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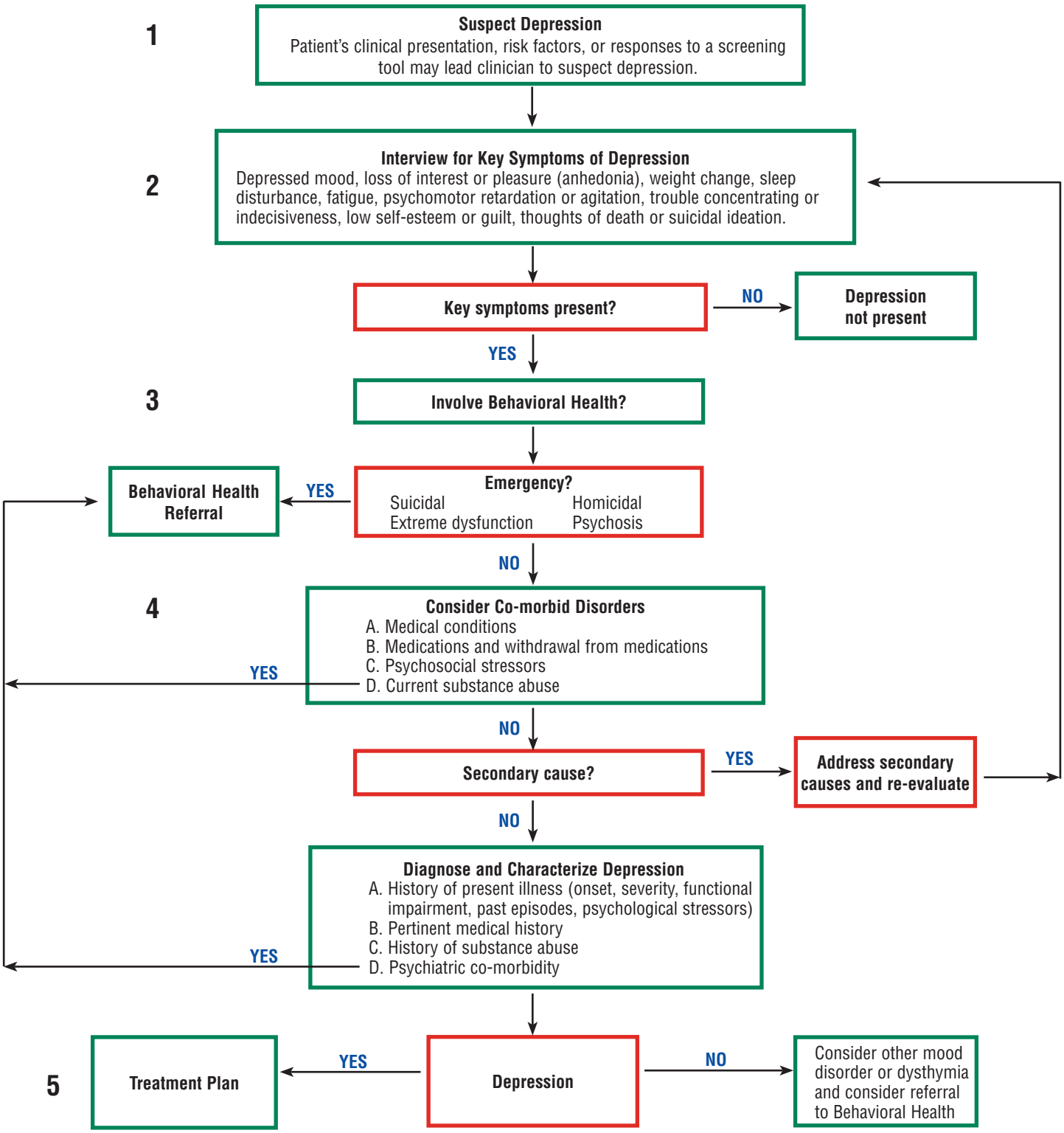
Treating Depression in Adults in Primary Care: Clinical Practice Guidelines

Guidelines are designed to assist clinicians by providing a framework for the evaluation and treatment of patients. These guidelines outline the preferred approach for most patients. They are not intended to replace a clinician's judgement or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

DIAGNOSING DEPRESSION IN ADULTS



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TREATMENT PLAN FOR DEPRESSION IN ADULTS

Select and Initiate Therapy
A) Mild DD* – Pharmacotherapy or psychotherapy
B) Moderate / Severe DD** – Pharmacotherapy with or without psychotherapy

Consider Medication When:
- Depression is moderate to severe
- Patient has had prior positive response to medication
- Patient has had recurrent depressive episodes
- As adjunct to psychotherapy or if psychotherapy is unavailable

Educate about Depression and Medications
For antidepressant medications, compliance with a therapeutic dose is more important than the specific drug selected. The following educational messages may increase adherence:
A) Take the medication daily as prescribed.
B) Antidepressants must be taken daily for 4 to 6 weeks for a noticeable effect.
C) Continue to take medication even if you are feeling better: increased risk of relapse if stopped before 6 months.
D) Do not stop taking antidepressant without checking with your provider. Some antidepressants may have uncomfortable withdrawal symptoms.
E) Contact your provider if you have questions about your medication.
F) Be sure to make and keep a follow-up appointment.

Monitor Acute Treatment (first 12 weeks)
- Patients should have a minimum of three contacts during the acute phase
- Patients should be reminded to call within one week if they experience adverse medication reactions
- Consider referral to behavioral health if more severe symptoms present
- Certain patients (new, unstable, those on many medications, those with sudden onset) may need to be seen more often and may require close observation
- Once the depression has resolved, visits every 4-12 weeks are reasonable

Assess Response
- Pharmacotherapy – 4-6 weeks
- Psychotherapy – 6-12 weeks

CLEARLY BETTER

SOMEWHAT BETTER

NOT BETTER AT ALL

Continue Therapy
Assess response every 4-12 weeks

Adjust Therapy
- Pharmacotherapy – consider adjusting dose
- Psychotherapy – consider augmenting with medical therapy

Adjust or Change Therapy
- Augment or change treatment
- Consider referral to behavioral health
- Assess adherence to medication

Full Symptom Remission?

