanced meals. Avoid drinking alcohol and coffee. 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.
   - Complementary and alternative medicine approaches: The most notable complementary and alternative medicine therapies generally have a low level of evidence and include St. John's wort (more effective than placebo, comparable efficacy to first- and second-generation antidepressants, lower side effect profile) and acupuncture (possibly more effective than no treatment, unclear if effect comparable to medication or psychotherapy, unclear adverse risk profile due to inadequate reporting in studies). Furthermore, data remain inconclusive on the efficacy of meditation, yoga,

SAdenosylmethionine, and omega-3 fatty acids. Moderate quality evidence exists for the addition of music therapy to treatment as usual to decrease anxiety and improve functioning in depression. (17). Of note, St. John's wort has significant drug-drug interactions and should not be used in conjunction with SSRIs or MAO-inhibitors.

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/#; Call 1-800-95-6264
- National Suicide Prevention Lifeline: 1-800-273-TALK or 1-800-273-8255; Suicide & Crisis Lifeline: Call or text 988; The Lifeline provides 24/7, free and confidential support for people in distress, prevention, and crisis resources.
- 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*® ($84)	20mg daily	20-40mg daily max dose 20 mg for age >60 or hepatic impairment	• 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. Discontinue in patients with QTc interval >500ms.
escitalopram *Lexapro*® ($148)	10mg daily	10-20mg daily	• Minimal drug interactions compared with other SSRIs • Possible quicker onset in resolving panic-related symptoms	• Risk of QT prolongation

fluoxetine *Prozac*® ($320)	10-20mg daily (Elderly dose 10mg/day)	20-80mg daily	• Energizing feeling • Lower cost of care	• Longer half life • More agitation
Fluvoxamine ($158)	50mg daily	100-200mg daily Divide doses >100mg	• Less cognitive disturbance	• Similar side effect profile to other SSRIs
fluvoxamine CR ($611)	100mg daily	100-200mg daily		
paroxetine *Paxil*® ($95)	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 (CrCl <30mL/min dose 12.5mg/day)	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)	10 mg daily	20-40 mg daily	• May have lower incidence of sexual dysfunction • May lead to less weight	
vortioxetine *Trintellix*® ($560 – brand only)	5-10 mg daily	20 mg daily	• May be alternative to partial or non-responders to SSRIs due to multi-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, hypo-natremia in elderly persons; potential for drug-drug interactions; contraindicated with MAOI; Increased risk of bleeding with SSRIs and SNRIs (especially in combo with NSAIDs).

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)	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. Cigarette smoking reduces plasma levels of duloxetine

venlafaxine *Effexor*® ($66)	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® ($625)	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 venlafaxine
levomilnacipran *Fetzima*® ($573) (Brand only)	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)	
milnacipran *Savella*® ($557) (Brand only)	25-50mg twice daily	100-200mg daily Divide doses >100mg	• Less agitation than other SNRIs	

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 ($84)	50mg bid (Depression) 25-50mg hs (Insomnia)	150-400mg daily in divided doses (w/food)	• Sedative properties	• Over-sedation and/or possible orthostasis • Priapism
nefazodone *Serzone*® ($304)	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. Caution in patients with renal impairment

VI. Tricyclic Antidepressants (TCA's)

Drug name	Initial Dose	Dosing Range	Positives	Limitations
amitriptyline ($229)	25-50mg 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*® ($253)	25-50mg hs	50-150 mg/day as single or divided doses	• Well known therapeutic and toxic levels • Less anticholinergic	• Cardiac arrhythmias

amoxapine ($204)	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 *Silenor*® ($200)	75mg 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 ($238)	25-50mg hs	100-300mg 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 ($1080)	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 ($1460)	25-50 mg hs or in divided doses	75-300mg hs	• Patients with insomnia or anxiety	• Weight gain • Sedation

VII. Monoamine Oxidase Inhibitors (MAOIs)

Drug Name	Initial Dose	Dosing Range	Positives	Limitations
isocarboxazid *Marplan*® ($1022 – 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*® ($2451) (brandonly)	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*® ($442/28mg – 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

Discount cards like Good Rx provide deep discounts, making some medications listed above cost $10-20 a month.

