

## Major Depressive Disorder

DSM-IV-TR Diagnostic Code: 296.2X Single episode, 296.3X Recurrent

### Diagnostic Guidelines

1. Establish diagnostic accuracy as defined in DSM-IV-TR.
2. Depressed mood most of the day, nearly every day, as indicated either by subjective account or observation by others.
3. Evaluate if vegetative symptoms are present: anhedonia (inability to experience pleasure), loss of energy, sleep disturbance, early AM waking, appetite disturbance, significant weight change, change in libido, inability to concentrate, forgetfulness, cognitive impairment, psychomotor retardation. Occasionally no subjective depressed mood is present; only anxiety and irritability are displayed.
4. Consider age – related manifestations of depression:
  - Children – somatic symptoms, withdrawal, change in attitude; psychosis .
  - Adolescents – increased impulsivity, substance abuse, irritability, change in attitude, boredom;
  - Geriatric – cognitive impairment (‘)pseudo-dementia), “I don’t know” or “I can’t” responses, somatic symptoms such as constipation; and in clients >35, rule out medical problems. Work up should include consideration of Hx/PE routine labs including thyroid function tests, CBC with diff, urine drug screen, EKG.
5. Consider co-morbid problems (dual diagnosis):
  - Substance abuse, e.g., alcohol abuse, cocaine or stimulant abuse; other psychiatric problems, e.g., personality disorder, panic or other anxiety disorder, somatization; and medical problems, e.g., thyroid and other endocrine dysfunction, depressogenic medications such as Valium or methyl dopa, central nervous system pathology, and hypertensive medication steroids.
6. Evaluate for:
  - Suicidal/violent thoughts and behavior; delusions or hallucinations indicating psychosis; anhedonia, depression worse in a.m. waking, much guilt, weight loss, reversed diurnal variation of mood, previous response to treatment with full recovery, previous response to somatic

treatment (antidepressant, ECT). This severe and recurrent subtype is particularly responsive to medication and/or ETC.

7. Consider contribution of psychosocial stressors, for example, death of a loved one, marital conflict, job loss, interpersonal conflict, and the need to consider these in treatment. For example, marital conflict may be a contributing factor to a client's major depression, and marital treatment may then be indicated. Differentiate from grief and adjustment disorders.
8. Has never had a manic episode or an unequivocal hypomanic episode.
9. Recurrent – Over 50% of people who have one episode of major depression will eventually have another episode, this rises to 70% after two episodes and 90% after three episodes.

### Treatment Guidelines

1. Treatment consists of an acute phase, during which remission is induced, a continuation phase, during which remission is preserved, and a maintenance phase, during which the client is protected against the recurrence of subsequent depressive episodes. Treatment selection is influenced by stage and severity of depressive episode.
2. Individual therapy using cognitive behavioral therapy and interpersonal therapy approaches has been found particularly effective. Consider focused, active and directive techniques which support the client's efforts to achieve clearly formulated goals. Similar considerations apply to family, marital and group therapies. These therapies are time limited, high therapist focused, and present focused.
3. Refer for psychiatric/medication evaluation if:
  - Psychotic symptoms, suicidal ideation or behavior; recurrent major depression; history of mood swings or mania; family history of mood disorder or substance abuse; previous responsiveness to medications or ECT; Concomitant substance abuse, medical problems, or meds; past history of psychiatric hospitalization; and age greater than 65, or moderate to severe impairment of functioning.
4. Is medication appropriate?
  - Medically clear for psychotropic medications – consult with primary care physician. Consider review of treatment, PE, labs. Factors suggestive of responsiveness: history of a previous positive response; Fhx responsiveness;

melancholia; vegetative signs; and absence of substance abuse, personality disorder, Somatization disorder.

5. Consider compliance: how likely is client to take medication as prescribed?
  - Review benefits and risks with client – obtain informed consent; success of medication: client is more likely to respond well to a medication to which she/he or a family member has previously responded well; consider potential side effects. Co-occurring personality disorder or substance abuse may negatively impact medication compliance. Confusion in geriatric clients on other medications or urinary retention in men with prostate enlargement; improved compliance and safety often offsets the increased cost of newer antidepressants.
6. To be effective, medication must be used in an adequate dose for a sufficient period of time, typically 4 to 6 weeks to determine responsiveness.
7. Research has shown that, in children and adolescents, SSRIs have demonstrated efficacy.
8. For medication failure or partial response, augmentation with other drugs should be considered.
9. ECT may be indicated in severe, treatment-resistant, or life threatening mood states or when medications are contraindicated.

