Major Depression in Primary Care

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Major depression in a primary care population is an important clinical entity. Although major depression is prevalent in primary care, it is frequently underdiagnosed and undertreated. The presence of major depression in the medically ill increases morbidity, mortality, and utilization of medical resources. Depression may be the initial manifestation of a medical disorder. The diagnosis of major depression in primary care requires a thorough work-up. This depressive disorder responds best to a combination of counseling and antidepressant medication. An algorithm is suggested to assist the clinician in the selection of an appropriate antidepressant.

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Major depression is an important clinical entity (1,2) commonly occurring in the primary care setting in 5% to 10% of general medical inpatients and 9% to 16% of general medical outpatients. Although the prevalence of major depression in the medical setting is quite high, this condition is often underdiagnosed and undertreated. Failure to adequately diagnose and treat major depression in a medically ill patient can have serious clinical consequences by increasing the morbidity and mortality rates in patients with coronary artery disease, myocardial infarction, stroke, renal failure, cancer, and other acute, life-threatening medical conditions. The presence of major depression is also associated with the high utilization of medical resources. In addition, depressive symptoms may be the initial manifestation of an underlying medical illness such as cancer of the pancreas, Cushing's syndrome, Addison's disease, hyperthyroidism, hypothyroidism, or Huntington's disease (3).

Diagnostic Criteria

For the diagnosis of major depression, "The Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association, 4th Edition" (DSM-IV) (4) places particular importance on the physical symptoms that accompany many depressive disorders (Table 1). Because many concurrent medical conditions can also produce these vegetative physical symptoms, the clinician is often uncertain whether to attribute these symptoms to the medical condition or to the depression. As a result, the depression in many of these patients is missed and goes untreated. This diagnostic pitfall can be avoided if the clinician looks for the psychological symptoms of depression, such as poor self-esteem, hopelessness, helplessness, suicidal ideation, brooding pessimism, tearfulness, depressed appearance, social withdrawal, and lack of emotional reactivity (5). Because of the safety of the newer antidepressants, when in doubt, the clinician should treat the patient for depression.

Diagnostic Work-up

Every depressed patient in a primary care environment requires a very careful evaluation. The patient's history establishes the presence of depression, excludes other possible psychiatric disorders, helps assess suicide potential, clarifies the psychosocial precipitants for the depression, and may yield the first clues for an underlying medical condition (6). In particular, the clinician should look for symptoms of medical disorders with a high prevalence of major depression (Table 2) (1,2,3). Conversely, all patients with established diagnoses of medical disorders known to have a high comorbidity with depression should be questioned carefully for the presence of major depression. A complete listing of all drugs taken by the patient (prescribed, over-the-counter, herbal, and illicit) can identify substances which may have induced or worsened the depression (Table 3). The patient's personal and family histories are often positive for affective disorders in medical patients with major depression (7). Similarly, a thorough physical examination with particular emphasis on the neurological is essential in detecting concurrent medical disorders in all depressed patients (2). Depending on the findings of the history and physical examination, certain laboratory studies may be helpful in confirming the diagnosis of many toxic and medically induced depressions (3) (Table 4).

Table 1. Criteria for Major Depressive Episode.

A. 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 (1) depressed mood or (2) loss of interest or pleasure.
   1. depressed mood
   2. markedly diminished interest or pleasure in most activities
   3. significant weight loss
   4. insomnia or hypersomnia
   5. psychomotor retardation or agitation
   6. fatigue or loss of energy
   7. feelings of worthlessness or inappropriate guilt
   8. diminished ability to think or concentrate, or indecisiveness
   9. recurrent thoughts of death, recurrent suicidal ideation without specific plan, or a suicide attempt or a specific plan for committing suicide

B. The symptoms do not meet criteria for a Mixed Episode.
C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The symptoms are not due to the direct physiological effects of a substance or a general medical condition.
E The symptoms are not better accounted for by bereavement.

Table 2. Prevalence of Major Depression in Certain Medical Conditions.

Condition	Prevalence (%)
Hemodialysis	6.5
Coronary artery disease	18
Cancer	25-38
Chronic pain	32
Neurological disorders	
Stroke	27
Parkinson's disease	28
Multiple sclerosis	57
Epilepsy	55
Huntington's disease	41
Dementia	11
Endocrine disorders	
Hyperthyroidism	31
Diabetes mellitus	24
Cushing's disease	66
HIV	30
Chronic fatigue	17

Table 3. Medications and Substances Associated with Depression.

- Antihypertensive Medications
  - Reserpine
  - Methyldopa
  - Beta-blockers
- Oral contraceptives
- Corticosteroids
- Benzodiazepines
- Histamine 2 receptor antagonists
- Certain cancer chemotherapy agents
- Psychoactive substances
  - Alcohol
  - Opiates
  - Anabolic steroids
  - Amphetamine or cocaine withdrawal

Table 4. Possible Laboratory Studies for Depressed Patients in Primary Care.

