Diagnosis and treatment of depression in adults: 2012 clinical practice guideline.

Major Recommendations

Recommendations are identified as either "strong" or "weak." For definitions of the recommendation strength, see the end of the "Major Recommendations" field.

Depression Screening

1. The Patient Health Questionnaire 9 (PHQ9) or PHQ2 is recommended for depression screening. (Strong recommendation)
    a. The Geriatric Depression Scale (GDS or GDS15) is an option as a screening instrument for older patients who have difficulty completing the PHQ9. (Weak recommendation)
    b. The Edinburgh Postpartum depression scale is an option as a screening tool for pregnant or postpartum women. (Weak recommendation)

Note: The PHQ9 is recommended as the preferred diagnosis and tracking instrument.

First-Line Treatment

2. Antidepressant medication or referral to behavioral health clinicians for evidence-based psychotherapy are recommended as first-line treatment in patients with mild to moderate major depressive disorder (MDD). (Weak recommendation)
    a. Given the lack of evidence on a clearly superior approach for mild to moderate MDD, clinicians may base treatment decisions on patient and clinician preference, potential side effects, and cost. (Weak recommendation)

Note: Evidence-based psychotherapy can include Interpersonal Therapy, Cognitive Behavioral Therapy (CBT), or Problem-Solving Therapy

3. The combination of antidepressants and referral to behavioral health for evidence-based psychotherapy is recommended as first-line treatment for patients with severe or chronic MDD. (Strong recommendation)
4. First-line antidepressant use
    a. Any class of antidepressant (selective serotonin reuptake inhibitor [SSRI], tricyclic antidepressant [TCA], serotonin–norepinephrine reuptake inhibitor [SNRI],

norepinephrine reuptake inhibitor [NRI], or dopamine agonist [DA]) is recommended for first-line treatment of MDD. (Strong recommendation)

   b. Given the equivalence of therapeutic effect, clinicians may base the choice of antidepressant on patients' prior response, patient and clinician preference, potential side effects, and cost. (Weak recommendation)

5. Behavioral activation in the primary care setting is an option for patients with mild to moderate depression. (Weak recommendation)

Note: Behavioral activation is a discrete, time-limited, structured psychological intervention, derived from the behavioral model of affective disorders.

6. Monitoring patients who are prescribed antidepressants for signs of new or worsening suicidal ideation is recommended. (Strong recommendation)
   a. Consultation or collaboration with a psychiatrist before prescribing TCAs or venlafaxine for patients with suicidal ideation or who have made previous suicide attempts is an option. (Weak recommendation)
   b. Consultation with specialty behavioral health for patients with MDD who are expressing suicidal intent or plan is an option. (Strong recommendation)
7. Atypical antipsychotics are not recommended as first-line treatment for (non-psychotic) MDD. (Strong recommendation)
8. Use of *Hypericum* (St. John's wort)

   a. *Hypericum* (St. John's wort) is not generally recommended for patients with severe MDD. (Weak recommendation)
   b. The Guideline Development Team (GDT) makes no recommendation for or against providing *Hypericum* (St. John's wort) to patients with mild to moderate MDD.

Pregnancy and Breastfeeding

9. Paroxetine is not recommended in pregnant women. (Strong recommendation)
10. The GDT makes no recommendation for or against other antidepressant medications. (Weak recommendation)
11. Starting fluoxetine and/or citalopram in breastfeeding women is not generally recommended. If used, the medications should be used with caution, and only in patients who had good results with these medications during pregnancy or a previous depression episode. (Weak recommendation)

Second-Line Treatment

12. Assessing adherence to the initial treatment regimen for patients with MDD whose symptoms fail to remit after first-line treatment is recommended. (Strong recommendation)
13. For patients with MDD whose symptoms fail to remit after adherence to first-line treatment, recommended alternatives include:
    a. Combine antidepressant and psychotherapy. (Strong recommendation)
    b. Increase the dose of the initial antidepressant. (Strong recommendation)
    c. Switch to a different antidepressant of the same or different class. (Strong recommendation)
    d. Switch from psychotherapy to antidepressants or antidepressants to psychotherapy. (Strong recommendation)
    e. Combine pharmacologic treatment (monitoring for toxicity, side effects and drug interactions) with selective serotonin reuptake inhibitors and:
        I. Low-dose TCAs
        II. Bupropion
        III. Mirtazepine
        IV. Lithium

        (Strong recommendation)

14. Consulting psychiatry before prescribing atypical antipsychotics for MDD is recommended. (Strong recommendation)
15. Augmentation with pindolol for patients with MDD whose symptoms fail to remit after adherence to first-line treatment is not recommended. (Strong recommendation)
16. Benzodiazepines for depression treatment augmentation or antidepressant side-effect management are not generally recommended. (Weak recommendation)

Adjunctive Treatment Strategies

17. Exercise as an adjunctive strategy (in addition to antidepressants or psychotherapy) for treating MDD is recommended. (Strong recommendation)
18. Internet patient cognitive-behavioral therapy self-help programs as an adjunct strategy (in addition to antidepressants or psychotherapy) for treating MDD is an option. (Weak recommendation)
19. Selected bibliotherapy as an adjunct strategy (in addition to antidepressants or psychotherapy) for treating MDD is an option. (Weak recommendation)

Note: Bibliotherapy (e.g., reading therapy, self-help books therapy) is the use of books to help people understand mental health conditions.

