Complete Summary

GUIDELINE TITLE

Practice guideline for the treatment of patients with major depressive disorder.

BIBLIOGRAPHIC SOURCE(S)

American Psychiatric Association practice guideline for the treatment of patients with major depressive disorder. Am J Psychiatry 2000 Apr;157(4 Suppl):1-45. [325 references]

GUIDELINE STATUS

This is the current release of the guideline. It is a revision of a previously issued version (Practice guideline for major depressive disorder in adults. Washington [DC]: American Psychiatric Press, Inc; 1993. 51 p., and Am J Psychiatry 1993 Apr;150[4 Suppl]:1-26).

According to the guideline developer, this guideline is still considered to be current as of February 2005, based on a review of literature published since the original guideline publication.

In addition, a Guideline Watch, which summarizes significant developments in practice since the publication of the original guideline, was published in 2005 and is available from the American Psychiatric Association Web site (see also the "Availability of Companion Documents" field below).

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

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

- May 2, 2007, Antidepressant drugs: Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.
- October 25, 2006, Effexor (venlafaxine HCl): Published retrospective studies report that venlafaxine overdosage may be associated with an increased risk of fatal outcome.
- May 12, 2006, Paxil (paroxetine) and Paxil CR: Changes to the Clinical Worsening and Suicide Risk subsection of the WARNINGS section in the

prescribing Information related to adult patients, particularly those who are younger adults.

- December 8, 2005, Paxil (paroxetine): Pregnancy category changed from C to D and new data and recommendations added to the WARNINGS section of prescribing information.
- September 27, 2005, Paxil (paroxetine) and Paxil CR: Changes to the Pregnancy/PRECAUTIONS section of the Prescribing Information to describe the results of a retrospective epidemiologic study of major congenital malformations in infants born to women taking antidepressants during the first trimester of pregnancy.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **
SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Major Depressive Disorder

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Neurology
Psychiatry

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

1. To assist the physician faced with the task of implementing specific antidepressant treatment(s) for an adult patient diagnosed as suffering from major depression according to the criteria for this disorder defined in DSM-IV.
2. To summarize the specific forms of somatic, psychotherapeutic, psychosocial, and educational treatments that have been developed to deal with major depressive disorder and its various subtypes.

TARGET POPULATION

Adults (over the age of 18) suspected of having major depressive disorder

INTERVENTIONS AND PRACTICES CONSIDERED

The various interventions considered for treatment of a major depressive episode may be used alone or in combination. Furthermore, the psychiatrist must decide whether to conduct treatment on an outpatient, partial hospitalization, or inpatient basis.

Psychotherapeutic Interventions

- Psychotherapeutic management
- Psychodynamic psychotherapy and psychoanalysis
- Brief psychodynamic psychotherapy
- Interpersonal therapy
- Behavior therapy
- Cognitive behavior therapy
- Marital therapy and family therapy
- Group therapy

Somatic Interventions

- Antidepressant medications including:
    1. Cyclic antidepressants, which include the tricyclic antidepressants as well as the tetracyclic antidepressant medication maprotiline
    2. Selective serotonin-reuptake inhibiting antidepressants, which currently include fluoxetine, sertraline, paroxetine, fluvoxamine, and citalopram
    3. Monoamine oxidase (MAO) inhibitors, which include the commonly used phenelzine, isocarboxazid, and tranylcypromine
    4. Other antidepressant medications, including bupropion, nefazodone, trazodone, venlafaxine, mirtazapine, and reboxetine (for which U.S Food and Drug Administration approval is anticipated)
    5. St. John's wort (whole plant product)
- Electroconvulsive therapy
- Light therapy

MAJOR OUTCOMES CONSIDERED

- Control of depressive symptoms
- Rate of remission, relapse and recurrence of major depression
- Morbidity and mortality due to major depression

