CareFirst BlueCross BlueShield

Clinical Practice Guidelines *for Depression in Adults in the Primary Care Setting*

Disease Criteria

Major Depression

The essential feature of a Major Depressive episode is a period of at least 2 weeks during which there is depressed mood or the loss of interest or pleasure in nearly all activities.

Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either depressed mood or loss of interest or pleasure.

- Depressed mood
- Loss of interest or pleasure in nearly all activities
- Thoughts of death/suicidal
- Weight loss/gain
- Fatigue/loss of energy
- Insomnia/hypersomnia
- Psychomotor retardation/agitation
- Worthlessness/guilt
- Impaired concentration

Dysthymia

This is a depression of less severity than Major Depression that usually begins in childhood and adolescence, and must be present for at least 2 consecutive years without a period of greater than 2 months of absence of symptoms.

Depressive Disorder Not Otherwise Specified (NOS)

This is a depression that does not strictly meet the severity or duration criteria of the other diagnoses.

Screening

A patient self-reported questionnaire is recommended (refer to Appendices 1 & 2 for examples of patient screening tools and Appendix 3 for patient questionnaire scoring guidelines). Screening may be completed by the patient during the office visit.

Screening is recommended for:

- All new patients
- Existing patients (at least annually)
- High-risk patients (e.g., stroke, dementia, diabetes, coronary artery disease, chronic pain)

Suicidality Assessment

An essential part of the initial evaluation of clinical depression is assessing suicide potential. The evaluation should include:

- Assessment of suicide risk factors: hopelessness, general medical illnesses, family history of substance use and/or suicide, psychotic symptoms, living alone with little social support, prior suicide attempts.
- Direct inquiry about the content and frequency of suicidal ideation, intent, and plans.
- Factors that argue against the patient making an attempt.
- Patient's access to means of suicide and lethality of those means.

If the evaluation reveals any significant degree of suicidal risk, then an immediate call should be made to the mental health provider for psychiatric assessment at the appropriate level of care.

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Goals of Treatment

- Reduce if not remove all symptoms of the disease.
- Restore occupational and psychosocial functioning.
- Reduce the likelihood of relapse and recurrence.

Types and Evaluation of Treatment

- **Psychotherapy** – Patients with mild to moderate clinical depression (usually Dysthymia or Depressive Disorder NOS) may be selected for psychotherapy alone, if the patient prefers. If symptoms do not significantly improve within 2 to 3 months, then medication should be strongly considered.
- **Medication** – Patients with moderate to severe clinical depression (usually Major Depression) are appropriately selected for medication, whether or not formal psychotherapy is also used.
- **Medication and Psychotherapy** – This combination may hold a particular advantage for complicated, chronic depressions. It may also be advantageous for patients with only a partial response to either treatment alone.
- **ECT** – This is a first-line treatment option for only certain patients. It is recommended that this option be selected only after psychiatric consultation.

Initial Medication Selection and Management

- A selective serotonin reuptake inhibitor (SSRI) would usually be the first choice unless the patient has a history or risk of intolerable side effects, is taking other essential medications that put the patient at risk for significant drug interactions, or has a personal or family history of a positive response to another class of antidepressants. Some authorities recommend lower starting doses for women.
- Starting dosages may have to be reduced to lessen side effects and improve compliance. It is highly recommended in the elderly to reduce these starting dosages by half.

Note: Be aware of drug interactions and side effects. (Refer to Appendix 4 for guide to antidepressants)

Office Visit Frequency

- Frequent office visits with the prescribing physician during the first 4 -12 weeks of treatment are usually necessary to assess efficacy and side effects, as well as make any medication adjustments to optimize response.
- **A first follow-up visit is recommended within 1 to 4 weeks after the initial prescription.** At follow-up visits re-assess the diagnosis of depression and measure changes in symptom severity (depression scores) and patient function. (Refer to Appendix 6 for an example of a depression monitoring tool).
- **The patient should be seen at least 3 times in the critical 12 weeks acute treatment phase.**
- If treating a patient in concert with a behavioral health therapist conducting psychotherapy, then only one of these 3 follow-up visits need to be with the PCP.
- It is recommended to advise the patient to call the PCP between visits for any side effect problems.
- Continue to monitor for safety.

