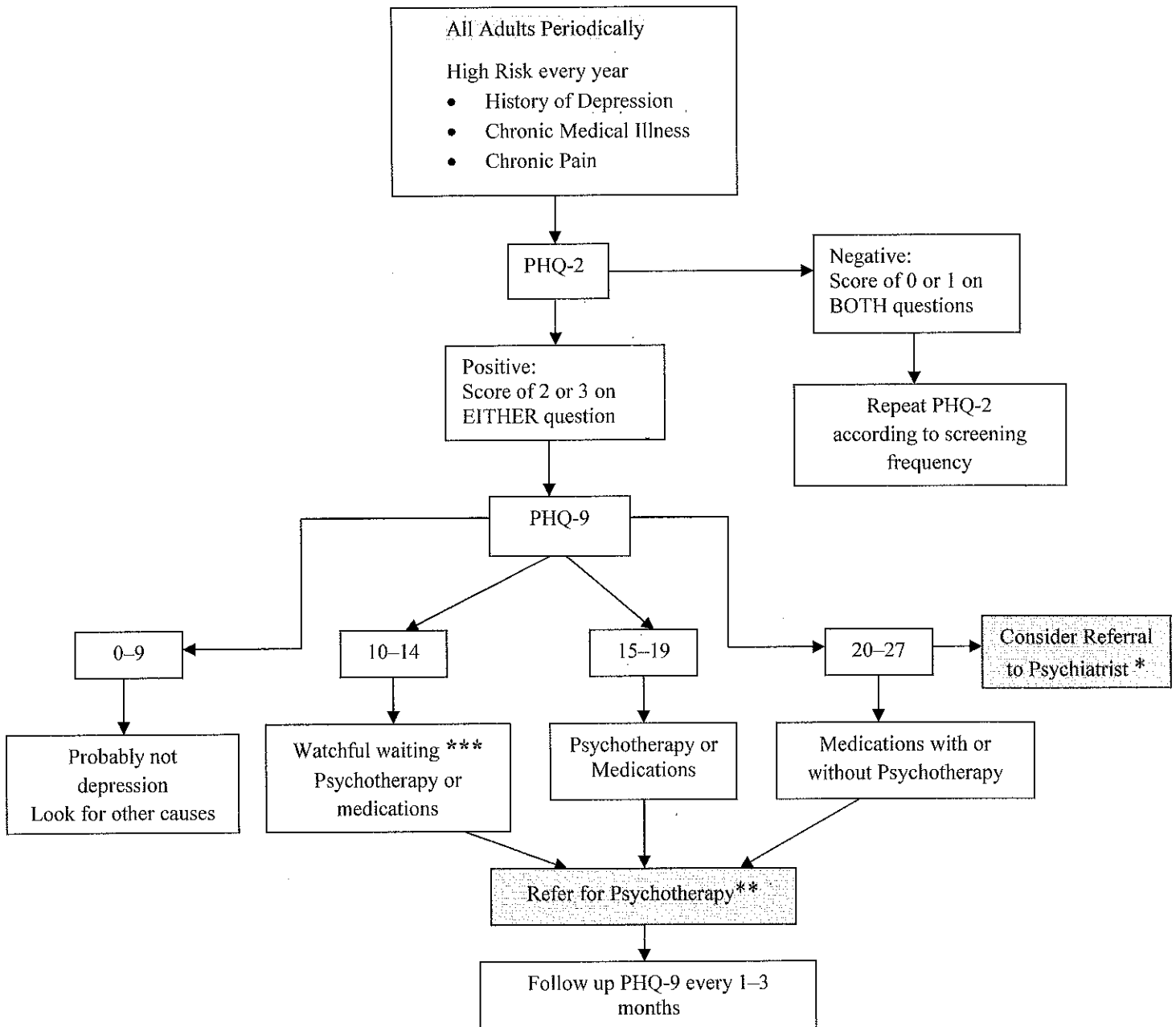


Guideline for the Treatment of Major Depressive Disorder in Adults in Primary Care Settings