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Studies were identified through an extensive review of the literature by using MEDLARS for the period 1971-1999. The key words used were affective disorder, major depression, depressive disorder, seasonal affective disorder, melancholia, unipolar depression, endogenous depression, dysthymic disorder, dysthymia, postpartum depression, pseudodementia, antidepressant medications, tricyclic antidepressive agents, monoamine oxidase inhibitors, lithium, and electroconvulsive therapy and included the concepts of melancholia, neurotic depression, and major depression. In addition, the key words for the psychotherapy search were psychotherapy (not otherwise specified); behavior therapy, including aversive therapy, biofeedback (psychology), cognitive therapy, desensitization (psychologic), implosive therapy, and relaxation techniques (meditation); psychoanalytic therapy, including existentialism, free association, transactional analysis, psychotherapy (brief); and psychotherapy (group), including family therapy and marital therapy. Major review articles and standard psychiatric texts were consulted. The Agency for Health Care Policy and Research Evidence Report on Treatment of Depression--Newer Pharmacotherapies (Rockville [MD]: Agency for Health Care Policy and Research. March 1999 [Evidence Report/Technology Assessment: no: 7]) was reviewed in its entirety. Review articles and relevant clinical trials were reviewed in their entirety; other studies were selected for review on the basis of their relevance to the particular issues discussed in this guideline.

NUMBER OF SOURCE DOCUMENTS

169 source documents

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Once a topic is chosen for guideline development, a work group is formed to draft the guideline. By design, the work group consists of psychiatrists in active clinical practice with diverse expertise and practice experience relevant to the topic. Policies established by the Steering Committee guide the work of systematically reviewing data in the literature and forging consensus on the implications of those data, as well as describing a clinical consensus. These policies, in turn, stem from criteria formulated by the American Medical Association to promote the development of guidelines that have a strong evidence base and that make optimal use of clinical consensus.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Each recommendation is identified at falling into one of three categories of endorsement, indicated by a bracketed Roman numeral following the statement. The three categories represent varying levels of clinical confidence regarding the recommendation:

[I] indicates recommended with substantial clinical confidence.

[II] indicates recommended with moderate clinical confidence.

[III] indicates options that may be recommended on the basis of individual circumstances.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline is written in successive drafts, each being revised on the basis of comments received from an increasing number of people: early drafts are sent to the Steering Committee and about 50 expert reviewers; later drafts are sent to members of the Assembly, the District Branches, the Board of Trustees, and other American Psychiatric Association (APA) components. Drafts are available to any APA member by request through their District Branch. In addition, individual

experts who are not APA members along with relevant professional, scientific, and patient organizations are asked to review the drafts. Once all comments have been considered, a final draft is sent to the Assembly and Board of Trustees for their approval. Thus each guideline is reviewed by hundreds of psychiatrists and other interested parties prior to publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation is identified as falling into one of three categories of endorsement, by a bracketed Roman numeral following the statement. The three categories represent varying levels of clinical confidence regarding the efficacy of the treatment for the disorder and conditions described.

[I] indicates recommended with substantial clinical confidence.

[II] indicates recommended with moderate clinical confidence.

[III] indicates options that may be recommended on the basis of individual circumstances.

Successful treatment of patients with major depressive disorder is promoted by a thorough assessment of the patient [I]. 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 susceptible patient is protected against the recurrence of subsequent major depressive episodes. Psychiatrists initiating treatment for major depressive disorder have at their disposal a number of medications, a variety of psychotherapeutic approaches, electroconvulsive therapy (ECT), and other treatment modalities (e.g., light therapy) that may be used alone or in combination. The psychiatrist must determine the setting that will most likely ensure the patient's safety as well as promote improvement in the patient's condition [I].

A. **Psychiatric Management**

Psychiatric management consists of a broad array of interventions and activities that should be instituted by psychiatrists for all patients with major depressive disorder [I]. Regardless of the specific treatment modalities selected, it is important to continue providing psychiatric management through all phases of treatment. The specific components of psychiatric management that must be addressed for all patients include performing a diagnostic evaluation, evaluating safety of the patient and others, evaluating the level of functional impairments, determining a treatment setting, establishing and maintaining a therapeutic alliance, monitoring the patient's psychiatric status and safety, providing education to patients and families, enhancing treatment adherence, and working with patients to address early signs of relapse.