NO

YES

Monitor Treatment
Patient should continue to be seen every 1-6 weeks by provider or behavioral health practitioner

Continuation Therapy
- Pharmacotherapy – continue for 6-9 months
- Psychotherapy – consider resolution of unresolved psychosocial issues

CLEARLY BETTER

Assess Response
4-6 weeks following therapy change

NOT BETTER

Has patient been asymptomatic for 6-9 months?

NO

Consider
- Changing treatment
- Augmenting treatment
- Re-evaluating diagnosis
- Consult with behavioral health

YES

- Discontinue treatment or consider maintenance therapy ***
- Continue ongoing assessment

Footnotes

* **Mild depressive disorder:** Depression without prominent vegetative symptoms, suicidal ideation, or significant functional impairment.

** **Moderate to severe depression disorder**: Depression with significant neurovegetative symptoms, hopelessness, or suicidal ideation.

*** **Maintenance therapy** (1 year to lifetime) should be considered for patients who have had 3 or more episodes of depression.

There are three types of depression that should be recognized by primary practitioners.

Depression is the most important because of its associated disability and its treatability.

- Depression is characterized by a persistent disturbance in mood of at least two weeks duration that is usually accompanied by diminished interest in life, and significant impairment in the individual's social, occupational, and physical functioning.
- The point prevalence of depressive disorder in the Western industrialized nations is 2.3-3.2% for men and 4.5-9.3% for women. The lifetime risk for depressive disorder is 7-12% for men and 20-25% for women.[1]

Chronic minor depression (dysthymia) is also common but more difficult to treat than a primary depression.

Adjustment disorder with depressed mood is by far the most common depressive disorder in primary care, but much less is known about its prevalence, associated disability, and treatment.[5] Occasionally this is known as pathological grief, if symptoms persist beyond 3 months or worsen, depression should be considered.

1. SUSPECT DEPRESSION

Physical complaints are extremely common in depression and are often the primary manifestation of the illness. Somatic manifestations of depression include fatigue, insomnia, anorexia, weight loss, gastrointestinal disturbances, and a variety of pain complaints. Anxiety and agitation are common as secondary symptoms.[5]

Common Presentations of patients with depression include:

- multiple office visits
- numerous unexplained symptoms
- work or relationship dysfunction
- sleep disturbance
- multiple worries and distress

Risk Factors for depression include:

- prior episodes
- family history of depressive disorder
- female gender
- postpartum period
- peri/postmenopausal period
- medical co-morbidity
- lack of social support

Screening Instruments have been developed for use in various clinical settings, including ambulatory primary care. The primary objective of these well-tested tools is to obtain input from the patient regarding their symptoms related to depression. These tools tend to be fairly sensitive, but not too specific in the recognition of depression. These are generally self-administered and then reviewed by the practitioner. Screening patients is recommended when depression is suspected.

Information on several tools is listed below. One simple means of screening is to ask two questions while completing an exam:

1) Over the past two weeks have you ever felt down, depressed, or hopeless?, and
2) Have you felt little interest or pleasure in doing things?

In addition, the CES-D screening tool is included in with this guideline and may be copied without charge.

DEPRESSION SCREENING TOOLS	CONTACT	COST
CES-D, Center for Epidemiological Studies Depression Scale	Tool included in guideline.	No charge
PRIME-MD	See your Pfizer pharmaceutical representative	No charge
Beck Depression Inventory - Fast Screen for Medical Patients	Psychological Corporation Harcourt Brace PO Box 839954 San Antonio, TX 78283-3954 800-2118378	$1.20 per tool (discount for quantity)
Geriatric Depression Scale	http://www.stanford.edu/~yesavage/GDS.html	No charge
Postpartum Depression Screening Scale by Cheryl Beck at University Connecticut	Western Psychological Services 12031 Wilshire Boulevard Los Angeles, CA 90025-1251 1-310-478-2061 www.wpspublish.com	$1.20 per tool
Zung	See your GlaxoSmithKline or Lilly pharmaceutical representative	No charge

2. INTERVIEW FOR KEY SYMPTOMS OF DEPRESSION

A Detailed Clinical Interview is used to confirm the diagnosis of depression. Questions include:

- Are you often sad, down, blue or teary?
- Do you have your usual interest in and look forward to enjoyable activities?
- Are you able to have fun or joy?
- Do you have sleep disturbances, changes in appetite and energy level?

DSM IV Symptoms[3]

The diagnosis of depression requires that the patient have five or more of the nine symptoms. Symptoms must be present during the same two-week period of time, nearly every day, and represent a change from previous functioning.
At least one of the symptoms must be either 1.) depressed mood or 2.) loss of interest or pleasure.

At least five of the following:

1. Depressed mood
2. Loss of interest or pleasure
3. Weight loss or gain (or appetite loss or gain)
4. Sleep disturbance
5. Fatigue
6. Psychomotor retardation or agitation
7. Trouble concentrating or indecisiveness
8. Low self-esteem or guilt
9. Thoughts of death or suicidal ideation

History of the Present Illness should detail the onset and severity:

- **Mild** – five or six depressive symptoms with minor impairment in functioning
- **Moderate** – symptoms and functional impairment between mild and severe
- **Severe** – most depressive symptoms present with clear-cut impairment of functioning

3. INVOLVE BEHAVIORAL HEALTH

Emergency "Same Day" Behavioral Health Consultation/Evaluation should be considered for:

- suicidal thoughts and/or plans that make the patient's safety uncertain
- assaultive and/or homicidal plans which make the safety of others uncertain
- loss of touch with reality (psychosis)
- significant or prolonged inability to work and care for self and/or family

Referral to a Behavioral Health Specialist is recommended when there is:

- psychiatric co-morbidity (for example, mania or hypomania, obsessive compulsive disorder, or eating disorders)
- concern regarding the possibility of suicide and/or homicide
- alcohol or substance abuse
- psychosis with the depression
- a patient who is pregnant or wants to become pregnant
- diagnostic uncertainty
- no improvement with medications prescribed by the primary physician