Secondary Adjustment Strategies

- Early signs of positive response can occasionally be seen after one week, but usually 4 to 6 weeks is required for a full response.
- Adequate treatment for 6 to 8 weeks is necessary before concluding that a patient is not responsive to a particular medication.
- If side effects are tolerable, then titration of the dosage upward is a first adjustment strategy to consider.
- Occasionally, titration of the dosage downward is a first adjustment strategy if it is concluded that the depressive symptoms are responding but side effects are interfering.
- Either of these strategies can certainly be followed during the first 6 to 8 weeks if judged as useful to increase response.
- If a patient is deemed unresponsive to a particular SSRI or has intolerable side effects, then a trial of a different SSRI often yields positive results.
- Other medication alternatives include selecting an antidepressant from a different class, combining antidepressants, or adding augmentation medications such as stimulants, lithium, or thyroid hormone.
- Combining antidepressants and adding augmentation medications are best managed by a psychiatrist.

Antidepressant Side Effects

Side effects account for as many as two-thirds of all pre-mature discontinuations of antidepressants. Most side effects are early onset and time limited and includes decreased appetite, nausea, diarrhea, agitation, anxiety, and headache. These side effects can be managed by temporary aids to tolerance. Persistent or late onset side effects, which may include apathy, fatigue, weight gain, and sexual dysfunction, may require additional medications or a switch in antidepressants.

Strategies for managing antidepressant side effects include:

- Allow the patient to verbalize his/her complaint about side effects.
- Wait and provide support. Some side effects will subside over 1 to 2 weeks.
- Lower the dose temporarily.
- Treat the side effects. (Refer to Appendix 5)
- Change to a different antidepressant.
- Discontinue medications and start psychological counseling.

Continuation of Treatment

- If this is an episode of clinical depression in a patient with a good premorbid mood history and without significant family history of depression, then effective medication should be continued for at least 12 months before considering discontinuation.
- Generally, medications should be discontinued through a gradual taper to avoid any uncomfortable physical withdrawal.
- If this is a chronic or recurrent clinical depression, “double depression” (Major Depressive episode in a patient with Dysthymia), or depression in a patient with a positive family history, then indefinite maintenance on effective antidepressant medication should be considered.
- Risk factors for recurrence of Major Depressive Disorder (MDD) include a prior episode of MDD, Dysthymia, additional psychiatric diagnosis, the presence of a comorbid medical disorder, or a comorbid substance abuse disorder.

Psychiatric Referral

Referral for psychiatric consultation, treatment, and/or psychotherapy can occur at any time at the PCP's discretion and/or the patient's choice. In all cases, the mental health provider should communicate and coordinate with the PCP, after obtaining the patient's permission.

It is strongly recommended that referral to the mental health provider be considered in any of the following circumstances:

- Significant evidence of danger to self or others
- Suspicion of Bipolar Disorder (note—Strongly consider psychiatric referral to any member who describes periods of (1) too much energy, and (2) lack of need for sleep. Use of antidepressant medications with Bipolar members may further destabilize the clinical picture.)
- Presence of psychotic symptoms
- Treatment-resistant depression
- Depression during pregnancy and postpartum
- Childhood depression
- Depression with comorbid psychiatric/ substance use disorders
- Depression with eating disorders
- Depression with Dementia
- Depression with severe/chronic medical disorder

Algorithm for Clinical Practice Guidelines for Depression in Adults in the Primary Care Setting Refer to Appendix 7.

References

Agency for Health Care Policy and Research: Depression in Primary Care, Vol 1-11, April 1993.

Agency for Health Care Policy and Research: Treatment of Depression-Newer Psychopharmacotherapies. Evidence Report Technology Assessment # 7. Publication # 99-E014.

