

**Neighborhood Health Plan of Rhode Island and
Beacon Health Strategies, LLC
Present**

**CLINICAL PRACTICE GUIDELINE
FOR THE**

**Diagnosis and Treatment of
Depressive Disorders in
Adult Primary Care Patients**

January 2009

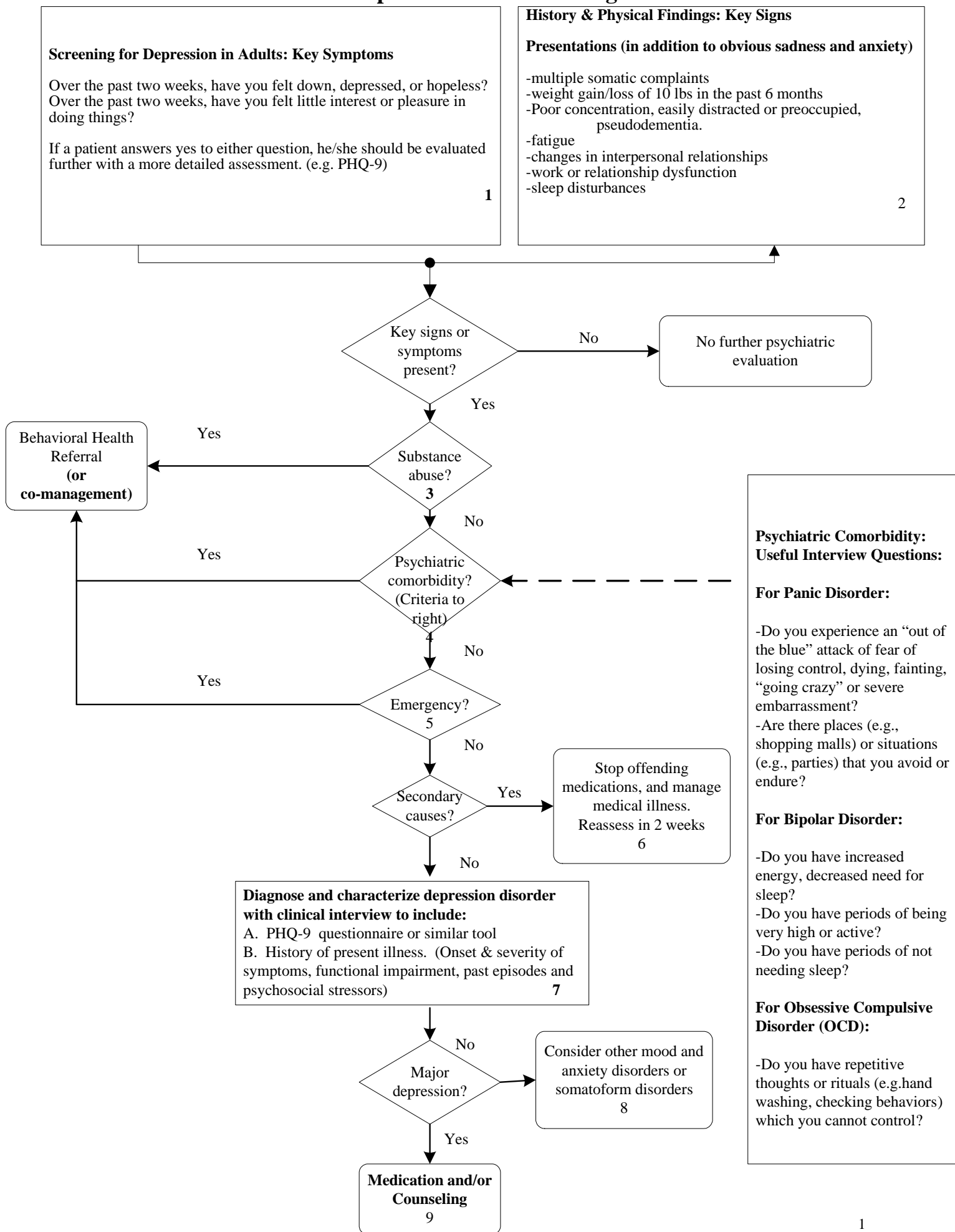
Goals

To support Neighborhood Health Plan of Rhode Island practitioners in identifying and treating depression in adult primary care patients.