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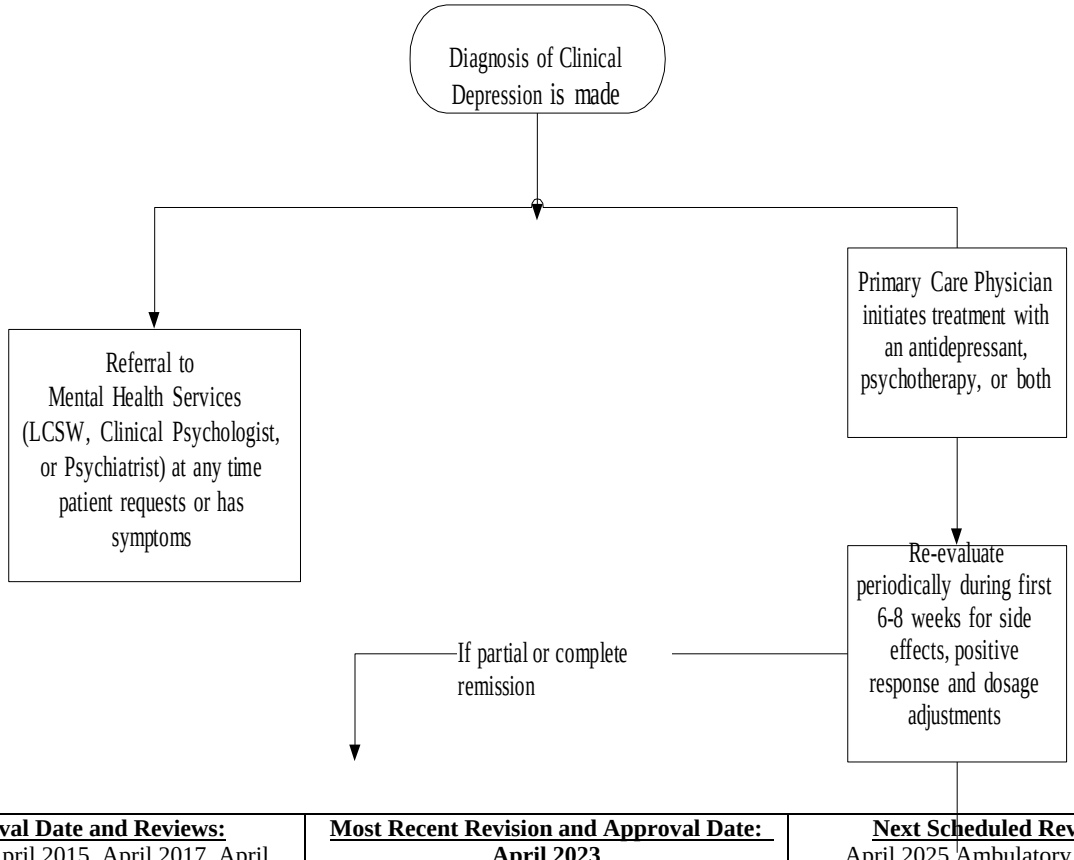
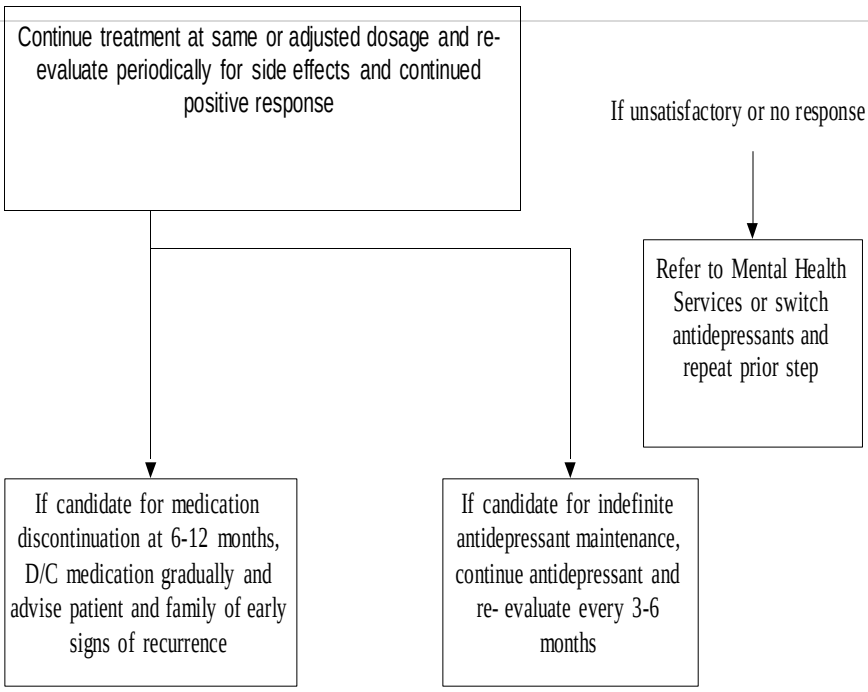
APPENDIX A: Clinical Depression Treatment Algorithm