- Complete blood count
- Blood chemistries
- Thyroid function studies
- Electrocardiogram (EKG)
- Cortisol levels
- Arterial blood gases
- Electroencephalogram (EEG)
- Blood and urine toxicology
- Brain scanning

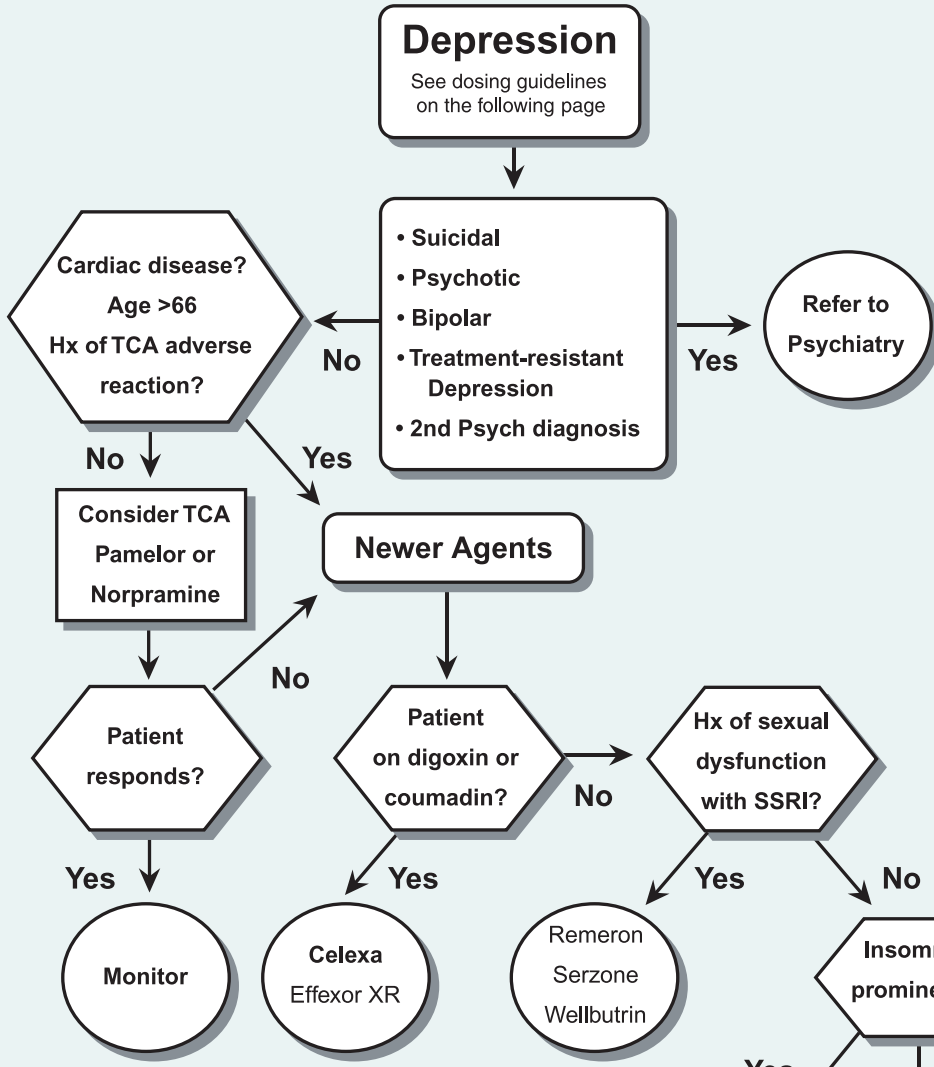
Course and Prognosis

When depression accompanies a medical illness, the presence of one complicates the course of the other. The presence of a medical condition is one of the best predictors for persistence of a depressive disorder (8). Conversely, depression has been shown to increase the morbidity and mortality of numerous medical illnesses (3).

Treatment

Successful management of major depression in primary care involves the identification and treatment of all concurrent medical conditions, psychotherapy, and use of antidepressant medications. In particular, all medical conditions and drugs that

Treatment Guideline for Depression



CHECK PDR FOR FOR POSSIBLE ADVERSE DRUG REACTIONS OR INTERACTIONS

Disclaimer. Guidelines may not be appropriate for all individuals. Use clinical judgement in the application of this guideline for your patient.