American Medical Association Report 4 of the Council of Scientific Affairs, Approved by the AMA House of Delegates, December 2000. Women's Health: Sex and Gender Based Differences in Health and Disease, page 2, lines 25-29.

American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, fourth edition: Primary Care Version, 1995.

American Psychiatric Association: Practice Guideline for Major Depressive Disorder in Adults, 1993.

American Psychiatric Association Practice Guideline for the Treatment of Patients with Major Depressive Disorder, Second Edition, April 2000.

Apler, JT: Fluoxetine treatment in depressed patients who failed treatment with sertraline. Presented at the 34th Annual Meeting of the American College of Neuropsychopharmacology, December 11-15, 1995, San Juan, Puerto Rico.

Blehar MC, Oren DA. Women's Increased Vulnerability to Mood Disorders: Integrating Psychobiology and Epidemiology. Depression 1995;3:3-12.

Brown, WA: Are patients who are intolerant to one seratonin selective reuptake inhibitor intolerant to another? J. Clin Psychiatry 1995; 56:30-34.

Harris RZ, Benet LZ, Schwartz JB, Gender Effects in Pharmacokinetics and Pharmacodynamics,.Drugs 1995;50 (2): 222-39.

Hoffman E, Women's Health and Complexity Science, Academic Medicine, 75,11, 1102-1106, November 2000.

MacArthur Foundation's Initiative on Depression and Primary Care. Depression Management Tool Kit.2004 Trustees of Dartmouth College, V 1.3, June 2004.

Montano, CB: Recognition and Treatment of Depression in a Primary Care Setting. J Clin Psychiatry December 1994; 55[12,suppl]: 18-34.

Murray CJL, Lopez AD eds, The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Diseases, Injuries, and Risk Factors in 1990 and projected to 2020. Cambridge MA: Harvard University Press, 1996.

National Institutes of Health, Office of Director, Agenda for Research on Women's Health for the 21st Century, NIH Publication 99-4386, 1999.

Pollock BG II, The Endocrine-Treatment Interface: Gender Differences in Psychotrophic Metabolism. Psychopharmacol Bull 1997; 33:235-41.

Sternbach HS. The seratonin syndrome. Atn J Psychiatry 1991; 148; 705-713.

Thase, ME: Treatment-resistant depression, In Blom. FE: Psychopharmacology: The Forth Generation. New York, Raven Press, 1995.

Weissman MM, Olfson M, Depression in Women: Implications for Health Care Research. Science 1995; 269; 799-801.

Whooley MA, Avins AL, Miranda J, Browner WS: Case-finding instruments for depression, two questions are as good as many. J Gen Intern Med 1997;12:439-445.

Zarate, Ca: Does intolerance and lack of response with fluoxetine predict the same will happen with sertraline? J Clin Psychiatry, in press.

Zung, WWK. The role of rotating scales in the identification and management of the depressed patient in the primary care setting. J Clin Psychiatry 1990; [6,suppl]:72-76.

The Clinical Practice Guidelines for Depression in Adults in the Primary Care Setting were approved by the Quality Improvement Council in April, 2009.

Clinical Resources

Appendix 1 *(Adapted from Whooley Depression Screen)*

Patient Screening Tool

Patient Name:____ Date: ______________________

Depression Screen

Please answer each question by circling Yes or No.

During the past month, have you often been bothered by feeling down, sad, and hopeless?	YES	NO
During the past month, have you noticed a decrease in you interest or pleasure in doing things?	YES	NO

Bipolar Screen

Has there ever been a 4 day or longer period when you had racing thoughts, talked faster than usual, felt unusually good, and didn't need your usual amount of sleep?	YES	NO