B. **Acute Phase**

1. Choice of an initial treatment modality

In the acute phase, in addition to psychiatric management, the psychiatrist may choose between several initial treatment modalities, including pharmacotherapy, psychotherapy, the combination of medications plus psychotherapy, or electroconvulsive therapy [I]. Selection of an initial treatment modality should be influenced by both clinical (e.g., severity of symptoms) and other factors (e.g., patient preference).

a. Antidepressant medication

   If preferred by the patient, antidepressant medications may be provided as an initial primary treatment modality for mild major depressive disorder [I]. Antidepressant medications should be provided for moderate to severe major depressive disorder unless electroconvulsive therapy is planned [I]. A combination of antipsychotic and antidepressant medications or electroconvulsive therapy should be used for psychotic depression [I].

b. Psychotherapy

   A specific, effective psychotherapy alone as an initial treatment modality may be considered for patients with mild to moderate major depressive disorder [II]. Patient preference for psychotherapeutic approaches is an important factor that should be considered in the decision. Clinical features that may suggest the use of psychotherapeutic interventions include the presence of significant psychosocial stressors, intrapsychic conflict, interpersonal difficulties, or a comorbid axis II disorder [I].

c. Psychotherapy plus antidepressant medications

   The combination of a specific effective psychotherapy and medication may be a useful initial treatment choice for patients with psychosocial issues, interpersonal problems, or a comorbid axis II disorder together with moderate to severe major depressive disorder [I]. In addition, patients who have had a history of only partial response to adequate trials of single treatment modalities may benefit from combined treatment. Poor adherence with treatments may also warrant combined treatment modalities.

d. Electroconvulsive therapy

   Electroconvulsive therapy should be considered for patients with major depressive disorder with a high degree of symptom severity and functional impairment or for cases in which psychotic symptoms or catatonia are present [I]. Electroconvulsive therapy may also be the treatment modality of choice for patients in whom there is an urgent need for

response, such as patients who are suicidal or refusing food and nutritionally compromised [II].

2. Choice of specific pharmacologic treatment

   Antidepressant medications that have been shown to be effective are listed in the full-text guideline document -- see the table titled "Commonly Used Antidepressant Medications" [II]. The effectiveness of antidepressant medications is generally comparable between classes and within classes of medications. Therefore, the initial selection of an antidepressant medication will largely be based on the anticipated side effects, the safety or tolerability of these side effects for individual patients, patient preference, quantity and quality of clinical trial data regarding the medication, and its cost (for more information, see Section V.A.1 of the original guideline document) [I]. On the basis of these considerations, the following medications are likely to be optimal for most patients: selective serotonin reuptake inhibitors (SSRIs), desipramine, nortriptyline, bupropion, and venlafaxine. In general, monoamine oxidase inhibitors (MAOIs) should be restricted to patients who do not respond to other treatments because of their potential for serious side effects and the necessity of dietary restrictions. Patients with major depressive disorder with atypical features are one group for whom several studies suggest monoamine oxidase inhibitors may be particularly effective; however, in clinical practice, many psychiatrists start with selective serotonin reuptake inhibitors in such patients because of the more favorable adverse effect profile.

   a. Implementation

      When pharmacotherapy is part of the treatment plan, it must be integrated with the psychiatric management and any other treatments that are being provided (e.g., psychotherapy) [I]. Once an antidepressant medication has been selected, it can be started at the dose levels suggested in the full-text guideline document -- see the table titled "Commonly Used Antidepressant Medications" [I]. Titration to full therapeutic doses generally can be accomplished over the initial week(s) of treatment but may vary depending on the development of side effects, the patient's age, and the presence of comorbid illnesses. Patients who have started taking an antidepressant medication should be carefully monitored to assess their response to pharmacotherapy as well as the emergence of side effects, clinical condition, and safety [I] (see "Management of Medication Side Effects" in the original guideline document.). Factors to consider in determining the frequency of patient monitoring include the severity of illness, the patient's cooperation with treatment, the availability of social supports, and the presence of comorbid general medical problems. Visits should also be frequent enough to monitor and address suicidality and to promote treatment adherence. In practice, the frequency of monitoring during the acute phase of

pharmacotherapy can vary from once a week in routine cases to multiple times per week in more complex cases.

b. Failure to respond

If at least moderate improvement is not observed following 6-8 weeks of pharmacotherapy, a reappraisal of the treatment regimen should be conducted [I]. Section II.B.2.b in the original guideline document reviews options for adjusting the treatment regimen when necessary. Following any change in treatment, the patient should continue to be closely monitored. If there is not at least a moderate improvement in major depressive disorder symptoms after an additional 6-8 weeks of treatment, the psychiatrist should conduct another thorough review. An algorithm depicting the sequence of subsequent steps that can be taken for patients who fail to respond fully to treatment is provided in the full-text guideline document --see "Acute Phase Treatment of Major Depressive Disorder."