4. CONSIDER CO-MORBID DISORDERS

In evaluating patients with the symptoms of depression, the primary care practitioner must determine if the depression is a primary process or is a symptom of other medical conditions. Screening for other medical conditions should be based on clinical judgement

Medical Conditions: Many medical conditions (cancer, coronary artery disease, diabetes mellitus, cerebral vascular accident, hypothyroidism, hyperthyroidism) are risk factors for depression. Depressive disorder, when present, should be considered an independent condition and specifically treated. Treatment may include optimizing treatment for the medical condition and/or providing specific treatment for the depression. When depression and a medical condition co-exist, there are several plausible explanations:

- The medical disorder biologically causes the depression (for example, hypothyroidism may cause depression).
- The medical disorder triggers the onset of depression in those who are genetically predisposed to depression.
- The perceived severity of the illness causes depression (for example, a patient with cancer becomes depressed as a psychological reaction to prognosis and pain).
- The medical disorder and the depression are not causally linked.

It is important for the physician to differentiate among these several explanations in patients with concomitant medical disorder(s) and depression.[2]

Medications: Some medications may cause depressive symptoms:

DRUG causing Depression	Potential Alternatives
Clonidine, Methyldopa, Reserpine	Other antihypertensive agent (diuretics, ACE-I, CCB, ARB, etc)
Lipophilic beta blockers (propranolol)	Atenolol or metoprolol
Corticosteroids	Minimize dose as allowed
Sedatives/Hypnotics	Consider taper off
Benzodiazepines	Minimize use
Estrogens/Progesterones	Addition of Vitamin B6, use lower progestin
Anti-Parkinson Medications	No alternatives
Anti-convulsants	Consider diagnosis and alternatives
Indomethacin	Other NSAIDS
Interferons (HepC, MS)	No alternatives

Other Psychiatric Disorders: Patients with depressive symptoms or in a depressive episode may have a co-existent non-mood psychiatric disorder.

- **Substance abuse:** depressed patients with concurrent substance abuse should discontinue the abused substance and their depression should be reevaluated 4-8 weeks later when they are drug-free. If depressive disorder is still present, it should be treated as a primary mood disorder. Alcoholism is rarely a consequence of depression, but many alcoholics develop depressive symptoms or the syndrome of depression.
- **Anxiety, panic, obsessive-compulsive, or phobic disorders** are often accompanied with depressive symptoms. Depression can also mask underlying psychiatric disorders. Anxiety symptoms are frequent in depressive episodes. The depression may precede the panic or anxiety disorder, or the anxiety disorder may be part of the longitudinal course of the mood disorder. When a patient has anxiety symptoms, the existence of depressive symptoms should be evaluated. For those patients whose disorder has some obsessive features, the mood disorder is the initial focus of treatment.
- **Eating disorders**: young women who present with any mood disorder should be interviewed for symptoms of anorexia nervosa and/or bulimia. One-third to one-half of patients with eating disorders have a concurrent depressive syndrome. If both depression and an eating disorder are present, the eating disorder, generally, should be the principal therapeutic target.

Grief Expression: Bereavement is depressive symptoms beginning within 2-3 weeks of the death of a loved one.3 Bereavement is considered a normal, relatively benign state that most often resolves without treatment. In those bereaved patients who meet the diagnostic criteria for a depression two months following the loss, the diagnosis of a depressive disorder may be made.

5. TREATMENT PLAN

The Initial Objectives of Treatment, in order of priority, are:

1. Reduction and ultimately removal of all signs and symptoms of the depressive syndrome.
2. Restoration of psychosocial and occupational function to that of the asymptomatic state.
3. Reduction of the likelihood of relapse or recurrence.

The Four Treatment Domains For Depressive Disorder

Factors considered in making treatment recommendations are the severity of symptoms, presence of psychosocial stressors, presence of co-morbid conditions, and patient preferences.

1. **Psychotherapy** alone is not recommended for the acute treatment of patients with severe and/or psychotic depressive disorders.

2. **Medication**: for essentially all patients, the practitioner who provides the medication also provides support, advice, reassurance, and hope, as well as, medication monitoring. This “clinical management” is critical with depressed patients whose pessimism, low motivation, low energy, and sense of social isolation or guilt lead them to give up, not comply with treatment, or to drop out of treatment.

   Selection of a particular medication should take into consideration:
   - Prior positive/negative response to medication
   - History of first degree relatives’ responses to medication
   - Concurrent medications that make selected medications more or less risky

   See formulary, cost, and drug information on antidepressant therapies at the end of this guideline.

3. **Combination of medication and psychotherapy**

4. **Electroconvulsive Therapy (ECT)**

Patient Education on the treatment of depression is important for patient compliance with therapy. For antidepressant medications, compliance with a therapeutic dose is more important than the specific drug selected. The following educational messages may increase adherence:

- Take the medication daily as prescribed.
- Antidepressants must be taken daily for 2-4 weeks for a noticeable effect.
- Continue to take medication even if you are feeling better, increased risk of relapse if stopped before 6 months.
- Do not stop taking antidepressant without checking with your provider. Some antidepressants may have uncomfortable withdrawal symptoms.
- Contact your provider if you have questions about your medication.
- Be sure to make and keep follow-up appointments.

Treatment Plan Phases

1. **Acute Treatment (first 12 Weeks)** aims to remove all signs and symptoms of the current episode of depression and to restore psychological and occupational functioning (a remission).

   The patient should be seen a minimum of three times during the acute phase. At least one of those encounters should be with the prescriber. Patient non-compliance is high in those with depression, and the practitioner must assertively engage the patient in follow-up care and assessments.
   - Patients should have a minimum of three contacts during the acute phase (first 12 weeks)
   - Patients should be reminded to call within one week if they experience adverse medication reactions
   - Consider referral to behavioral health if more severe symptoms present.
   - Certain patients (new, unstable, those on many medications, those with sudden onset) may need to be seen more often and may require close observation
   - Once the depression has resolved, visits every 4-12 weeks are reasonable.