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Clinical Resources

Appendix 2 *Adapted from PHQ – 9 (Nine Symptom Depression Checklist)*

Patient Questionnaire

Patient Name:____ Date: _______________________

1. Over the last 2 weeks, how often have you experienced any of the following problems?
(Place a ✔ in the response box)

	Not at all 0	Several days 1	More than half the days 2	Nearly every day 3
a. Little interest or pleasure in doing things.	☐	☐	☐	☐
b. Feeling down, sad, or hopeless.	☐	☐	☐	☐
c. Trouble falling asleep/staying asleep, sleeping too much.	☐	☐	☐	☐
d. Feeling tired or having little energy.	☐	☐	☐	☐
e. Poor appetite or overeating.	☐	☐	☐	☐
f. Feeling bad about yourself - or that you are a failure or have let yourself or your family down.	☐	☐	☐	☐
g. Trouble concentrating on things, such as reading the newspaper or watching television.	☐	☐	☐	☐
h. Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that you are moving around more than usual.	☐	☐	☐	☐
i Thoughts that you would be better off dead or of hurting yourself in some way.	☐	☐	☐	☐

2. How difficult have these problems made it to do your work, take care of things at home, or get along with other people? (Circle response.)

Not difficult at all   Somewhat difficult   Very difficult   Extremely difficult

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Clinical Resources

Appendix 3

Patient Questionnaire Scoring Guideline

Appendix 1 – Patient Screening Tool

How to score Patient Screening Tool

This is a screening tool for both Major Depression and Bipolar Disorder. The first 2 screening questions relate to Major Depression and the 3rd question relates to Bipolar Disorder. A positive response to either screen does not confirm a diagnosis, rather a trigger for further evaluation. Strongly consider a psychiatric referral if the patient screens positive for Bipolar Disorder, since the diagnosis and treatment usually requires specialty oversight including the use of mood stabilizing agents and NOT antidepressants.

Appendix 2 – Patient Questionnaire

How to Score Patient Questionnaire

Major Depressive Syndrome is suggested if:

- Of the 9 items (a-i), 5 or more are checked as at least “More than half the days” and
- Either item a or b is positive, that is, at least “More than half the days”

Other Depressive Syndrome is suggested if:

- Of the 9 items (a-i), if b, c, or d are checked as at least “More than half the days” and
- Either item a or b is positive, that is, at least “More than half the days”

If depression is suspected, the score can be used to plan and monitor treatment. To score the questionnaire, tally each response by the number value under the answer headings:

- Not at all = 0
- Several days = 1
- More than half the days = 2
- Nearly every day = 3

Add the numbers together to total the score. Interpret the score by using the following guide.

Guide for Interpreting Patient Questionnaire Score

Score	Action
≤ 4	The score suggests the patient may not need depression treatment.
5 - 14	Physician uses clinical judgment about treatment, based on patient’s duration of symptoms and functional impairment.
≥ 15	Warrants treatment for depression, use antidepressant, psychotherapy and/or a combination of treatment.

A functional health assessment is reflected in Question 2, which asks the patient how emotional difficulties or problems impact work, things at home, or relationships with other people. Patient responses can be one of four: not difficult at all, somewhat difficult, very difficult, or extremely difficult. A response of very difficult or extremely difficult suggests that the patient’s functionality is impaired. After treatment begins, functional status is again measured to see if the patient is improving.