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|---------------------------------|--|
| <u>Definition</u> | Depression is a mood disorder ranging from mild to severe with symptoms that can be disabling, cause behavioral changes, and may frequently present with somatic complaints. |
| <u>Evaluation</u> | <p>In general, five (5) of nine (9) symptoms over a two week period with one of the symptoms either depressed mood or loss of interest and pleasure</p> <p>Affective Symptoms:</p> <ul style="list-style-type: none"> ◆ Depressed mood (e.g., sad, tearful, apprehensive), most of the day, nearly every day <p>Cognitive Symptoms:</p> <ul style="list-style-type: none"> ◆ Impaired thinking or concentration (indecisiveness, wandering thoughts, racing thoughts, sometimes memory problems), nearly every day <p>Psychological Symptoms:</p> <ul style="list-style-type: none"> ◆ Feelings of worthlessness or excessive or inappropriate guilt nearly every day ◆ Recurrent thoughts of death or suicide, active (a plan) or passive ("I wouldn't care if...") ◆ Loss of interest or pleasure (the so-called anhedonia) in all or almost all activities, most of the day, nearly every day <p>Physiological Symptoms:</p> <ul style="list-style-type: none"> ◆ Change in appetite nearly every day, weight loss or gain ◆ Insomnia or hypersomnia nearly every day ◆ Fatigue or loss of energy nearly every day ◆ Psychomotor retardation or agitation nearly every day |
| <u>Associated Features</u> | While not on the official DSM criteria for major depression, irritability, increased expressions of anger and mood liability are often associated with episodes of major depression and these features should trigger a screening for depression. |
| <u>Precipitating</u> | Life events can trigger a depressive episode in susceptible individuals. Such events could include loss of a job or loved one, a traumatic event, the postpartum period, or relationship problems. Many major chronic medical diseases have a high comorbidity with MDD. A few of these are myocardial infarction, stroke, cancer, Parkinson's disease, diabetes, epilepsy, dementias, thyroid disease, substance abuse, and renal disease. |
| <u>Risk Factors</u> | <ul style="list-style-type: none"> ◆ Alcohol use or abuse ◆ Other substance abuse ◆ Prior episode(s) of depression ◆ Family history of depression or bipolar disorder ◆ Female Gender (2:1) ◆ Lack of social support |
| <u>Existing Screening Tools</u> | Depression rating scales can be useful in initial and follow-up assessment. PHQ-9 (Patient Health Questionnaire), the Beck Depression Inventory Primary Care Version, and the Zung Self-Rating Depression Scale are self-administered in 10 minutes. |
| <u>Somatic Episodes</u> | Depressed individuals often present with a variety of medical symptoms. These can include malaise/fatigue, dizziness, joint/back/head pain, abdominal/pelvic pain, muscle tension and pain, bowel problems. In geriatric patients, somatic symptoms may be more frequent than in other patients and affective symptoms may be less frequent. In addition to being components of depression, somatic symptoms can sometimes represent other medical or psychiatric conditions in the depressed patient. These possibilities should be evaluated appropriately. |
| <u>Differential</u> | <p>It is important to rule out the existence of medical disorders that may be commonly associated with depressive symptoms:</p> <ul style="list-style-type: none"> • Use appropriate laboratory tests including at a minimum – TSH, metabolic and liver profiles, CBC, and other tests based specifically on clinical findings. • Review medications and potential side effects • Conduct an appropriate review of systems • Screen for substance abuse <p>Practitioners should always ask about prior manic episodes, since bipolar disorder, if present, requires a different treatment approach.</p> |

Sources: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, 2000. U.S. Dept. of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, 1993, 1998. Anthem East Depression Guideline, 2001. University of Michigan Health System, Guidelines for Clinical Care, Depression 2004. American Psychiatric Association, Treatment Recommendations for Patients With Major Depressive Disorder, 2001, National Institute of Clinical Excellence, Management of depression in primary and secondary care, 2004. Kaiser Permanente Care Management Institute, Adult primary care depression guidelines, 2004. MHACO Behavioral HealthCare Program Quality Improvement Committee, 2016.

Depression Screening & Initial Treatment



Referrals:

* **Consider referral:** To psychiatrist or other mental health clinician for severe symptoms, esp. if suicidal risk