Limitations

The Clinical Practice Guideline Committee (CPGC) provides this product for the educational benefit of the contracted practitioners of the Neighborhood Health Plan of Rhode Island. **This document is a guideline, and is not meant to replace any practices based on clinical judgment, experience or specific aspects of individual patient situations.**

Depression Evaluation Algorithm



Psychiatric Comorbidity: Useful Interview Questions:

For Panic Disorder:

- Do you experience an “out of the blue” attack of fear of losing control, dying, fainting, “going crazy” or severe embarrassment?
- Are there places (e.g., shopping malls) or situations (e.g., parties) that you avoid or endure?

For Bipolar Disorder:

- Do you have increased energy, decreased need for sleep?
- Do you have periods of being very high or active?
- Do you have periods of not needing sleep?

For Obsessive Compulsive Disorder (OCD):

- Do you have repetitive thoughts or rituals (e.g. hand washing, checking behaviors) which you cannot control?

NEIGHBORHOOD HEALTH PLAN OF RHODE ISLAND CLINICAL PRACTICE
GUIDELINE FOR THE DIAGNOSIS AND TREATMENT OF DEPRESSIVE
DISORDERS IN PRIMARY CARE PATIENTS OVER AGE 18

1. **Screening for Depression in Adults**--Now recommended by the United States Preventive Services Task Force for all adults.¹⁸
 - a. Over the past two weeks, have you felt down, depressed, or hopeless?
 - b. Over the past two weeks, have you felt little interest or pleasure in doing things?

If a patient answers yes to either question, he/she should be evaluated further with a more detailed assessment found on page 8.

This screen may be administered orally or as a written, patient self-administered questionnaire, by the PCP or a member of his or her staff (R.N., L.P.N., M.A.). One positive answer triggers further assessment.

2. **Somatic Presentations**--All practitioners should maintain a high index of suspicion for the presence of depressive disorders in patients with the following somatic presentations in addition to sadness and anxiety
 - a. Weight gain/loss of 10 lbs in the past 6 months
 - b. Pseudodementia, mild forgetfulness, poor concentration, preoccupation
 - c. Fatigue
 - d. Sleep disturbances
 - e. Multiple somatic concerns, unexplained
3. **Psychosocial Functioning** – Practitioners should also maintain a high level of suspicion for the presence of depressive disorders when there are reported problems with the patient’s ability to work and/or with relationships
 - a. Change in interpersonal relationships
 - b. Work or relationship dysfunction

**If at least one somatic or psychosocial factor present, perform clinical interview.

4. **Substance Abuse**

The CAGE questions should be used to screen for substance abuse, as follows:

- C** Felt you ought to **cut** down on your drinking or drug use?
- A** Had people **annoy** you by criticizing your drinking or drug use?
- G** Felt bad or **guilty** about your drinking or drug use?
- E** Had a drink or used drugs as an **eye opener** first thing in the morning to steady your nerves or get rid of a hangover or to get the day started?

5. **Assess Complicating Factors–Psychiatric Co-morbidities**

Patients with underlying bipolar illness, panic disorder, and obsessive compulsive disorder may present with symptoms suggestive of unipolar depression as the primary disorder. They are unlikely to improve however, unless the underlying psychiatric disorder is identified and effectively treated. For this reason it is important to utilize the suggested screening questions, along with a careful history, to reveal co-morbid psychiatric disorders. Other co-morbid diagnoses in this category would include post traumatic stress disorder and domestic abuse.

Be alert to diagnose unresolved grief in the bereaved patient. Normal grief does not include suicidal ideation, psychotic symptoms, morbid preoccupation with worthlessness, marked functional impairment, or the persistence of depressive symptoms for more than two months. Counseling should be should be part of the treatment plan for patients with unresolved grief.

6. **Emergency Referrals**

Patients who are actively suicidal or psychotic should be referred promptly for formal psychiatric evaluation, utilizing Crisis Assessment Teams and emergency department facilities, when necessary. The following characteristics identify patients with increased risk for fatal suicide attempts:

- Prior suicide attempts
- Family history of death by suicide
- Older males, particularly if living alone
- Substance abuse
- Psychosis
- Lack of social supports and/or isolation

“SAD PERSONS Scale”

Suicide Risk Assessment

Sex (Attempts 3:1 F:M; completions 1:3 F:M)

Age (Bimodal: <19 >45)

Depression

Previous Attempts

Etoh abuse

Rational thinking loss (psychosis)

Social supports lacking

Organized plan

No spouse

Sickness (medical illness, cancer, AIDS, etc.)