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

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**

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 weeks
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 weeks
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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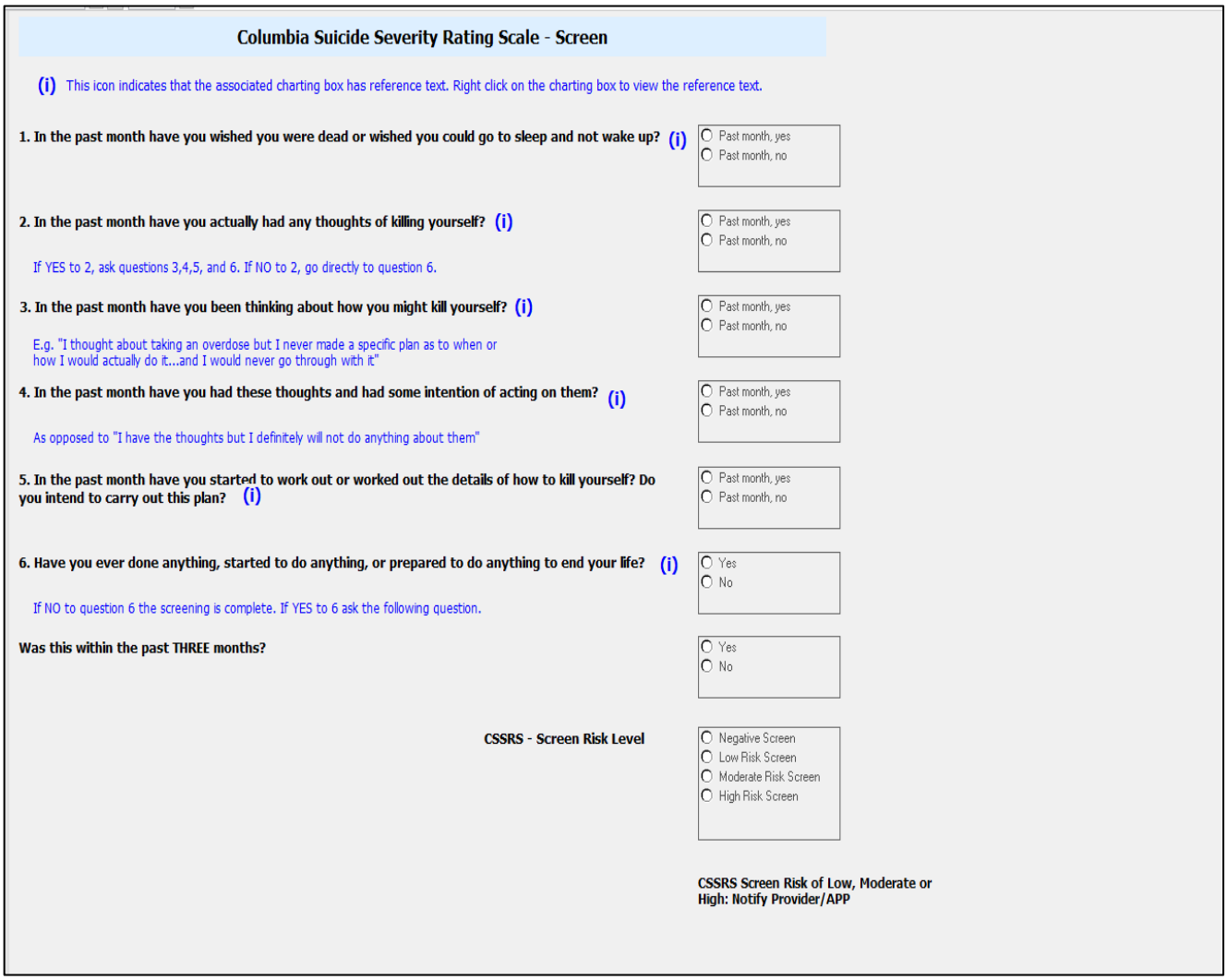
APPENDIX F: Columbia Suicide Severity Rating Scale-Screen



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