#### **Issues of Concern:**

**Major Depressive Disorder has a high mortality: current research notes a 15% suicide rate.**

In the American Psychiatric Association's guideline for a Major Depressive Disorder, there were two areas of concern addressed. The first area was suicide risk and antidepressants and the second was hepatotoxicity with nefazodone:

#### **SUICIDE CONCERNS**

“Because patients with major depressive disorder are at greater risk of suicide, the guideline indicates that they should be assessed for suicide risk initially and over the course of treatment. The guideline also notes that “the risk of suicide in some patients recovering from major depressive disorder increases transiently as they develop the energy and capacity to act on self-destructive plans made earlier in the course of their illness” (1). The guideline describes factors associated with an increased risk of suicide in patients with major depressive disorder but notes that “the ability to predict suicide attempts and completed suicide is poor, with both many

false positives (i.e., patients who appear more likely to make attempts or complete suicide but who do not) and false negatives (i.e., patients who appear less likely to make attempts or complete suicide but who do)” (1).

### **RISKS WITH ANTI-DEPRESSANTS (CHILDREN)**

With respect to children and adolescents, the guideline recommends caution when basing treatment decisions on adult data. All of these general principles remain true. Recent research has raised concern about the safety of antidepressant use for children and adolescents and has led the FDA to add additional warnings, including a black box warning, to the labeling of all antidepressant medications (9).

Although the APA practice guideline focused on treatment of adults, not children and adolescents, discussion of this research is appropriate in this watch. In 23 short-term (4- to 16-week) trials involving more than 4,400 patients receiving nine antidepressant drugs (selective serotonin reuptake inhibitors [SSRIs] and others), suicidal thinking or behavior was observed in 78 individuals. The average risk of suicidal thinking or behaviors was 3.8% for participants receiving a drug compared with 2.1% for those given placebo, suggesting an approximately twofold increase in risk (10).

Consequently, in the new labeling, the FDA notes that pooled analyses of placebo-controlled antidepressant trials (available at <http://www.fda.gov/ohrms/dockets/ac/04/briefing/2004-4065b1.htm>) have shown an increased risk of suicidal thinking or behavior in children and adolescents with major depressive disorder, obsessive-compulsive disorder, and other psychiatric disorders. However, it is important to note that no suicides occurred in any of these trials. Furthermore, according to the Centers for Disease Prevention and Control, suicidal thinking and suicide attempts are common among adolescents, occurring respectively in about 17% and 8.5% of adolescents each year. As a result of such attempts, only 0.002% of girls and 0.012% of boys ultimately die (11), highlighting the fact that suicidality (i.e., suicidal thoughts and behaviors) and suicide are not equivalent.”

### **MEDICATION RECOMMENDATIONS**

“The guideline recommends the serotonin modulator nefazodone as an effective medication for the treatment of depression. However, before initiating or continuing treatment with nefazodone, consideration should be given to the recent reports of life-threatening hepatic failure in patients treated with nefazodone (2–8). These reports have led the Food and Drug Administration (FDA) to change the drug’s labeling, adding a black box warning of possible liver failure leading to death and/or a need for

transplant and contraindicating the drug in patients who were withdrawn from it because of evidence of liver injury. According to the warning, the reported rate of liver failure resulting in death or transplant in the United States is about 1 case per 250,000–300,000 patient-years of nefazodone treatment. This represents a rate of about three to four times the estimated background rate of liver failure and is probably an underestimate. There are no known predictors of the development of liver toxicity and failure with nefazodone; toxicity and failure have been reported in individuals early in the course of treatment as well as in persons receiving stable dosages for many months. The FDA warns that patients with preexisting liver disease should not be treated with nefazodone and that patients should be advised to immediately report symptoms that may indicate liver dysfunction, such as jaundice, anorexia, gastrointestinal complaints, and malaise.”

### Major Depressive Disorder Bibliography

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