Asking about thoughts of suicide, and any past attempts, should be part of every evaluation for depression. Even highly trained psychiatrists are not very good at predicting suicide. However, the “**SAD PERSONS Scale**” is a mnemonic to help the clinician assess the patient for known suicide risk factors. Rather than assigning an actual numeric value, the scale should be used to assist the clinician in determining the patient’s overall risk.

If a patient does voice suicidal thoughts and meets a number of the **SAD PERSONS** criteria, the clinician should take this seriously and do everything possible to assure the patient’s safety, even if this is against the patient’s wishes. The PCP should enlist expert help for the at risk patient. This might include calling the mental health specialist on site, if there is one, calling a crisis team to come evaluate the patient, or calling 911 to get an ambulance to take the patient to an emergency room for an acute psychiatric assessment.

7. **Identify symptoms caused by a general medical disorder or medication prescribed for another illness** (see list below).

Perform a history and physical examination to assess for medical illness prior to prescribing medication. Various general medical illnesses and medications can cause mood symptoms or disorders. After optimization of treatment for a medical illness, or modification of a patient’s medications, the depressive disorder should be reassessed, and if not resolved, treated. The most common offending drugs include corticosteroids (oral), long acting benzodiazepines, interferon, oral contraceptives, and clonidine. Recent literature reviews have not confirmed previously suspected causal links between beta blockers and depression.¹⁶

Reference List of Medications That Can Cause Depression (incidence > 5%)

Accutane	Corticosteroids (oral)	Nifedipine
Interferon (Interon A)	Depakote	Oral contraceptives
Actimmune	Digoxin	Prazosin
Agenerase (for HIV)	Diltiazem	Procainamide
Alcohol	Disulfiram	Prograf (for transplants)
Amphetamine withdrawal	Ethambutol	Ranitidine
Anabolic steroids	Guanethidine	Reserpine
Androderm	Hydralazine	Rebetron combination therapy
Aricept	Klonopin	Revia (like disulfiram)
Arimidex (antineoplastic)	Lamictal (anticonvulsant)	Rilutek (ALS agent)
Baclofen	Levodopa	Sandostatin
Barbiturates	Lupron	Thiazide diurectics
Benzodiazapines	Meridia (weight loss)	Topamax (anticonvulsant)
Casodex (prostate cancer)	Methyldopa	Verapamil
Cellcept	Methylphenidate	Zoladex (prostate cancer or endometriosis)
Clonidine	Metoclopramide	

Patient with Major Depressive Episode. Assess with the PHQ-9 Depression Screening Tool:

PHQ-9 Depression Screening Tool

Patient Health Questionnaire (9-item)*

Name _____ Date _____

Not at all Several days More than half the days Nearly every day

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Please circle your responses)

1. Little interest or pleasure in doing things.....	0	1	2	3
2. Feeling down, depressed, or hopeless.....	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much..	0	1	2	3
4. Feeling tired or having little energy.....	0	1	2	3
5. Poor appetite or overeating.....	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down.....	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television.....	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual.....	0	1	2	3
9. Thoughts that you would be better off dead or hurting yourself in some way.....	0	1	2	3

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

10. Not difficult at all Somewhat difficult Very difficult Extremely difficult

Scoring Instructions:

PHQ score is the sum of responses for question 1 through 9

Interpreting the Scores:

Depression severity levels according to PHQ scores are:

0-4 = no or minimal symptoms

5-9 = minor symptoms

10-14 = moderate symptoms

15-19 = moderate to severe symptoms

20 or more = severe symptoms

} Scores ≥ 10 are strongly suggestive of major depression (sensitivity 88%, specificity 88%)**

Patients with borderline PHQ-9 scores may warrant treatment if they indicated significant functional impairment in their response to question 10.

*The Patient Health Questionnaire (PHQ) was developed by Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke, and colleagues. For research information, contact Dr. Spitzer at rls@columbia.edu.