References:
(1) Steffens et al. Psychotropic drug interactions. Psychopharmacology 24-53,1997
(2) American Psychiatric Association, Practice Guideline for Major Depressive Disorder in Adults. Am. J. Psychiatry 150:1-26,1993
(3) PDR, 1999

SYMPTOMS OF DEPRESSION

- Depressed Mood
- Loss of Interest/Anhedonia
- Guilt / Worthlessness
- Weight Gain/Loss
- Insomnia/Hypersomnia*
- Loss of Concentration*
- Fatigue*
- Recurrent thoughts of Suicide
- Inactivity/Agitation

[*Indicates Common Symptoms]

SYMPTOMS OF ANXIETY

- Restlessness*
- Easily Fatigued*
- Difficulty Concentrating*
- Sleep Disturbance*
- Irritability
- Muscle Tension

ALPHABETICAL LIST OF DOSING REGIMENS

Not a complete list of all drugs. Prices subject to change

CELEXA (CITALOPRAM) **20 mg Q a.m., Usual dose 20-40 mg** **Max dose = 60 mg** **• AVAILABLE AS FIRST LINE THERAPY BY PRIOR AUTHORIZATION** **• ONLY 40 MG TAB OHP APPROVED $22 (15 tabs 40 mg)*****	PROZAC (FLUOXETINE) 20 mg Q a.m. FOR MOST ADULTS 10 mg Q a.m. FOR GERIATRICS TITRATE Q MONTH MAX DOSE = 80 mg/day $60 (30 caps 20 mg)**
EFFEXOR XR (VENLAFAXINE XR) 37.5 mg Q a.m., X I WEEK then 75mg Q a.m. MAX DOSE = 225mg CHECK BP FOR DOSE > 200 MG/DAY • ONLY 75 MG and 150 MG CAPS OHP APPROVED $51 (55 caps 75mg)**	REMERON (MITRAZAPINE) 15 MG Q h.s. TITRATE Q 2 WEEKS MAX DOSE=45 mg/day • ONLY 30 mg TAB OHP APPROVED $52.41(30 tabs 30 mg)***
NORPRAMIN (DESIPRAMINE) 50 mg Q h.s. TITRATE DOSE Q 3 WEEKS MAX DOSE = 300 mg/day MAX DOSE GERIATRICS =150 mg Therapeutic level > 125 ng/ml $29.84 (60 caps generic 75mg)***	**SERZONE (NEFAZODONE)** 50 mg/ BID x 1 WEEK 100mg/ BID x 1 WEEK 150 mg/ BID x 1 WEEK RANGE 300-600 mg/day **Contraindicated with Propulsid,Hismanal,Seldane** **Dose reduction with Xanax and Halcion** **$49 (61 caps 150 mg)****
PAMELOR (NORTRIPTYLINE) 25 MG Q. h.s. TITRATE DOSE Q 3 WEEKS MAX DOSE=150 mg/day Therapeutic level 50-150 ng/ml $ 73.08(60 caps generic 50 mg)***	WELLBUTRIN (BUPROPRION) 100 mg q B.I.D. x 3 DAYS then 100 mg T.I.D. no single dose over 150 mg MAX DOSE = 450 mg/day MAX DOSE FOR SR = 400 mg/day SR FORM AVAILABLE BY PRIOR AUTHORIZATION ONLY $68.08 (90 tabs 100 mg) ***
PAXIL (PAROXETINE) **10 mg Q h.s. FOR PANIC DISORDER** **20 mg Q h.s. FOR DEPRESSION** **10 mg Q h.s. FOR GERIATRICS** **TITRATE DOSE Q 3 WEEKS** **MAX DOSE = 50 MG/DAY** **$28 (40 m 17 tabs)****	**ZOLOFT (SERTRALINE)** **50 mg Q a.m.** **TITRATE DOSE Q 3 WEEKS** **MAX DOSE=200 mg/day** **• ONLY 100 MG TAB OHP APPROVED** **$44 (100 mg 26 tabs)****

- START LOW DOSES IN GERIATRIC PATIENTS AND PATIENTS WITH PANIC DISORDER.
- TITRATE DOSES UNTIL:
  1. RESPONSE 2. SIDE EFFECTS OR 3. MAXIMUM DOSE.
- MAINTAIN EFFECTIVE DOSE X 6 MONTHS THEN TRY TO TITRATE DOSE DOWNWARD.

** Claims data 1998 after $10.00 co-pay.
*** No claims data available.
Estimate after $10 co-pay

could be inducing the depression should be vigorously addressed. Whenever possible, those medications should be replaced by medications that do not cause or worsen depression. On the other hand, if the medical condition is chronic or if the depression-inducing medication is essential (e.g. steroids), then the depression should be treated like a primary affective disorder with psychotherapy and antidepressants (3).

Counseling

Counseling the depressed medical patient requires a comprehensive assessment of the presenting problem, exploration of the precipitating events, and flexible psychosocial interventions (9). Psychologically, depression in these patients is triggered by multiple losses. The medically ill often sustain losses of health, autonomy, financial resources, social support, and physical abilities (2). The goals of psychotherapy are to improve self-esteem, correct misunderstandings about the medical illnesses, reduce shame and isolation, promote acceptance of the limitations imposed by the illness, and facilitate the expression of fears and concerns (10). Psychoeducational group therapy is an effective treatment modality for depression and, remarkably, has been shown to improve survival rates in metastatic breast cancer and malignant melanoma patients (11,12).