3. Choice of specific psychotherapy

Cognitive behavioral therapy and interpersonal therapy are the psychotherapeutic approaches that have the best documented efficacy in the literature for the specific treatment of major depressive disorder, although rigorous studies evaluating the efficacy of psychodynamic psychotherapy have not been published [II]. When psychodynamic psychotherapy is used as a specific treatment, in addition to symptom relief, it is frequently associated with broader long-term goals. Patient preference and the availability of clinicians with appropriate training and expertise in the specific approach are also factors in the choice of a particular form of psychotherapy.

a. Implementation

When psychotherapy is part of the treatment plan, it must be integrated with the psychiatric management and any other treatments that are being provided (e.g., medication treatment) [I]. The optimal frequency of psychotherapy has not been rigorously studied in controlled trials. The psychiatrist should take into account multiple factors when determining the frequency for individual patients, including the specific type and goals of psychotherapy, the frequency necessary to create and maintain a therapeutic relationship, the frequency of visits required to ensure treatment adherence, and the frequency necessary to monitor and address suicidality. The frequency of outpatient visits during the acute phase generally varies from once a week in routine cases to as often as several times a week. Regardless of the type of psychotherapy selected, the patient's response to treatment should be carefully monitored [I].

If more than one clinician is involved in providing the care, it is essential that all treating clinicians have sufficient ongoing contact with the patient and with each other to ensure that relevant information is available to guide treatment decisions [I].

b. Failure to respond

If after 4-8 weeks of treatment at least a moderate improvement is not observed, then a thorough review and reappraisal of the diagnosis, complicating conditions and issues, and treatment plan should be conducted [I]. Figure 3 and Section II.B.3.b. in the original guideline document review the options to consider.

4. Choice of medications plus psychotherapy

In general, the same issues that influence the specific choice of medication or psychotherapy when used alone should be considered when choosing treatments for patients receiving combined modalities [I].

5. Assessing the adequacy of response

It is not uncommon for patients to have a substantial but incomplete response in terms of symptom reduction or improvement in functioning during acute phase treatments. It is important not to conclude the acute phase of treatment for such patients, as a partial response is often associated with poor functional outcomes. When patients are found to have not fully responded to an acute phase treatment, a change in treatment should be considered as outlined in the full-text guideline document -- see "Acute Phase Treatment of Major Depressive Disorder" [II].

C. **Continuation Phase**

During the 16-20 weeks following remission, patients who have been treated with antidepressant medications in the acute phase should be maintained on these agents to prevent relapse [I]. In general, the dose used in the acute phase is also used in the continuation phase. Although there has been less study of the use of psychotherapy in the continuation phase to prevent relapse, there is growing evidence to support the use of a specific effective psychotherapy during the continuation phase [I]. Use of electroconvulsive therapy in the continuation phase has received little formal study but may be useful in patients for whom medication or psychotherapy has not been effective in maintaining stability during the continuation phase [II]. The frequency of visits must be determined by the patient's clinical condition as well as the specific treatments being provided.

D. **Maintenance Phase**

Following the continuation phase, maintenance-phase treatment should be considered for patients to prevent recurrences of major depressive disorder [I]. Factors to consider are discussed in the full-text guideline document -- see the table titled "Considerations in the Decision to Use Maintenance Treatment" -- and Section II.D of the original guideline document.

In general, the treatment that was effective in the acute and continuation phases should be used in the maintenance phase [II]. In general, the same full antidepressant medication doses are employed as were used in prior phases of treatment; use of lower doses of antidepressant medication in the maintenance phase has not been well studied. For cognitive behavioral therapy and interpersonal therapy, maintenance phase treatments usually involve a decreased frequency of visits (e.g., once a month). The frequency of visits in the maintenance phase must be determined by the patient's clinical condition as well as the specific treatments being provided. The frequency required could range from as low as once every 2-3 months for stable patients who require only psychiatric management and medication monitoring to as high as multiple times a week for those in whom psychodynamic psychotherapy is being conducted.

E. **Discontinuation of Active Treatment**

The decision to discontinue active treatment should be based on the same factors considered in the decision to initiate maintenance treatment, including the probability of recurrence, the frequency and severity of past episodes, the persistence of dysthymic symptoms after recovery, the presence of comorbid disorders, and patient preferences [I]. In addition to the factors listed in the full-text guideline document -- see the table titled "Considerations in the Decision to Use Maintenance Treatment" and the table titled "Risk Factors for Recurrence of Major Depressive Disorder" -- patients and their psychiatrists should consider the patient's response, in terms of both beneficial and adverse effects, to maintenance treatments.