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Clinical Resources

Appendix 4

Guide to Antidepressants

Antidepressant*	Therapeutic Dose Range (mg/day)	Initial Suggested Dose	Titration Schedule**	Advantages	Disadvantages
Serotonin Reuptake Inhibitors (SSRIs)					
citalopram (Celexa)‡	20 – 40	20 mg once daily	Maintain 20 mg for 1 week before dose increase. If no response, increase in 20 mg increments every 7 days as tolerated.	Possibly fewer cytochrome P450 interactions. Generic available.	
escitalopram (Lexapro)‡	10 - 20	10 mg once daily for escitalopram	Increase to 20 mg once daily after 1 week.	s-enantiomer more potent than racemic, 10 mg dose usually effective for most FDA approved for anxiety disorders.	
fluoxetine (Prozac)‡ **(Prozac Weekly)**	20 -80	20 mg once daily, usually in morning 90mg once weekly (maintenance only)	Maintain 20 mg for 4 weeks. Increase in 10-20 mg increments at intervals of 4 weeks. In children >=8 years, initially 10-20mg once daily. Increase 10mg increments after 1 week. (max 60mg daily)	Long half-life good for poor adherence, missed doses. Generic available. Less frequent discontinuation symptoms.	Slower to reach steady state. Sometimes too stimulating. Possibly more cytochrome P450 interactions.
paroxetine (Paxil)‡ **Paroxetine controlled release (Paxil CR)‡**	10 – 50 (40 in elderly) 25 – 62.5 (50 in elderly)	20 mg once daily, usually in morning (10 mg in elderly) 25 mg daily usually in morning (12.5 mg in elderly)	Maintain 20 mg for 1 week before dose increase. Increase in 10 mg increments at intervals of approximately 7 days up to a maximum of 50 mg/day. Increase by 12.5 mg at weekly intervals,	FDA approved for most anxiety disorders. Generic available. May cause less nausea and GI distress.	Sometimes sedating. Occasionally more anticholinergic-like effects. Possibly more cytochrome P450 interactions. May have more frequent discontinuation symptoms.
sertraline (Zoloft)‡	25 - 200	50 mg once daily (25mg in elderly)	Maintain 50 mg for 1 week. at intervals of 7 days as tolerated.	FDA approved for anxiety disorders. Safety shown post MI. Generic available.	
Serotonin and Norepinephrine Antagonist					
mirtazapine (Remeron)‡	15 - 45	15 mg at bedtime (7.5mg in elderly)	Increase in 15 mg increments (7.5 mg in elderly) every 1-2 weeks as tolerated.	Few drug interactions. Less or no sexual dysfunction. Less sedation as dose increased. May stimulate appetite. Generic available.	May initially stimulate appetite.

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Clinical Resources

Appendix 4 *(continued)*

Guide to Antidepressants

Antidepressant*	Therapeutic Dose Range (mg/day)	Initial Suggested Dose	Titration Schedule**	Advantages	Disadvantages
Norepinephrine and Dopamine-Reuptake Inhibitor					
bupropion extended release†‡ (Wellbutrin XL)	300 – 450	150 mg once daily in morning	After no less than 4 days titrate to usual dose of 300mg once daily as tolerated.	Stimulating. Less or no sexual dysfunction. Generic available.	At higher dose, may induce seizures in persons with seizure disorder. Stimulating. Usually b.i.d. dosing, unless more expensive XL.
bupropion‡ sustained release† (Wellbutrin SR)	300 - 400		Increase to 150 mg twice daily after 4 days. Increase to 200 mg twice daily if insufficient response after several weeks. 8 hours between doses and initially not at bedtime. With hepatic disease only 100 mg total per day.		
Serotonin and Norepinephrine Reuptake Inhibitor					
venlafaxine‡ (Effexor,	75 -375	75 mg per day in 2-3 divided doses	Dose should be divided twice daily. or three times a day unless XR. Increase by 75mg per day in intervals >=4 days.	XR version can be taken once daily. Helpful for anxiety disorders. Possibly fewer cytochrome P450) interactions. Generic available.	May increase blood pressure at higher doses. Twice daily dosing unless XR. Expensive.
Effexor XR)‡	75 -225	75 mg per day	For extended release (XR) give 37.5 once daily then increase to 75 mg per day after 4-7 days, If needed after >=4 days increase to 225 mg per day. Norepineprhine effect only occurs above 150 mg.		
duloxetine (Cymbalta)	30-60	30-60mg per day	30-60 mg may be given as a single dose or two divided doses		