**Validation of this screening tool is summarized in Kroenke et al, Journal of General Internal Medicine, Vol 16, p 607, Sept 2001.

8. **Non-major Depression Branch of Algorithm:** If patient does not meet the criteria for Major Depressive Episode, assess for presence of dysthymic disorder [two or more years of depressed mood >50% of time plus 2 or more associated symptoms (poor appetite or overeating, insomnia or hypersomnia, low energy or fatigue, low self-esteem, poor concentration or difficulty making

decisions, feelings of hopelessness)]. Patients with dysthymic disorder may be treated similarly to patients with major depression. If the patient is over 18, and is given an ICD-9 diagnosis of Dysthymic Disorder, or Depressive Disorder, and fills a prescription for an antidepressant, the patient should be seen for three follow-up visits within twelve (12) weeks of the visit at which the diagnosis is made, and continue the antidepressant for at least six (6) months. At least one follow-up visit should be with a provider licensed to prescribe drugs. The 2009 HEDIS ® specifications measure patients 18 years of age and older diagnosed with a new episode of major depression, treated with an antidepressant medication, and who remained on an antidepressant medication treatment for 12 weeks (Effective Acute Phase Treatment) and 6 months (Effective Continuation Phase Treatment).

9. Treatment Plan

a. Objectives of treatment:

1. Acute symptom remission. This necessitates some measurement of symptom severity during and at the end of treatment to determine whether remission has been attained (PHQ-9 is a useful tool for follow up monitoring)
2. Reduction of likelihood of recurrence of depression
3. Return to previous level of occupational and psychosocial function

b. Treatment Considerations

1. Pharmacologic Therapy vs. Psychotherapy (see Table I for medication treatment)
 - Pharmacologic and/or non-pharmacologic interventions (psychotherapy, exercise) are effective in treating both depression and anxiety disorders. Factors to consider in making treatment recommendations are symptom severity, presence of psychosocial stressors, presence of co-morbid conditions, and patient preferences.
 - Depression treatment should take health beliefs into account. It is important to adequately assess a patient's expectations and beliefs in the controllability of depressive symptoms and functioning in order to treat depression effectively and to minimize the risk of relapse and recurrence
2. Pharmacologic Therapy
 - Treatment options for major depression may include pharmacology and psychotherapy. For patients with mild to moderate depression, psychotherapy and/or pharmacology are indicated. For severe depression, (PHQ 9 score \geq 15), pharmacologic therapy is indicated and mental health referral may also be indicated.
 - If the initial medication response is incomplete after six weeks of a possibly therapeutic dose (e.g., partial positive response to medication), increase the dose, if side effects allow, and wait another four to six weeks to reassess. If medication response is still incomplete, add or substitute another medication, or add another treatment modality. When considering how long to continue medication after remission of acute symptoms, two issues need to be considered: Continuation and Maintenance treatment

Acute Phase involves remission of acute symptoms (usually 3 months.)

Continuation treatment, (usually lasting 6-12 months after the acute treatment), consists of prolonged administration of treatment after disappearance of acute depressive symptoms and aims to maintain a euthymic state.

Maintenance treatment consists of long-term efforts to prevent recurrence and can extend for years. It should be strongly considered for all patients at the risk of recurrence. (Continuation treatment and Maintenance Treatment should consist of full dose antidepressant therapy.)

Risk factors for recurrence include:

1. More than one previous major depressive episode.

2. Two prior episodes with associated family history of bipolar disorder, psychosis or severe depression.
3. Pre-existing dysthymia.
4. Severe episodes.
5. Seasonal patterns.

Note on suicide risk and antidepressants:

Patients with depressive disorders are at greater risk for suicide and therefore should be assessed for suicidal ideation at treatment initiation and over the course of treatment. Patients treated with any antidepressant should be monitored regularly for changes in behavior or thinking regarding suicidal ideation, **especially at the beginning of therapy or when the dose is increased or decreased.** Worsening of symptoms could be due to the underlying disease or a result of drug therapy. See SAD PERSONS mnemonic for risk factors. Recent FDA Black Box warning are included below, because additional information continues to become available on the issue of antidepressants and suicide risk, go to <http://www.fda.gov> for periodic updates.