CLINICAL ALGORITHM(S)

The original guideline contains a clinical algorithm depicting the sequence of subsequent steps that can be taken for patients who fail to respond fully to treatment.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations delineated in this guideline are in some instances based on data distilled from randomized prospective clinical trials, while in other areas they are based on individual case reports along with the collective experience and judgment of well-regarded senior psychiatrists.

To identify the type of evidence supporting the major recommendations in the full-text practice guide, each is keyed to one or more references and each reference is followed by a letter code in brackets that indicates the nature of the

supporting evidence. Minor recommendations not keyed to references may be assumed to be based on expert opinion.

The bracketed letter following each reference indicates the nature of the supporting evidence, as follows:

[A] Randomized controlled clinical trial

[B] Nonrandomized case-control study

[C] Nonrandomized cohort study

[D] Clinical report with nonrandomized historical comparison groups

[E] Case report or series

[F] Expert consensus

[G] Subject review subsuming multiple categories A-E

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved patient care.
- Education of psychiatrists, other medical and mental health professionals, and the general public about appropriate and inappropriate treatments.
- Identification of those areas where critical information is lacking and where research could be expected to improve clinical decisions.
- Aid those charged with overseeing the utilization and reimbursement of psychiatric services with developing more scientifically based and clinically sensitive criteria.

POTENTIAL HARMS

Side effects of antidepressant medication:

- Dizziness, sedation, and feeling medicated: Associated with many antidepressants. Amitriptyline, doxepin, and trazodone are experienced as most sedating, nortriptyline and amoxapine as less sedating, and fluoxetine, sertraline, bupropion, protriptyline, and desipramine as least sedating.
- Peripheral anticholinergic side effects: The most common undesirable consequences of muscarinic blockade are dry mouth, impaired ability to focus at close range, constipation, and urinary hesitation. All tricyclic antidepressants have some degree of antimuscarinic action; desipramine has the lowest potency in this regard. While monoamine oxidase inhibitors are not anticholinergic, their side effects may resemble anticholinergic symptoms.
- Weight gain: Tricyclic antidepressants, monoamine oxidase inhibitors, and lithium all have the capacity to induce weight gain. Bupropion, fluoxetine, sertraline, and trazodone do not usually induce weight gain, and bupropion

and fluoxetine (and perhaps sertraline) may actually cause some (usually transient) degree of appetite and weight loss.

- Sexual dysfunction: While loss of erectile or ejaculatory function in men and loss of libido and anorgasmia in both sexes may be complications of virtually any antidepressant agent, these side effects appear to be most common with the monoamine oxidase inhibitors, fluoxetine, and probably sertraline and to be least common with bupropion.
- Neurological side effects, such as seizures or myoclonus: Overall, for most agents and for patients without specific risk factors who receive antidepressants administered within the recommended dose range, the risk of seizures is most often reported to be less than 1 percent. Fluoxetine, sertraline, trazodone, and monoamine oxidase inhibitors carry a lower risk of inducing seizures. Risk increases with dose for all offending agents. Tricyclic antidepressants sometimes induce mild myoclonus
- Cardiovascular effects, such as orthostatic hypotension: A common side effect of tricyclic antidepressants, trazodone, and monoamine oxidase inhibitors.
- Insomnia and anxiety: Fluoxetine may precipitate or exacerbate anxiety and sleep disturbance in some patients. Anxiety may be minimized by introducing the agent at a low dose; insomnia may be effectively treated by the addition of trazodone, up to 100 mg at bedtime. Other antidepressants, including desipramine and bupropion, may also increase anxiety in some patients.

Side effects associated with electroconvulsive therapy

- Cognitive: transient postictal confusional state and anterograde and retrograde memory interference.
- Cardiovascular: transient rise in heart rate, cardiac workload, and blood pressure.
- Cerebrovascular: transient rise in intracranial pressure and blood-brain barrier permeability.

Side effects associated with light therapy

- Possibly include headache, eye strain, irritability, and insomnia, adverse ocular effects.

Subgroups Most Likely to be Harmed:

The following subgroups would be most likely to be harmed by electroconvulsive therapy:

- Patients with the presence of significant cardiovascular disease. Electroconvulsive therapy is an indication for caution and general medical or cardiology consultation.
- Patients with evidence of increased intracranial pressure or cerebrovascular fragility. These patients should only receive electroconvulsive therapy after careful general medical, neurological, or neurosurgical evaluation.