   Treatment response should be assessed every 4-6 weeks for drug therapy and every 6-12 weeks for psychotherapy. See sample flow sheet to assess response to therapy. Most patients respond partially to medication within 2-3 weeks and full symptom remission is typically seen in 6-8 weeks. If the patient does not respond at all by 6 weeks (4 weeks in severely ill), or responds only partially by 12 weeks, other treatment options should be considered including:
   - Assess medication adherence
   - Continue medication at a corrected dose
   - Change medication
   - Augment with a second medication (not advised until initial trial adequate in time and dosage)
   - Refer for professional psychotherapy. Most patients receiving time-limited psychotherapy respond partially by 5-6 weeks and fully by 10-12 weeks.
   - Obtain a behavioral health consultation

2. **Continuation Therapy (next 6 - 9 months)** is intended to prevent relapse.

   - The patient should remain on medication for at least 6 months after symptoms resolve.
   - Once the patient has been asymptomatic for at least 6 to 9 months following an episode, recovery from the episode is declared. At recovery, treatment may be stopped.

3. **Maintenance Therapy (1 Year to lifetime)** is aimed at preventing a new episode. Patients who have had three or more episodes of depression should be considered for long-term maintenance medication therapy.

References:

1. Clinical Practice Guideline Number 5: Depression in Primary Care, 1: Detection and Diagnosis. Rockville, MD: US Dept of Health and Human Services, Agency for Health Care Policy and Research; 1993. AHCPR publication 93-0550.
2. Clinical Practice Guideline Number 5: Depression in Primary Care, 2: Treatment of Major Depression. Rockville, MD: US Dept of Health and Human Services, Agency for Health Care Policy and Research; 1993. AHCPR publication 93-0550.
3. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC, American Psychiatric Association, 1994.
4. Kupfer DJ, Frank E, Perel JM, et al. Five-year outcome for the maintenance therapies in recurrent depression. Arch Gen Psychiatry. 1992; 49: 769-73.

5. Peden JG, Lichstein PR. Proceedings of a Symposium: Management of Depression in Primary Care. Am J Med. 1996; 10(suppl 6A): 10S-25S.
6. Rush AJ. Strategies and Tactics in the Management of Maintenance Treatment for Depressed Patients. J Clin Psychiatry. 1999; 60(suppl 14): 21-6.
7. Thase ME. Treatment of Severe Depression. J Clin Psychiatry. 2000; 61(suppl 1): 17-25.
8. Beck AT, Rush AJ, Shaw BF, et al. Cognitive Therapy of Depression: A Treatment Manual. New York, Guilford, 1979.

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Postpartum Depression: Detection and Treatment

Postpartum depression (PD) occurs in approximately one of 10 childbearing women and is considerably underdiagnosed. If left untreated, the disorder can have serious adverse effects on the mother and her relationship with others, and on the child's development.

PD may begin 24 hours to 1 year after delivery. When its onset is abrupt and symptoms are severe, women are more likely to seek help early in the illness. In cases with an insidious onset, treatment is often delayed, if it is ever sought. Untreated, PD may resolve within several months but can linger into the second year postpartum. After the initial episode, women who have had PD are at risk for both nonpuerperal and puerperal relapses.

A simple screening instrument can be used to increase the detection of postpartum depression. The CES-D instrument included in this guideline is appropriate to use in postpartum assessment and diagnosis.

The **mainstay of treatment** has been **antidepressant therapy, alone or in combination with psychotherapy**.[1]

1. Recognizing Postpartum Depression

Risk Factors

- Dissatisfaction with the **marital relationship**.
- Amount of **social support** from a spouse and other significant persons.
- **Previous history of mood disorders**.

Screening for PD

The detection of PD is often complicated by several factors.

- Most women expect a period of adjustment after having a baby.
- Societal pressures to be a "good mother."
- Concern that sharing depressive thoughts might mean that their child could be taken from them.
- Delayed detection of PD by providers' minimizing a woman's distress in an effort to be reassuring.

Screening tools are available and should be administered if the women has risks for depression or depression is suspected. The CES-D tool included in this guideline is an appropriate tool for assessing PD.

Distinguishing PD

- The **"baby blues,"** subclinical mood fluctuations characterized by mild depressive symptoms typically peak 3 to 5 days after delivery and resolve by the 10th postnatal day. These include:
  - tearfulness
  - irritability
  - fatigue
  - anxiety
  - mood lability
  - sensitivity

Women who experience the "baby blues" have an increased risk for PD later in the postpartum period.

The criteria for diagnosing depression apply to the diagnosis of PD as well.
Depression symptoms include:

- Lack of pleasure or interest
- Frequent thoughts of death or suicide
- Sleep disturbance (insomnia or hypersomnia)
- Feelings of worthlessness or inappropriate guilt
- Diminished concentration or indecisiveness
- Symptoms that may be confused with normal sequelae of childbirth
- Agitation or retardation
- Weight loss
- Loss of energy

PD must be distinguished from postpartum psychosis, which occurs in 0.2% of childbearing women. Most puerperal psychoses have their onset within the first month of delivery and are manic in nature. Warning signs heralding the onset of puerperal psychosis include:

- An inability to sleep for several nights
- Agitation
- Irritable mood
- Avoidance of the infant
- Delusion or hallucinations often involve the infant.

2. Treatment of Postpartum Depression

Antidepressant medication is the mainstay of treatment for moderate to severe postpartum depression. While there are no absolute contraindications to using particular antidepressant medications during pregnancy or lactation, there are no specific Food and Drug Administration approved antidepressants labeled for peripartum use.[6]

Medications and Lactation

Most SSRI's are a FDA pregnancy risk Category C. Exception is sertraline which is Category B. The majority of expert opinion feels the benefit outweighs the risk in treatment with a SSRI. SSRI's should be a first choice recommendation.

- The goal is to effectively treat the depression.
- Initiating or continuing therapy should not interfere with the decision to start or continue to breastfeed.
- Breastfeeding should not interfere with the decision to initiate treatment of depression.

If the woman is breastfeeding, some agents may be preferred over others.