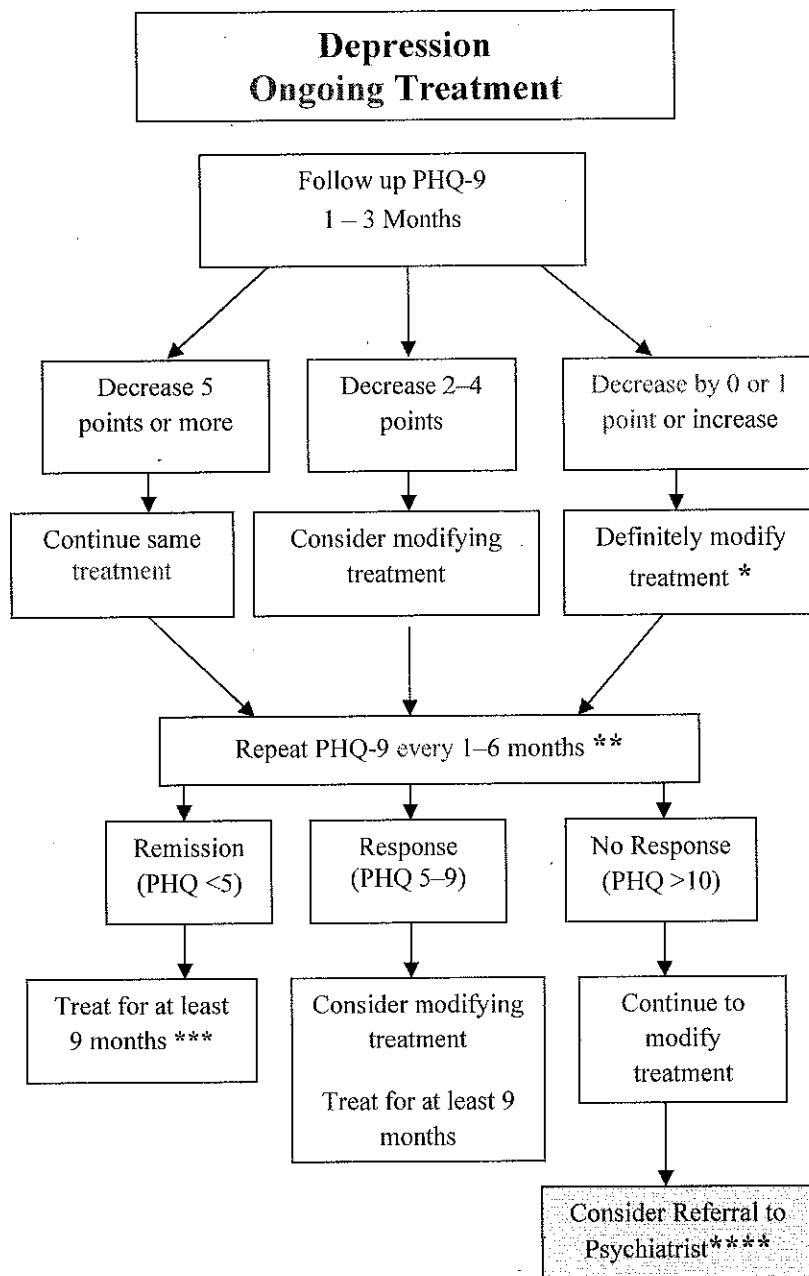
** **Refer:** For those who choose psychotherapy as initial treatment

*** Watchful waiting means:

- Contact is made with the patient about once a month and monitoring their PHQ-9 score, but not starting active treatment.
- Self-care activities such as exercise or relaxation are usually a component of watchful waiting.
- If the patient's symptoms have not resolved after 2-3 months, active treatment should be considered.

For more information on Mental Health visit:

<http://www.mainehealth.org/mentalhealthintegration>



*** Modifying Treatment:** All of these options are reasonable; select based upon patient preference and details of individual situation:

- Increase medication dose
- Change medication(s)
- Add a medication(s)
- Add psychotherapy

**** Frequency of PHQ - determination based on:**

- Severity of symptoms: More Severe - more frequent
- Duration of symptoms : Longer Duration - less frequent
- No more often than monthly
- No less often than every 6 months while on Rx

***** Duration of treatment**

- 1st episode 9-12 months
- 2nd episode 12-24 months
- 3rd or more episode or chronic depression:
consider ongoing maintenance Rx

****** Referral:** Consider referral to psychiatrist or other mental health clinician for those not responding after 2-3 trials of treatment

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<http://www.mainehealth.org/mentalhealthinte>

SSRI's (Selective Serotonin Re-uptake Inhibitors)

ALL PATIENTS UNDER 25 YEARS OF AGE SHOULD BE WARNED THAT SSRI's MAY BE ASSOCIATED WITH INCREASED SUICIDAL THINKING. THIS IS RARE BUT WARNING IS MANDATED BY THE FDA.

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| Advantages: <ul style="list-style-type: none"> • Low morbidity and mortality in overdose • Single daily dose (except fluvoxamine/Luvox) • Often does not need dose titration • Minimal cardiac toxicity | Disadvantages: <ul style="list-style-type: none"> • Sexual dysfunction • Expensive • Drug-drug interactions • May precipitate hypomania or mania in susceptible patients |
| Side effects: <ul style="list-style-type: none"> • Sexual dysfunction • Sweating • Anxiety • Headache • Nausea • Diarrhea • Akathisia • Sedation or insomnia • Long-term weight gain | If stopped abruptly, may cause non-dangerous (but uncomfortable) withdrawal syndrome with: <ul style="list-style-type: none"> • Flu-like symptoms • Insomnia • Nausea • Dizziness • Lethargy • Irritability • Paresthesias • Sweating • Tremors (less likely with fluoxetine/Prozac) • This list is not all-inclusive |