The following subgroups are more vulnerable to light therapy and would require attention and consultative supervision of the appropriate specialist if light therapy were conducted:

- Patients with retinal diseases or ordinary photosensitivity.
- Patients with systemic lupus erythematosus.
- Patients with a history of skin cancer.

Patients with the following concurrent general medical disorders are most likely to be adversely affected by pharmacotherapy:

- *Asthma.* Individuals with asthma who receive monoamine oxidase inhibitors should be cautioned regarding interactions with sympathomimetic bronchodilators.
- *Cardiac disease.* The presence of specific cardiac conditions complicates or contraindicates certain forms of antidepressant medication therapy, notably use of tricyclic agents; the cardiac history should therefore be carefully explored before the initiation of medication treatment.
- *Dementia.* Individuals with dementia are particularly susceptible to the toxic effects of muscarinic blockade on memory and attention. Therefore, individuals suffering from dementia generally do best when given antidepressant medications with the lowest possible degree of anticholinergic effect, e.g., bupropion, fluoxetine, sertraline, trazodone, and, of the tricyclic agents, desipramine or nortriptyline. Alternatively, some patients do well given stimulants in small doses.
- *Epilepsy.* Consideration should be given to concomitant prescription of an antiepileptic (or elevating the dose of an existing antiepileptic).
- *Glaucoma.*Medications with anticholinergic potency may precipitate acute narrow-angle glaucoma in susceptible individuals (i.e., those with shallow anterior chambers). Patients with glaucoma receiving local miotic therapy may be treated with antidepressant medications, including those possessing anticholinergic properties, provided that their intraocular pressure is monitored during antidepressant medication treatment.
- *Hypertension.* Antihypertensive agents and tricyclic antidepressant medications may interact to either intensify or counteract the effect of the antihypertensive therapy. The action of antihypertensive agents that block alpha receptors (e.g., prazosin) may be intensified by antidepressant medications that block these same receptors, notably the tricyclic antidepressants and trazodone. Tricyclic antidepressants may antagonize the therapeutic actions of guanethidine, clonidine, or alpha-methyldopa. Concurrent antihypertensive treatment, especially with diuretics, increases the likelihood that tricyclic antidepressants, trazodone, or monoamine oxidase inhibitors will induce symptomatic orthostatic hypotension. Beta-blockers, especially propranolol, may be a cause of major depressive disorder in some patients; individuals who have become depressed after initiation of treatment with one of these medications should be changed to another antihypertensive regimen. Dose-dependent elevations in blood pressure with venlafaxine are usually mild, although more severe elevations have been observed, making this agent less preferable in patients with hypertension.
- *Obstructive uropathy.* Benzodiazepines, trazodone, and monoamine oxidase inhibitors may retard bladder emptying.
- *Parkinson's disease.* Amoxapine, an antidepressant medication with dopamine-receptor blocking properties, should be avoided for patients who have Parkinson's disease. Lithium may in some instances induce or exacerbate parkinsonian symptoms. Bupropion, in contrast, exerts a beneficial effect on the symptoms of Parkinson's disease in some patients but

may also induce psychotic symptoms, perhaps because of its agonistic action in the dopaminergic system. Monoamine oxidase inhibitors (other than selegiline, also known as L-deprenyl, a selective type B monoamine oxidase inhibitor recommended in the treatment of Parkinson's disease) may adversely interact with L-dopa products. Selegiline loses its specificity for monoamine oxidase-B in doses greater than 10 mg/day and may induce serotonin syndrome when given in higher doses in conjunction with serotonin-enhancing antidepressant medications.

CONTRAINDICATIONS

CONTRAINDICATIONS

Prostatism and other forms of bladder outlet obstruction are relative contraindications to the use of antidepressant medication compounds with antimuscarinic effects.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guideline is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgment regarding a particular clinical procedure or treatment course must be made by the physician in light of the clinical data presented by the patient and the diagnostic and treatment options available.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The American Psychiatric Association develops derivative products including patient guides, quick reference guides, and quality of care indicators with research studies to evaluate the effectiveness of the guideline.