RECOMMENDED GUIDELINES FOR TREATMENT DURATION

EPISODE	TREATMENT DURATION
First	Up to 1 year (minimum 6 months)
Second	4-5 years
Second with complicating factors	Indefinitely
Third	Indefinitely

3. Psychotherapy

- Outcome studies^{6, 7, 8} support the efficacy of various psychotherapeutic approaches (cognitive-behavioral, interpersonal, structured educational group therapy).
- Consider early referral for psychotherapy if psychosocial issues are prominent and/or patient requests it. Psychotherapy may have maximum benefit as symptom severity diminishes.
- Supportive therapy by the PCP in the primary care setting is not the same as a course of psychotherapy with a mental health professional. However, education, support and reassurance by the PCP are critical. Support/reassurance includes asking the patient for his/her ideas regarding the cause of the depression, and about their expectations of recovery. It is helpful to inform patients that they have a good chance of improving with an antidepressant.

Exercise

Physical activity is a useful tool for easing depression symptoms. Among individuals with major depression, exercise therapy is feasible and is associated with significant therapeutic benefit, especially if exercise is continued over time. When prescribing an exercise regimen, several caveats apply:

- Anticipate barriers: Hopelessness, lack of interest (or motivation) and fatigue can make physical exertion difficult
- Keep expectations realistic; some patients are vulnerable to guilt and self-blame if they fail to carry out the regimen
- Introduce a feasible plan: Walking-alone or in a group-is often a good option
- Accentuate pleasurable aspects: The specific choice of exercise should be guided by the patient's preferences, and must be pleasurable
- State specifics: A goal of 30 minutes of moderate-intensity exercise, 3-5 days a week is reasonable for otherwise healthy adults

- Repetitive, aerobic exercises (e.g., running, walking, cycling, swimming) have a serotonergic effect in the brain and may augment the effects of the medications

c. Patient Education

1. Successful treatment of depression requires tailored and on-going patient education, beginning at the time of diagnosis. Enrollment in a formal depression disease management program can enhance compliance and treatment outcomes.^{18,19} Written materials are helpful to reinforce information shared during discussions. Education topics should include:
 - The cause (e.g. biologic, not personality), symptoms and natural history of major depression
 - Treatment options (empiric trials)
 - How to monitor symptoms and side effects
 - Follow-up regimen (office visits and/or telephone contacts)
 - Length of treatment
2. When antidepressant therapy is prescribed, the following key messages should be highlighted to support medication adherence and completion:
 - Most people need to be on medication at least 6 months.
 - It may take 1-6 weeks before improvement is seen and felt.

1. Pregnancy and Lactation (See Warning at end of Guideline)

Paxil use should be avoided in pregnancy because of studies suggesting an increased risk of congenital heart disease. Other SSRIs and Effexor can be used in pregnancy, with a preference for Sertraline, which yields very low levels in breastfed infants.

Two studies have suggested that SSRIs can cause pulmonary hypertension as a rare neonatal complication, so some prescribers withhold these agents in the third trimester, (though there is no specific FDA advisory in this regard) even though this is a very high risk time for relapse in women being treated for depression. The risk of this rare neonatal complication and the relative benefit of relapse prevention should be part of the risk/benefit discussion before such a decision is made.

There are many reports of transient jitters and poor feeding in neonates who have been exposed to SSRIs in utero, but these findings do not contraindicate the use of these agents in depressed women who are likely to relapse without continuation of treatment.

It is important to note that the primary physician for the infant should have a discussion with the parent regarding the risks versus benefits on continuing SSRIs while breastfeeding. The FDA has recommended that the labeling of these agents include warnings about these symptoms and that any decision to continue or discontinue these medications needs to include a documented discussion of risks and benefits.

Table I

Antidepressant Treatment Protocol

I. If antidepressant is prescribed:

- A. Start with an SSRI. (See Table II).
- B. A bedtime dose of Trazodone (right at bedtime) can be added for insomnia which persists or develops on SSRI therapy.
- C. Schedule follow-up care:
 - a. 2 weeks after starting the medication to trouble shoot, answer questions, assess side effects, etc.
 - b. 3 office visits within 12 weeks after antidepressant treatment is begun.
- D. If no improvement after four weeks of antidepressant treatment at a possibly effective dose, increase the dose.
- E. If better with the increased dose, but not in remission, after 8 weeks, increase the dose further, or add an antidepressant from another class and continue on that combo for 6 weeks before changing.
- F. If not remitted (0-2 symptoms and no impairment) by week 14 of treatment, try a different SSRI, or switch to a drug from another class.