Antidepressants

The newer antidepressants are highly efficacious and safe in the treatment of major depression in a primary care population. The selection of the best agent for a specific patient depends on the side effect profile of the antidepressant, compatibility with concurrent medical conditions and medications, target symptoms, and previous treatment response (3). The algorithm on pages 81-82 is included to assist the clinician in the choice of an appropriate antidepressant.

The tricyclic antidepressants (TCAs) are potent, cost-effective agents but have significant anticholinergic, orthostatic, sedative, and quinidine-like side effects. The use of TCAs in patients with first-degree heart block or bundle branch block can result in a higher degree heart block, and all patients over the age of 50 should have an electrocardiogram (EKG) before receiving a TCA. The use of TCAs should be avoided when the corrected Q-T interval is greater than 440 milliseconds.

Selective serotonin re-uptake inhibitors (SSRIs) are also effective antidepressants. However, there are two areas of concern with this group of antidepressants: the high prevalence of sexual side effects and inhibition of the P450 2D6 liver isoenzyme system. The clinician should be cautious when other medications that are metabolized by this system are concurrently prescribed with an SSRI.

Bupropion is a norepinephrine and dopamine re-uptake blocker that should not be prescribed to patients with eating disorders or epilepsy.

Venlafaxine inhibits the re-uptake of norepinephrine, serotonin, and dopamine. It does not inhibit any of the liver isoenzymes and, therefore, is compatible with most other medications. Another unique feature of venlafaxine is its plasma protein binding. Only 30% of venlafaxine is bound to plasma proteins, making it the safest antidepressant for patients on digoxin or Coumadin.

Nefazodone is an SSRI that also inhibits the 5HT-2 post-synaptic serotonin receptor resulting in the absence of sexual side effects. Because nefazodone inhibits the P450 3A4 cytochrome liver isoenzyme system, the clinician must avoid prescribing other medications that are metabolized by the 3A4 isoenzyme system. For example, co-administration of nefazodone with terfenadine or astemizole can result in cardiotoxicity.

Mirtazapine has both noradrenergic and serotonergic activity, in addition to inhibiting the 5HT-2 and 5HT-3 post-synaptic serotonin receptors. As a result, mirtazapine does not cause nausea or sexual side effects (3); however, because of its strong antihistamine properties, mirtazapine is very sedating and a potent appetite stimulant.

Non-Pharmaceutical Treatments

Electroconvulsive therapy (ECT) can be life saving for patients who have depressions resistant to antidepressant medications and can be utilized safely in most medically ill patients. Although there are no absolute medical contraindications for ECT, those clinical situations that increase the risk for this procedure include the presence of a space-occupying cerebral lesion, increased intracranial pressure, recent myocardial infarction, recent hemorrhagic cerebrovascular accident, unstable aneurysm, retinal detachment, and pheochromocytoma. Before receiving ECT, every patient should have complete medical and psychiatric history, physical examination, mental status examination, complete blood count, serum electrolytes, liver function tests, EKG, and anesthesia consultation. Some patients may also require computed tomography (CT) or magnetic resonance imaging (MRI) of the head, electroencephalogram (EEG), or chest x-ray (13).

Transcranial magnetic stimulation (TMS) is an evolving treatment option for depression in which magnetic fields are applied to certain areas of the brain. Because there is no electrical stimulus and no seizure induction, TMS is associated with fewer side effects, including less memory loss, when compared with ECT (14).

Conclusions

Major depression is prevalent in primary care, especially among patients with neurological and endocrine disorders, and has serious consequences in the medically ill in terms of medical utilization, morbidity, and mortality. Fortunately, depression in these patients is responsive to a combination of counseling and antidepressant medication.

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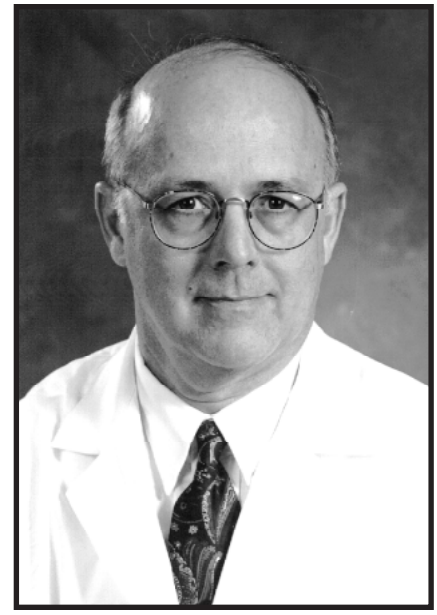

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