- **Sertraline or paroxetine** may be preferred SSRIs, since no adverse effects have been reported thus far in nursing infants.[11,12] Several studies have shown infant serum levels of sertraline to be nondetectable or less than 5ng/ml and its metabolite concentration to be less than 10ng/ml.[7,8] In six reports, paroxetine serum concentrations were measured in 27 infants and were found to be nondetectable in 24 infants and less than 20 ng/mL in the remaining three.[8,12]
- **Fluoxetine** has had several case reports of adverse effects in the infant, including colic, delayed weight gain, irritability, and disturbed sleep.[13,22] For this reason, fluoxetine should generally not be considered first line treatment with a new diagnosis of depression.
- The remaining SSRIs, as well as, bupropion and venlafaxine are not known to be contraindicated in nursing women, but less information is known about these medications during lactation. A decision to use these medications should be based on a patient-specific risk-benefit evaluation, and the infant should be observed closely for side effects.[14]

Women with severe depression, suicidal ideation, or psychosis should be referred for psychiatric care. Such women require a comprehensive, multifaceted approach to treatment, including crisis intervention, pharmacotherapy, psychotherapy, and strengthening social support networks.

Support groups available to women include:

- Postpartum Support International (telephone: 805-967-7636) (http://www.chss.iup.edu/postpartum/) and
- Depression After Delivery (telephone: 800-944-4PPD) (http://pubs.ama-assn.org/cgi-bin/buffer/http://www.depressionafterdelivery.com/

Postpartum Depression References:

1. Epperson, C. Neill for the American Academy of Family Physicians. Postpartum Major Depression: Detection and Treatment. http://www.aafp.org/afp/990415ap/2247.html Available from Internet. accessed 3/29/02
2. Wile J, Arechiga M. Sociocultural aspects of postpartum depression. In: Miller LJ,ed. Postpartum Mood Disorders. Washington, DC: American Psychiatric Press; 1999:83-98.
3. Beck CT. Postpartum Depression: a metasynthesis. Quality Health Research, Apr 12, 2002 (4):453-72
4. Gold, L.H. Postpartum disorders in primary care: diagnosis and treatment. Primary Care, Mar 29, 2002; 29(1):27-41.
5. Robling SA, Paykel ES, Dunn VJ, et al. Long-term outcome of severe puerperal psychiatric illness. Pschol Med. 2000; 30:1263-1271.
6. Miller, LJ. Postpartum depression. J Am Med Asso, Feb 13, 2002; 287(6): 762-69.
7. Wisner KL, Perel JM, Findling RL. Antidepressant treatment during breast-feeding. Am J Psychiatry. 1996;153(9):1132-1137.
8. Burt VK, Suri R, Altshuler L, Stowe Z, Hendrick VC, Muntean E. The use of psychotropic medications during breast-feeding. Am J Psychiatry. 2001;158(7):1001-1009.
9. Susman VL, Katz JL. Weaning and Depression: Another Postpartum Complication. Am J Psychiat. 1988: 145: 49850
10. Brent NB, Wisner KL. Fluoxetine and carbamazepine concentrations in a nursing mother/infant pair. Clin Pediatr. 1998;37:41-44.
11. American Academy of Pediatrics Committee on Drugs. The transfer of drugs and other chemicals into human milk. Pediatrics. 2001;108(3):776-789.
12. Stowe ZN, Cohen LS, Hostetter A, Ritchie JC, Owens MJ, Nemeroff CB. Paroxetine in human breast milk and nursing infants. Am J Psychiatry. 2000;157(2):185-189.
13. Chambers CD, Anderson PO, Thomas RG, et al. Weight gain in infants breastfed by mothers who take fluoxetine. Pediatrics. 1999;104(5):e61.
14. Howard CR, Lawrence RA. Xenobiotics and Breastfeeding. Ped Clinics of North America 48(2) April 2001; 495-500
15. Ohman R, Hagg S, Carleborg L, Spigset O. Excretion of paroxetine into breast milk. J Clin Psychiatry. 1999;60(8):519-523.
16. Hendrick V, Stowe ZN, Altshuler LL, et al. Fluoxetine and norfluoxetine concentrations in nursing infants and breast milk. Biol Psychiatry. 2001;50(10):775-782.
17. Yoshida K, Smith B, Craggs M, Kumar RC. Fluoxetine in breast-milk and developmental outcome of breast-fed infants. Br J Psychiatry. 1998;172:175-179.
18. Kristensen, JH, Ilett KF, Hackett LP, Yapp P, Paech M, Begg EJ. Distribution and excretion of fluoxetine and norfluoxetine in human milk. Br J Clin Pharmacol. 1999;48(4):521-527.
19. Epperson N, Czarkowski KA, Ward-O'Brien D, et al. Maternal sertraline treatment and serotonin transport in breast feeding mother-infant pairs. Am J Psychiatry. 001;158(11):1631-1637
20. Hale TW. Medications and Mother's Milk, Amarillo TX, Pharmasoft Medical Publishing 2000
21. American Academy of Pediatrics, The Transfer of Drugs and other Chemicals into Human Milk. Pediatric 108(3) September 201; 776-789
22. Wisner KL, Parry BL, Piontek CM. Postpartum Depression. New England Journal of Medicine 347(3) July 18, 2002.

The Center for Epidemiologic Studies Depression (CES-D) Scale

Please select the choice, for each item below, that best describes how you **felt over the past week:**		Rarely or none of the time (<1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of the time (3-4 days)	Most or all of the time (5-7 days)
1	I was bothered by things that usually don't bother me.	0	1	2	3
2	I didn't feel like eating, my appetite was poor.	0	1	2	3
3	I felt that I could not shake off the blues even with help from my family and friends.	0	1	2	3
4	I felt that I was not as good as other people.	0	1	2	3
5	I had trouble keeping my mind on what I was doing.	0	1	2	3
6	I felt depressed.	0	1	2	3
7	I felt that everything I did was an effort.	0	1	2	3
8	I felt hopeless about the future.	0	1	2	3
9	I thought my life had been a failure.	0	1	2	3
10	I felt fearful.	0	1	2	3
11	My sleep was restless.	0	1	2	3
12	I was unhappy.	0	1	2	3
13	I talked less than usual.	0	1	2	3
14	I felt lonely.	0	1	2	3
15	People were unfriendly.	0	1	2	3
16	I did not enjoy life.	0	1	2	3
17	I had crying spells.	0	1	2	3
18	I felt sad.	0	1	2	3
19	I felt that people disliked me.	0	1	2	3
20	I could not get "going."	0	1	2	3

Total all answers chosen. ***(Scoring may be eliminated when tool is reproduced for use.)***
Total score of 22 or higher, indicates possible major depression
Score 15-21, indicates possible mild to moderate depression
Score 14 and below, indicates no depression

For original work on this scale: Radloff, LW. (1977). A self-report depression scale for research in the general population. Applied Psychological Measurement 1(3), 385-401.