There is no need for a washout period when switching to a second SSRI; taper off one SSRI while titrating up on the second one.

- G. If switching to another class (other than an MAO-I), decrease the first medication at the same time as starting a low dose of the new medication; gradually increase the dose of the new medication while weaning off the old medication.

II. If switched to drug from a different class:

- A. Increase dose if not improved after 4 weeks on a possibly therapeutic dose (See Table II).
- B. If not substantially improved after 6 weeks, **refer to behavioral health services.**
- C. If not remitted (0-2 symptoms and no impairment) by week twelve, **refer to behavioral health services.**

III. Once remitted:

- A. Drug treatment must be continued for a minimum of six months.
- B. Continue the drug longer, if two prior episodes or otherwise clinically indicated.
- C. Counsel to return if relapse of symptoms.

Table II

Antidepressant Medications (specific to Neighborhood Health Plan of Rhode Island's formulary)			
Medication	Starting Dose ⁺	Target Dose #	Adverse-Effects/Pregnancy Category
Selective Serotonin Reuptake Inhibitor (SSRI)			
Celexa (Citalopram)	20 mg QAM (increase by 20 mg Q week)	20-60 mg (elderly/hepatic impairment=20mg)	Nausea, dry mouth, sweating, somnolence, ejaculation disorder/Category C
Fluoxetine (Prozac)	20 mg QAM (increase by 20 mg Q 4 weeks) †	20-80 mg	Anorexia and weight loss, anxiety, sweating, insomnia, asthenia, tremor, headache, GI symptoms, lupus-like symptoms/Category C
Escitalopram <i>(Lexapro – non-formulary Covered only after failure of Celexa, Paxil, Prozac)</i>	10 mg QD	10-20 mg QD	Nausea, insomnia, ejaculation disorder, somnolence, fatigue, increased sweating, sexual dysfunction/ Category C
Paroxetine (Paxil)	10 mg QAM x 3 days then 20 mg /day	20–50 mg/day	Headache, sedation, dry mouth, insomnia, dizziness, nausea, constipation, tremor, sweating asthenia, sexual dysfunction/Category D
Sertraline (Zoloft)	50 mg QAM (increase 50 mg/day Q 1 week)	50-200 mg/day	GI complaints, tremor, headache, insomnia, male sexual dysfunction/Category C
Tetracyclic			
Mirtazapine (Remeron, Remeron SolTab)	15 mg QHS (increase 15 mg Q 1-2 weeks)	15-45 mg/day @ HS	Drowsiness, dizziness, constipation, significant increased appetite and weight gain, dry mouth, agranulocytosis/Category C
Trazodone (Desyrel)	50 mg TID (increase 50 mg/day Q 3-7 days). Primarily used in low dose (25-50mg, right at bedtime) for depression- or medication-related insomnia	150-400 mg/day (Divide doses for depression) 25-50mg right at bedtime for insomnia	Dry mouth, dizziness, drowsiness, nausea/vomiting, hypotension/Category C
Serotonin/Norepinephrine Reuptake Inhibitor (SNRI)			
Duloxetine (Cymbalta)	20 mg BID	40-60 mg QD	Nausea, dry mouth, constipation, decreased appetite, somnolence, fatigue, increased sweating/ Category C

KEY:

⁺ In geriatric patients, the appropriate dosage is widely variable, but in general is one-half the young adult dosage range for TCAs and for compounds with significant cardiovascular toxicity.

[#] Dosage increases as tolerated and as needed if no clinical improvement observed. † Administer with food.

NOTE: All drugs should be tapered when withdrawn.