| Medication | Brand Name(s) | Starting Dose (mg/day) | Usual Dose (mg/day) | How Supplied (mg) | Max Dose (mg/day) | Other useful information |
|--------------|------------------------|------------------------|---------------------|--|-------------------|---|
| citalopram | Celexa | 10–20 mgs | 20–40 mgs | 10,20,40 10 mg/5ml soln. | 60 mgs | Fewer drug-drug interactions |
| fluoxetine | Prozac, aka Serafem | 10–20 mgs | 20–40 mgs | 10,20,40 caps 10 scored tablet 5 mg/ml soln. (10, 20 Serafem) | 80 mgs | Very long half-life. Can be activating. 10 mg tablet can be cut for economy/dose titration |
| paroxetine | Paxil | 10–20 mgs | 20–40 mgs | 10,20,30,40 10 mg/5ml soln. | 50 mgs | More anti-cholinergic, more sedating than other SSRI's. Increased P450 effects compared to other SSRI's |
| sertraline | Zoloft | 25–50 mgs | 50–150 mgs | 25,50,100 20mg/ml soln. | 200 mgs | Diarrhea more common |
| escitalopram | Lexapro | 5–10 mgs | 10–20 mgs | 10,20 mgs | 20 mgs | SSRI Brand name only. No evidence of superiority to other SSRI's |

TCA's (Tricyclic Antidepressants)

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|---|---|
| Advantages: <ul style="list-style-type: none"> • Well documented • May be better for severe depression • Serum levels are available and meaningful • Inexpensive • Single daily dose usually well tolerated | Disadvantages: <ul style="list-style-type: none"> • Need to be titrated up from low starting dose • Potentially lethal in overdose • May cause cardiac arrhythmias • May lower seizure threshold • Over age 40, get baseline ECG for rhythm, QTc interval (less than 450) and heart block |
|---|---|

Side Effects: Dry Mouth, Blurred Vision, Constipation, Orthostatic hypotension, Cardiac arrhythmias, Dizziness, Sedation, Weight gain. This list is not all-inclusive.

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|---------------|---------|-----------|------------|--|---------|---|
| nortriptyline | Pamelor | 10–25 mgs | 75–100 mgs | 10,25,50,75 mgs (generic may vary in size availability) | 150 mgs | Twice as potent as other TCA's. Therapeutic serum level 50-150 ng/ml. May have "therapeutic window" |
|---------------|---------|-----------|------------|--|---------|---|

Others

This group includes the other most widely used antidepressants. This list is not all-inclusive.

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|----------------|--|-------------|-------------|--|--|---|
| bupropion | Wellbutrin, Wellbutrin SR and XR, all but XR are generic | 100 mgs | 150-300 mgs | 75,150 mgs regular, 100,150 mgs SR: (150 SR Zyban) | 150 mgs tid regular, 200 mgs bid SR; 450 mgs qd XR | Activating. Seizure risk in bulimics/epileptics. Rare sexual side effects. Max. single dose 150 mgs. Available as generic 75,100 mgs. |
| mirtazapine | Remeron, | 15-30 mgs | 15-45 mgs | 15,30,45 mgs | 60 mgs | Sedation, especially at 15 mgs. Give at HS. Increased appetite. Rare sexual side effects. |
| venlafaxine | Effexor | 25-37.5 mgs | 150-300 mgs | 37.5,75,150 mgs XR 25,27.5, 50,75,100 mgs | 375 mgs (divided dose, B.I.D. or T.I.D.) | XR and regular may be mixed. Stopping suddenly may cause serotonin withdrawal syndrome. |
| duloxetine | Cymbalta | 20-30 mgs | 30-60 mgs | 20,30,60 mgs | 60 mgs | More P450 interactions than other third generation antidepressants. |
| vilazodone | Viibrid | 10 mgs | 40 mgs | 10,20,40 mgs | 40 mgs | Titrate from 10 to 40 mgs over two weeks; take with food to optimize absorption. |
| desvenlafaxine | Pristiq | 50 mgs | 50 mgs | 50,100 mgs | 100 mgs | No evidence that doses over 50 mgs are more effective. |

Medication Combinations

When a single antidepressant is not achieving full remission, combining two antidepressants is usually tolerated and simpler than older augmentation strategies. Combination of agents with different mechanisms of action include:

- sertraline or citalopram with bupropion, mirtazapine or TCA
- mirtazapine with venlafaxine or bupropion