Consideration of Concurrent Conditions

Depression with:	First Line Therapeutic Options Best economic choice in bold	May be problematic
No additional comorbid conditions	**Fluoxetine** Citalopram Mirtazapine Sertraline Paroxetine Venlafaxine Bupropion Trazodone Escitalopram	TCA – side effect profile less desirable Nefazodone- hepatotoxity
Anxiety or Panic Disorder	Paroxetine Sertraline **Fluoxetine** Citalopram Mirtazapine Escitalopram Venlafaxine	TCA- ineffective for anxiety Bupropion- may increase anxiety
Eating Disorders (anorexia, bulimia)	**Fluoxetine** Paroxetine Sertraline	Bupropion Mirtazapine
Cardiac condition	**Mirtazapine** Paroxetine	TCA, Venlafaxine
Decreased appetite	TCA Mirtazapine	Venlafaxine, SSRI
Diabetes	SSRIs	TCAs, Mirtazapine (may increase carbohydrate cravings)
Dementia, Head Injury, Post-Stroke Patients	Citalopram Escitalopram Sertaline Bupropion	TCAs, Paroxetine, Mirtazapine
Glaucoma	**Fluoxetine** Sertraline Citalopram Buproprion Escitalopram	TCA, Paroxetine
Lactation	Sertaline, Paroxetine (See Postpartum Depression)	Fluoxetine
Liver disease	Sertaline Venlafaxine	TCA, Fluoxetine, Paroxetine, Citalopram, Trazodone, Mirtazapine, Escitalopram, Nefazodone
Obsessive Compulsive Disorder	Fluvoxamine (Nonformulary) **Fluoxetine** Sertraline Citalopram Paroxetine Escitalopram	TCA
Parkinsons	Bupropion Trazodone Desipramine Nortriptyline Amoxapine Protriptylline	SSRIs Venlafaxine, Nefazodone, Mirtazapine
Renal disease	**Fluoxetine** Citalopram Sertaline Escitalopram	Mirtazapine, Paroxetine, Venlafaxine TCA – levels not predictive
Seizures/Seizure disorder	**Fluoxetine** Sertraline Citalopram Escitalopram Paroxetine	Buproprion, Maprotiline, TCA (in overdose)
Symptoms of: oversedation, weight gain, or lethargy	Bupropion Venlafaxine **Fluoxetine** Citalopram Sertraline Paroxetine Escitalopram	Mirtazapine TCA Trazodone
Symptoms of: insomnia, weight loss, overstimulation	**Mirtazapine** **Trazodone**	Venlafaxine SSRI

Due to potential for drug-drug interaction and a long half-life, elderly patients and other patients using many medications may not be candidates for fluoxetine.

Physicians should carefully consider the potential risks and benefits of treatment when treating pregnant women during the third trimester. Neonates exposed to Effexor XR, other SNRIs or SSRIs late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support and tube feeding.

Depression Side Effect Profiles

Side effects may be observed early in treatment and improve over time. If side effects persist, alternatives may be considered.

Side Effect	First Line Therapeutic Options	May be Problematic
Agitation, Insomnia	Trazodone, Mirtazapine TCA	Fluoxetine, Sertraline, Paroxetine, Bupropion, Venlafaxine
Anticholinergic Side Effects (dry mouth, blurred vision, constipation, urinary retention)	Citalopram, Fluoxetine, Sertraline, Venlafaxine, Bupropion, Escitalopram	TCA, Mirtazapine, Paroxetine
GI sensitivity (nausea, vomiting)	Bupropion, TCA, Mirtazapine	Citalopram, Fluoxetine, Sertraline, Paroxetine, Venlafaxine, Nefazodone, Escitalopram
Headache	TCA, Mirtazapine	SSRI, Venlafaxine, Bupropion
Orthostatic hypotension	Citalopram, Fluoxetine, Sertraline, Paroxetine, Venlafaxine, Bupropion, Escitalopram	TCA, Mirtazapine
Sedation	Citalopram, Fluoxetine, Sertraline, Paroxetine, Venlafaxine, Bupropion, Escitalopram	TCA, Nefazodone, Trazodone, Mirtazapine
Sexual Dysfunction	Bupropion, Mirtazapine	Citalopram, Fluoxetine, Sertraline, Paroxetine, Venlafaxine, Trazodone, Escitalopram
Weight Gain	Citalopram, Fluoxetine, Sertraline, Paroxetine, Bupropion, Escitalopram, Venlafaxine	TCA, Trazodone, Mirtazapine

Antidepressant Drug Interactions

Interactions below are established in well-controlled studies. This is not a comprehensive listing of all potential interactions.
The chart is continued on the next page.