Table II (cont)

Antidepressant Medications			
Medication	Starting Dose ⁺	Target Dose #	Adverse-Effects
Dopamine Reuptake Inhibitor			
Bupropion (Wellbutrin)	100 mg BID/day 1 AM& PM, day 4 100 mg TID (increase up to 100 mg/day after 3 days AM, noon, PM) ‡	200-450 mg (not to exceed over 150 mg/dose)	Nausea/vomiting, seizures/tremors, agitation, insomnia, hypertension, anorexia, dry mouth, headache, migraine, constipation, dizziness, hypersensitivity reaction (arthralgia, myalgia, fever, rash)/Category C
Bupropion SR (Wellbutrin SR)	150 mg QD (increase to 150 mg BID after 4 days) ‡	150 mg BID-400 mg/day	Nausea/vomiting, seizures/tremors, agitation, insomnia, hypertension, anorexia, dry mouth, headache, migraine, constipation, dizziness, hypersensitivity reaction (arthralgia, myalgia, fever, rash)/Category C
Bupropion XL (Wellbutrin XL – now in generic form)	150mg QAM (increase to 300mg after 4 days)	300 to 450mg/day	Nausea/vomiting, seizures/tremors, agitation, insomnia, hypertension, anorexia, dry mouth, headache, migraine, constipation, dizziness, hypersensitivity reaction (arthralgia, myalgia, fever, rash)/Category C
Tricyclic (TCA)			
Desipramine (Norpramin)	25 mg TID (increase 25-50 mg/day Q 3-4 days)* ‡	50-250 mg/day	Nausea/vomiting, cardiovascular effects, anticholinergic effects, sedation, seizures/Category C
Nortriptyline (Pamelor, Aventyl)	25 mg (increase 25 mg/day Q 3-4 days)* ‡	60-150 mg/day (QD-TID)	Sedation, cardiovascular effects, anticholinergic effects, weight gain, seizures/Category C

KEY:

⁺ In geriatric patients, the appropriate dosage is widely variable, but in general is one-half the young adult dosage range for TCAs and for compounds with significant cardiovascular toxicity.

[#] Dosage increases as tolerated and as needed if no clinical improvement observed.

* May be given on a divided or once-a -day dosage schedule.

‡ Do not exceed > 150 mg for any single dose, and use with great caution, if at all, in elderly patients.

† Administer with food.

NOTE: All drugs should be tapered when withdrawn.

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse (www.guideline.gov): This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- On December 8, 2005, the U.S. Food and Drug Administration (FDA) has determined that exposure to paroxetine in the first trimester of pregnancy may increase the risk for congenital malformations, particularly cardiac malformations. At the FDA's request, the manufacturer has changed paroxetine's pregnancy category from C to D and added new data and recommendations to the WARNINGS section of paroxetine's prescribing information. FDA is awaiting the final results of the recent studies and accruing additional data related to the use of paroxetine in pregnancy in order to better characterize the risk for congenital malformations associated with paroxetine.

Physicians who are caring for women receiving paroxetine should alert them to the potential risk to the fetus if they plan to become pregnant or are currently in their first trimester of pregnancy. Discontinuing paroxetine therapy should be considered for these patients. Women who are pregnant, or planning a pregnancy, and currently taking paroxetine should consult with their physician about whether to continue taking it. Women should not stop the drug without discussing the best way to do that with their physician. See the [FDA Web site](#) for more information.

- On September 27, 2005, GlaxoSmithKline (GSK) and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of changes to the Pregnancy/PRECAUTIONS section of the Prescribing Information for Paxil and Paxil CR Controlled-Release Tablets to describe the results of a GSK retrospective epidemiologic study of major congenital malformations in infants born to women taking antidepressants during the first trimester of pregnancy. This study suggested an increase in the risk of overall major congenital malformations for paroxetine as compared to other antidepressants [OR 2.2; 95% confidence interval, 1.34-3.63]. Healthcare professionals are advised to carefully weigh the potential risks and benefits of using paroxetine therapy in women during pregnancy and to discuss these findings as well as treatment alternatives with their patients. See the [FDA Web site](#) for more information.
- On July 1, 2005, in response to recent scientific publications that report the possibility of increased risk of suicidal behavior in adults treated with antidepressants, the U.S. Food and Drug Administration (FDA) issued a Public Health Advisory to update patients and healthcare providers with the latest information on this subject. Even before the publication of these recent reports, FDA had already begun the process of reviewing available data to determine whether there is an increased risk of suicidal behavior in adults taking antidepressants. The Agency has asked manufacturers to provide information from their trials using an approach similar to that used in the evaluation of the risk of suicidal behavior in the pediatric population taking antidepressants. This effort will involve hundreds of clinical trials and may take more than a year to complete. See the [FDA Web site](#) for more information.

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