**There are more antidepressants than those listed in this table; however, this list provides a reasonable variety of drugs that have different side effects and act by different neurotransmitter mechanisms. Treatment of Parkinson's disease may include selegiline (Eldepryl), which is a selective monoamine oxidase inhibitor at low doses only. Because the use of many antidepressants is contraindicated in conjunction with a nonselective MAOI, caution with or discontinuation of Eldepryl may be in order. For pregnancy, TCAs and SSRIs (particularly fluoxetine, because of more data collected) are not associated with congenital malformation or developmental delay. SSRIs in the third-trimester are associated with a slight decrease in gestational age and correspondingly lower weight, and occasionally with neonatal withdrawal symptoms. Diarrhea, drowsiness, and irritability are occasionally seen in breast fed infants of mothers taking antidepressants. The risks of maternal depression on child development should be balanced against the effects of antidepressants on an individual basis.*

***For SSRIs, generally start at beginning of therapeutic range. If side effects are bothersome, reduce doses and increase slower. In debilitated or those sensitive to medications, start lower. For all antidepressants, allow four weeks at a therapeutic dose, assess for a response. If a partial or slight response then increase the dose. If no response or worse symptoms then consider switching drugs.*

†Generally avoid bupropion in patients with a history of seizures, significant central nervous system lesions, or recent head trauma.

Reference: Reents S et al, (accessed on April 1, 2007)). Clinical Pharmacology, Gold Standard Inc http://clinicalpharmacology.com..

‡ Drug on CareFirst BlueCross BlueShield Preferred Drug List as of March 2009. To review current formulary reference the Preferred Drug List at www.carefirst.com.

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Clinical Resources

Appendix 5

Side Effects Management Chart

Side Effect	Selective Serotonin Reuptake Inhibitors (SSRIs) & Effexor	Tricyclic Antidepressants (nortriptyline, amitriptyline, imipramine)	bupropion (Wellbutrin, Wellbutrin SR)	mirtazapine (Remeron)	Symptom Management Strategy
Sedation	+/-	++	-	+	■ Give medication at bedtime. ■ Try caffeine.
Anticholinergic – like symptoms Dry mouth/eyes, Constipation, Urinary retention, Tachycardia	+/-	++	-	+/-	■ Increase hydration. ■ Sugarless gum/candy. ■ Dietary fiber. ■ Artificial tears. ■ Consider switching medication.
G I distress Nausea	++	-	+	+/-	■ Often improves in 1-2 weeks. ■ Take with meals. ■ Consider antacids or H2 blockers.
Restlessness Jitters/ Tremors	+	+/-	++	-	■ Start with small doses, especially with anxiety disorder. ■ Reduce dose temporarily. *Consider adding a beta-blocker *Consider an antianxiety drug.
Headache	+	-	+	-	■ Lower dose. ■ Analgesics.
Insomnia	+	-	+	-	■ Take medication in A.M. ■ Try adding a serotonin uptake inhibitor.
Sexual Dysfunction	++	-	-	-	■ May be part of depression or medical disorders. ■ Decrease dose. ■ Consider an erectile dysfunction drug ■ Try adding an NDRI ■ Try adding an antianxiety drug ■ Try adding a serotonin/ histamine antagonist.
Seizures	-	-	+	+/-	■ Discontinue antidepressant
Weight gain	+/-	+/-	+/-	++	■ Exercise. ■ Diet. ■ Consider changing medications.
Agranulocytosis	-	-	-	+/-	■ Monitor for signs of infection, flu-like symptoms. ■ Stop drug, check WBC.

Key:
(-) Very Unlikely
(+/-) Uncommon
(+) Mild
(++) Moderate

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Appendix 6

Depression Monitoring Tool (Physician tool for reassessment)

Patient Name:____ Date: _________________________

Symptoms	Date: Week:	Date: Week:	Date: Week:	Date: Week:	Date: Week:
Interest					
Mood					
Sleep					
Fatigue					
Appetite/ weight					
Self-Esteem					
Concentration					
Psychomotor					
Death/Suicide					
Patient Questionnaire (PQ) Score					
Suicidality PQ – Question "i" score					
Functioning PQ – Question #2					
Patient Impression					
Behavioral Health Referral					
Medications/Dosage					
Compliance with Recommendations					