Interacting Medication	First Line Therapeutic Options Most Economic Choice in Bold	May be Problematic	Problematic Effect
Antivirals (Ritonavir)	Escitalopram, Citalopram Sertraline, Paroxetine, **Mirtazapine**	Bupropion, Fluvoxamine, Fluoxetine, Trazodone, Nefazodone	Ritonavir may inhibit the metabolism of Bupropion, Fluvoxamine, Fluoxetine, Trazodone, Nefazodone. Large increases of antidepressant levels. Ritonavir and fluoxetine may inhibit each other.
Atypical Antipsychotics (Clozapine)	**TCAs**	Citalopram , Fluoxetine Fluvoxamine, Sertraline	Certain SSRIs inhibit the hepatic metabolism of Clozapine. Monitor Clozapine levels and adjust dose appropriately.
Azole Antifungals	Escitalopram, Citalopram , Sertraline Paroxetine, Venlafaxine **Mirtazapine**, Bupropion	TCAs, Nefazodone, Trazodone	Inhibition of TCA metabolism by fluconazole (CYP2C) and ketoconazole (CYP3A4). Elevated TCA levels and increased therapeutic and adverse effects, including cardiac arrhythmias.
Beta Blockers (Metoprolol, Carvedilol, Propranolol)	Bupropion, **Mirtazapine**	SSRIs	Certain SSRIs may inhibit the metabolism of certain Beta Blockers (CYP2D6). Excessive beta blockade may occur. Interaction may be less likely with sotalol or atenolol.
Carbamazepine	Citalopram, Sertraline, Paroxetine, Venlafaxine, **Mirtazapine**	TCAs, Bupropion, Fluoxetine, Nefazodone, Trazodone	Induction of CYP3A4 by Carbamazepine may decrease levels of Bupropion, Nefazodone and TCAs. Fluoxetine and TCAs may inhibit the hepatic metabolism and increase blood levels of Carbamazepine.
Cimetidine	Citalopram, Sertraline, **Fluoxetine,** Paroxetine, Venlafaxine, Bupropion, Mirtazapine	TCAs	Increased TCA concentrations. Decrease TCA dose as needed. Ranitidine may be substituted.
Clonidine	Citalopram, Sertraline, **Fluoxetine,** Mirtazapine, Paroxetine, Venlafaxine	TCAs	Theoretical TCA inhibition of central alpha 2 adrenergic receptors. Loss of blood pressure control and possibly life threatening elevations in blood pressure. Avoid concomitant use.
Cyclosporine	Citalopram, Bupropion, **Mirtazapine**, Venlafaxine	Fluoxetine, Fluvoxamine, Paroxetine, Sertraline, Nefazodone	SSRI may increase Cyclosporine concentrations and toxicity (via CYP3A4). Monitor blood levels of Cyclosporine and adjust dose accordingly.
Cyproheptadine	**TCAs,** Mirtazapine, Bupropion	SSRIs, Nefazodone, Venlafaxine	Cyproheptadine is a serotonin antagonist and may reduce the antidepressant effect of the SSRI.
Lithium	Use caution	Fluoxetine, Sertraline	Possible increased lithium levels.
Methadone	Citalopram , Sertraline	Fluvoxamine	Fluvoxamine may inhibit the hepatic metabolism of methadone elevating methadone levels.
NSAIDS	**TCAs,** Mirtazapine, Trazodone	SSRIs	In a population-based cohort study, the combined use of SSRIs and NSAIDS increased the risk of GI adverse effects 10-fold compared with taking SSRIs alone.
Phenothiazines (Promethazine, Thioridazine)	**Bupropion,** Citalopram, Sertraline	Paroxetine, Fluoxetine	Elevated Phenothiazine levels may increase adverse effects due to inhibition of CYP2D6 by Paroxetine. Life-threatening arrhythmias with Thioridazine and Paroxetine have been reported.
Phenytoin	Citalopram , **Mirtazapine,** Venlafaxine	Fluoxetine, Paroxetine	Fluoxetine may inhibit the metabolism of hydantoins resulting in elevated Hydantoin blood levels.

Antidepressant Drug Interactions (continued)

Interacting Medication	First Line Therapeutic Options Most Economic Choice in Bold	May be Problematic	Problematic Effect
Propafenone	Citalopram, Sertraline	Fluoxetine, Paroxetine, Sertraline	Certain SSRIs may inhibit the metabolism (CYP2D6) of propafenone resulting in elevated propafenone levels. Monitor cardiac function.
Rifampin	Citalopram, Sertraline, **Fluoxetine,** Paroxetine, Venlafaxine, Bupropion, Mirtazapine	TCAs	Hepatic metabolism of TCA may be increased resulting in decreased pharmacological effect of TCA. Adjust dose as needed.
Statins	Escitalopram, Citalopram, Sertaline, **Paroxetine**	Nefazodone	Possible nefazodone inhibition of metabolism of HMG- CoA Reductase Inhibitors metabolized by the cytochrome P450 3A4 isozyme causing rhabdomyolysis and myalgias.
St. John's Wort	Bupropion, Mirtazapine, **TCAs**	SSRIs, Nefazodone, Venlafaxine	Possible additive serotonin reuptake inhibition. Increased sedative hypnotic effects.
Sympathomimetics (Phenylephrine, Dextroamphetamine, sibutramine, phentermine)	Use caution, Mirtazepine	SSRIs, TCAs	SSRIs increase sympathomimetic effects and increase risk of serotonin syndrome with Phenylpropanolamine and Dextroamphetamine. TCAs potentiate pressor response of direct acting sympathomimetics (Phenylephrine), dysrhythmias have occurred. The pressor response of indirect acting sympathomimetics (Ephedrine) has been decreased by TCAs.
Tacrine	Citalopram, Sertraline, **Fluoxetine,** Paroxetine, Venlafaxine, Mirtazapine, Bupropion	Fluvoxamine	Fluvoxamine may inhibit the hepatic metabolism (CYP1A2) of Tacrine. Monitor for hepatotoxicity, elevated pharmacological and adverse effects of Tacrine.
TCAs	Citalopram, Sertraline	Fluoxetine, Paroxetine	Fluoxetine may inhibit TCA hepatic metabolism.
Triptan Migraine Agents (Sumatriptan)	**TCAs,** Mirtazapine, Bupropion	SSRIs, Nefazodone, Venlafaxine	Possibly rapid, excessive accumulation of serotonin in the CNS - risk of serotonin syndrome.
Valproic Acid	Citalopram, Sertraline, **Fluoxetine,** Paroxetine, Venlafaxine	TCAs	Decreased first pass metabolism and inhibition of hepatic metabolism of TCA. Increased effects of TCA.