IMPLEMENTATION TOOLS

Clinical Algorithm
Patient Resources
Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Psychiatric Association practice guideline for the treatment of patients with major depressive disorder. Am J Psychiatry 2000 Apr;157(4 Suppl):1-45. [325 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1993 (revised 2000; reviewed 2005)

GUIDELINE DEVELOPER(S)

American Psychiatric Association - Medical Specialty Society

SOURCE(S) OF FUNDING

American Psychiatric Association (APA)

GUIDELINE COMMITTEE

Work Group on Major Depressive Disorder

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Work Group Members: T. Byram Karasu, M.D., Chair; Alan Gelenberg, M.D.; Arnold E. Merriam, M.D.; Philip Wang, M.D., Dr.P.H.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

This practice guideline has been developed by psychiatrists who are in active clinical practice. In addition, some contributors are primarily involved in research

or other academic endeavors. It is possible that through such activities many contributors have received income related to treatments discussed in this guideline. A number of mechanisms are in place to minimize the potential for producing biased recommendations due to conflicts of interest. The guideline has been extensively reviewed by members of American Psychiatric Association (APA) as well as by representatives from related fields. Contributors and reviewers have all been asked to base their recommendations on an objective evaluation of the available evidence. Any contributor or reviewer who has a potential conflict of interest that may bias (or appear to bias) his or her work has been asked to notify the APA Office of Research. This potential bias is then discussed with the work group chair and the chair of the Steering Committee on Practice Guidelines. Further action depends on the assessment of the potential bias.

GUIDELINE STATUS

This is the current release of the guideline. It is a revision of a previously issued version (Practice guideline for major depressive disorder in adults. Washington [DC]: American Psychiatric Press, Inc; 1993. 51 p., and Am J Psychiatry 1993 Apr;150[4 Suppl]:1-26).

According to the guideline developer, this guideline is still considered to be current as of February 2005, based on a review of literature published since the original guideline publication.

In addition, a Guideline Watch, which summarizes significant developments in practice since the publication of the original guideline, was published in 2005 and is available from the American Psychiatric Association Web site (see also the "Availability of Companion Documents" field below).

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Psychiatric Association (APA) Web site.

Print copies: Available from the American Psychiatric Press, Inc (APPI), 1000 Wilson Boulevard, Suite 1825, Arlington, VA 22209-3901; (703) 907-7322; (800) 368-5777; Fax (703) 907-1091.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- American Psychiatric Association practice guideline development process. In: Practice Guidelines for the Treatment of Psychiatric Disorders: Compendium 2000. Washington, DC: APA, 2000.
- Treating major depressive disorder: A quick reference guide for psychiatrists. Washington, DC: American Psychiatric Association, 2000. 25 p. Electronic copies: Available in Portable Document Format (PDF) from the American Psychiatric Association Web site.
- Fochtmann, LJ & Gelenberg, AJ. Guideline Watch: practice guideline for the treatment of patients with major depressive disorder, 2nd Edition. Arlington

(VA): American Psychiatric Association; 2005 Winter. 9 p. Electronic copies available in Portable Document Format (PDF) from the American Psychiatric Association Web site.

Print copies: Available from the American Psychiatric Press, Inc (APPI), 1000 Wilson Boulevard, Suite 1825, Arlington, VA 22209-3901; (703) 907-7322; (800) 368-5777; Fax (703) 907-1091.

Additionally, a continuing medical education (CME) course is available online at the American Psychiatric Association Web site.

PATIENT RESOURCES

The following is available:

- Treatment works. Major depressive disorder: a patient and family guide. Available in Portable Document Format (PDF) from the American Psychiatric Association (APA) Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on December 1, 1998. The information was verified by the guideline developer on January 11, 1999. The summary was updated by ECRI on February 1, 2001. The updated summary was verified by the guideline developer as of March 9, 2001. This summary was updated by ECRI on August 15, 2005, following the U.S. Food and Drug Administration advisory on antidepressant medications. This summary was updated by ECRI on October 3, 2005, following the U.S. Food and Drug Administration advisory on Paxil (paroxetine). This summary was updated by ECRI on December 12, 2005, following the U.S. Food and Drug Administration advisory on Paroxetine HCL - Paxil and generic paroxetine. This summary was updated by ECRI on May 31, 2006 following the U.S. Food and Drug Administration advisory on Paxil (paroxetine hydrochloride). This summary was updated by ECRI on November 21, 2006, following the FDA advisory on Effexor (venlafaxine HCl). This summary was updated by ECRI Institute on November 2, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs.

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2008 National Guideline Clearinghouse

Date Modified: 10/27/2008