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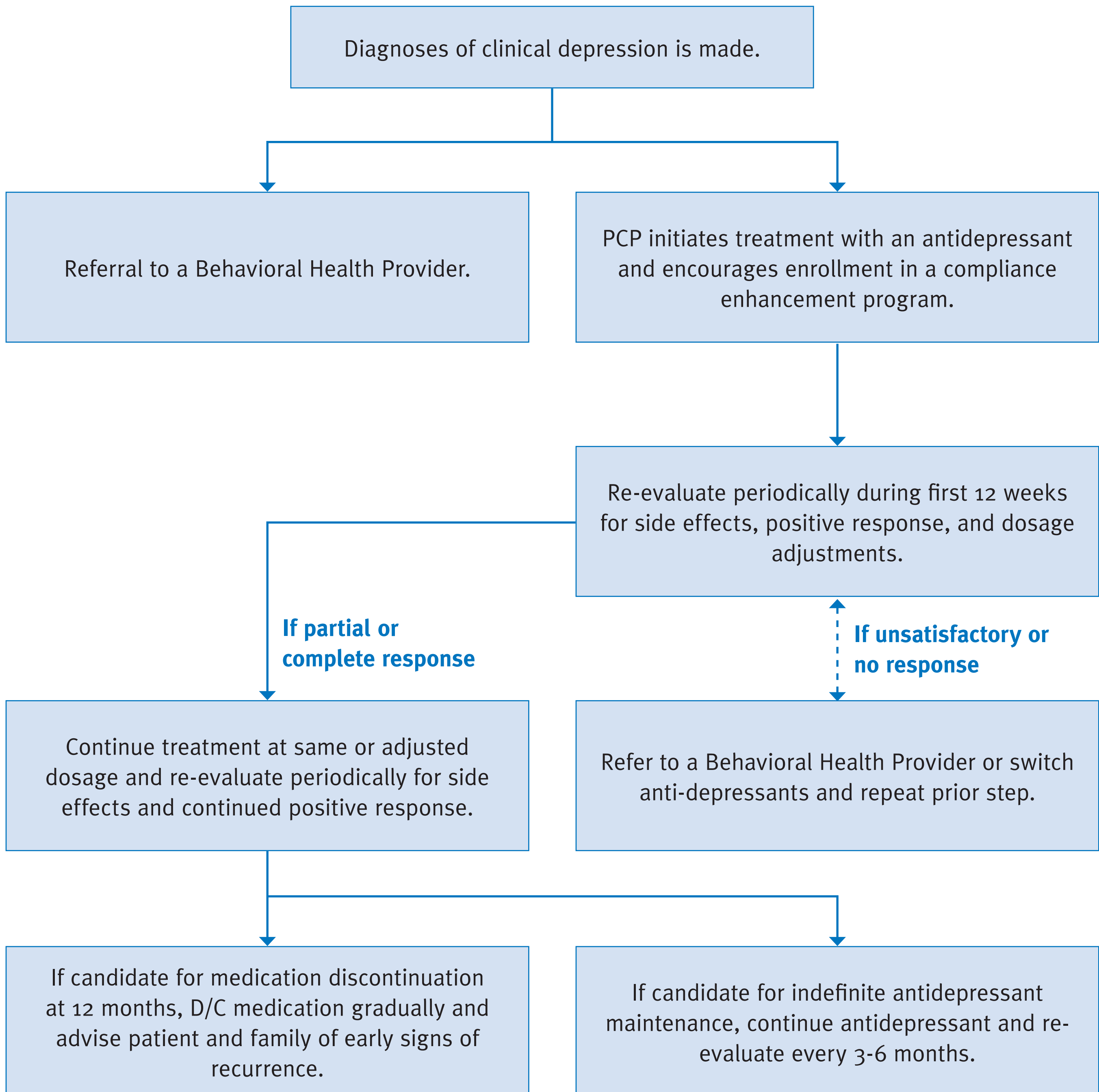
Appendix 7

Algorithm for Clinical Practice Guidelines for Depression in Adults in the Primary Care Setting



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