Source: Drug Interactions Facts and Comparisons, eFacts, www.efactsweb.com/, 2004

Product Dosage and HMO Formulary Comparison

PRODUCT	HOW SUPPLIED	DOSAGE RANGE / COMMENTS	U	P	G	D	N	RELATIVE COST
SELECTIVE SEROTONIN REUPTAKE INHIBITORS								
citalopram (Celexa)	10, 20, 40mg scored tab 10mg/5ml soln	20mg to 60mg QD	2	3	2	PA	2	$$
escitalopram (Lexapro)	5 unscored, 10, 20mg scored tab 5mg/5ml	10-20mg QD	2	2	2	2	2	$$
fluoxetine (generics)	10, 20, 40mg cap 10 ,20mg tab 20mg/5ml susp	10-80mg QD	1 *	$0*	1*	1*	1 *	$
paroxetine (generics)	10, 20, 30, 40mg tab	10-60mg QD	1	1	1	PA	2	$$
paroxetine (Paxil, CR)	10mg, 20mg scored tab 30mg, 40mg tab 12.5mg, 25, 37.5mg CR 10mg/5ml susp	10-60mg IR or 62.5mg CR QD lower for anxiety	2	3 2	2	NC	2	$$$
sertaline (Zoloft)	25, 50, 100mg scored tab 20mg/ml	50-200mg QD	2	2	2	2	2	$$$
NOREPINEPHRINE SEROTONIN ANTIDEPRESSANTS								
bupropion (generics)	75, 100mg IR tab 100,150, 200mg SR tab	200 mg SR BID IR TID = SR BID	1	1	1	1	1 2	$$$$
bupropion (Wellbutrin)	75,100mg IR tab 100, 150, 200mg SR tab 150, 300mg XL tab	200mg SR BID maximum IR TID = SR BID=XL QD	3 3	3 2	1 2	2 PA	3 3	$$$$
nefazodone (generics)	50, 100, 150, 200, 250mg tab	200mg to 600mg QD in divided doses	1	1	NC	1	3	$-$$
mirtazapine (generics) Remeron Sol Tab	7.5, 15, 30, 45mg tab 15, 30mg ODT 15, 30, 45mg ODT	15 to 45mg QD	1 2	1 3	1 1	2 1	2 3	$$-$$$
trazodone (generics)	50, 100, 150, 300mg tab	100 to 600mg QD in divided doses	1	1	1	1	1	$
venlafaxine (Effexor)	IR 25, 37.5, 50, 75, 100 tab ER 37.5, 75, 100mg cap	75mg to 225mg QD in divided doses 37.5 IR BID = 75mg ER	2	2	2	2	3 2	$$$-$$$$
TRI-CYCLIC ANTIDEPRSSANTS								
amitriptyline (generics)	10, 25, 50, 75, 100, 150mg tab	50mg to 150mg QD in divided doses	1	1	1	1	1	$
desipramine (generics)	10, 25, 50, 75, 100, 150mg coated tab	100mg to 300mg QD in divided or single doses	1	1	1	1	1	$
doxepin (generics)	10, 25, 50, 75, 100, 150mg cap 10mg/mL conc	75mg to 300mg QD in divided or single doses	1	1	1	1	1	$
imipramine (generics)	10, 25, 50, 75, 150mg tab 75, 100, 125, 150mg cap 25mg/5mL syrup	150mg to 300mg QD	1	1	1	1	1	$
nortriptyline (generics)	10, 25, 50, 75mg cap 10mg/5mL soln	60mg to 150mg QD in divided or single doses	1	1	1	1	1	$
MONOAMINE OXIDASE INHIBITORS								
phenelzine (Nardil)	15mg tab	60mg to 90mg QD in divided doses	2	2	2	2	2	$$
tranylcypromine (Parnate)	10mg tab	30mg QD in divided doses	2	3	2	2	2	$$

capsules only (40mg capsules not covered, tier 3 for PPIC) 20mg tablet not covered by PPIC

U=Unity P=Physicians Plus GHC= Group Health D=Dean N=Navitus 1,2,3 = Tier Copay

Depression Monitoring Flow Sheet #1

Patient Name _____ DOB/age_____

Date of Diagnosis _____

Date/Type of Contact						
Assessment of Progress: Score 1 if symptoms are worse Score 2 if there is no change in symptoms Score 3 if symptoms have improved						
CES-D Scale score/ Assessment score	/	/	/	/	/	/
Thoughts of death or suicidal ideation						
Patient impression of progress						
New stressors						
Other concerns or Assessments						
Assessment of Treatment						
Current Medication						
Medication compliance	Y N	Y N	Y N	Y N	Y N	Y N
Medication side-effects[1]: Sedation/agitation Dry mouth Headache Nausea/GI distress Constipation Diarrhea Dizziness Sexual dysfunction Other _____	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
Psychotherapy						
Initials of Provider						

1. Place check mark for presence of side-effect. Track progress by noting ongoing presence of side-effect.

Depression Monitoring Flow Sheet #2

Patient Name _____ DOB/age_____

Scoring Guide: 1 = poor/no change in symptoms
2 = OK/some improvement in symptoms
3 = good/much improved.

Date of Diagnosis _____

Date/Type of Contact						
Mood						
Interest in activities						
Appetite						
Sleep						
Psychomotor agitation or lethargy						
Energy level						
Self-esteem						
Concentration						
Thoughts of death or suicidal ideation						
Patient impression of progress						
Medication side-effects[1]:						
Sedation/agitation	☐	☐	☐	☐	☐	☐
Dry mouth	☐	☐	☐	☐	☐	☐
Headache	☐	☐	☐	☐	☐	☐
Nausea/GI distress	☐	☐	☐	☐	☐	☐
Constipation	☐	☐	☐	☐	☐	☐
Diarrhea	☐	☐	☐	☐	☐	☐
Dizziness	☐	☐	☐	☐	☐	☐
Sexual dysfunction	☐	☐	☐	☐	☐	☐
Other _____	☐	☐	☐	☐	☐	☐
Other concerns or assessments						
Initials of Provider Completing Assessment						

1. Place check mark for presence of side-effect. Track progress by noting ongoing presence of side-effect.