20. Behavioral health education classes as an adjunctive treatment option for patients with mild to moderate MDD is recommended. However, these classes should not be used in lieu of either antidepressant medication or psychotherapy. (Strong recommendation)
21. Light therapy as a primary or adjunctive treatment for non-seasonal forms of MDD is not generally recommended. (Weak recommendation)

Long-Term Treatment, Monitoring, and Follow-up

22. The PHQ9 is recommended to monitor outcomes of care over time. (Strong recommendation)
23. For patients who are starting treatment with antidepressants for MDD, a minimum follow-up of one patient contact within the first month, and at least one additional patient contact four to eight weeks after the first contact is recommended. Assessing for adherence, side effects, suicidal ideation, and patient response during both these visits is recommended. (Strong recommendation)
24. After achieving symptom remission, at least one follow-up contact during the fifth or sixth month of treatment in patients with MDD is recommended. Assessing for continuing symptom remission and dosage/treatment adjustment during this contact is recommended. (Strong recommendation)
25. For asymptomatic patients with MDD who are continuing on antidepressants beyond 12 months:
    a. At least one annual follow-up contact to assess for continuing symptom remission, the need for ongoing treatment, and dosage/treatment adjustment is an option. (Weak recommendation)
    b. Additional follow-up should be based on patient preference and response. (Weak recommendation)
26. Continuing antidepressants at the same dose for at least an additional six to 12 months for patients with MDD who achieve symptom remission with antidepressants is recommended. (Strong recommendation)
27. Based on patient and provider preference, a trial of antidepressant discontinuation is an option for patients in their first lifetime episode of MDD, who are being treated with antidepressants, achieve remission, and remain asymptomatic for six to 12 months after acute phase treatment. (Weak recommendation)
28. For patients with two or more lifetime episodes of MDD, who are being treated with antidepressants and remain asymptomatic after acute phase treatment, maintenance on the medication and dose with which they achieved remission for at least an additional 15 months to five years after acute phase treatment is recommended. (Strong recommendation)

29. For patients with chronic MDD (e.g., continual symptoms for more than two years) or double depression (MDD and dysthymia) who improve with antidepressants during acute phase treatment, continuing antidepressants for at least an additional 15 to 28 months after acute phase treatment is recommended. (Strong recommendation)
30. Cognitive behavioral therapy is recommended to decrease the risk of relapse in patients with depression who achieve symptom remission and are considered to be at increased risk of relapse who are unable or choose not to take or continue antidepressants. (Strong recommendation)

Definitions:

Determinants of the Recommendation Strength

Factor	Comment
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted.
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted.
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted.
Costs (resource	The higher the costs of an intervention--that is, the greater the resources

Factor	Comment
allocation)	consumed--the lower the likelihood that a strong recommendation is warranted.

Major depressive disorder (MDD)

Target Population

Adults with mild to moderate major depressive disorder

Interventions and Practices Considered

Screening/Diagnosis

1. Patient Health Questionnaire 9 (PHQ9) or PHQ2 for depression screening
2. Geriatric Depression Scale (GDS or GDS15) for older adults
3. The Edinburgh Postpartum depression tool for pregnant and postpartum women

Treatment/Management/Evaluation

1. First-line antidepressant treatment
    - Selective serotonin reuptake inhibitors (SSRIs)
    - Tricyclic antidepressants (TCAs)
    - Dopamine agonists (DAs)
    - Serotonin norepinephrine reuptake inhibitors (SNRIs)
    - Norepinephrine reuptake inhibitors (NRIs)
    - Combinations of antidepressants
2. Psychotherapy (interpersonal therapy, cognitive behavioral therapy, problem-solving therapy)
3. Combination of antidepressants and psychotherapy
4. Behavioral activation
5. *Hypericum* (St. John's wort) (Note: Considered but not generally recommended)

6. Monitoring patients who are prescribed antidepressants for signs of new or worsening suicidal ideation
7. Consultation with specialists (behavioral health, psychiatrist) for patients expressing suicidal ideation, intent, or plan
8. Antidepressant use in pregnancy and breastfeeding women
    - Avoiding use of paroxetine in pregnancy
    - Avoiding initiation of fluoxetine and/or citalopram in breastfeeding women
9. Second-line treatment for patients whose symptoms fail to remit
    - Combining antidepressants and psychotherapy
    - Increasing dose of initial antidepressant
    - Combined treatment with SSRI and low-dose tricyclic antidepressants, bupropion, mirtazepine, or lithium
    - Switching to a different antidepressant
    - Switching from psychotherapy to antidepressants or vice versa
10. Consulting psychiatry before prescribing atypical antipsychotics for depression
11. Adjunctive therapies
    - Internet patient cognitive-behavioral therapy (CBT) self-help programs
    - Selected bibliotherapy
    - Behavioral health education classes
    - Light therapy (not generally recommended as a primary or adjunctive treatment for non-seasonal forms of depression)
12. Long-term treatment, monitoring, and follow-up
    - PHQ9 to monitor outcomes of care
    - Consideration of appropriate length of treatment with antidepressants
    - Follow-up at specified intervals, including assessment for adherence, side effects, suicidal ideation, and response to treatment
    - Trial of antidepressant discontinuation
    - Cognitive behavioral therapy (CBT)

Note: Augmentation with pindolol and benzodiazepines for depression treatment augmentation or antidepressant side-effect management were considered but not recommended.

Major Outcomes Considered

- Accuracy, sensitivity, and specificity of screening tools
- Change in symptom/symptom score

- Quality of life
- Patient adherence to treatment
- Hospitalizations
- Mortality
- Spontaneous abortion or congenital malformations
- Perinatal complications (mother and child)
- Long-term behavioral sequelae
- Relapse rates
- Adverse effect of treatment

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Search Strategy

A comprehensive literature search was performed in February and March 2011 to identify rigorous external Adult Depression Guidelines. The Guidelines International Network (GIN) and TRIP databases were used to search for full guidelines relating to major depressive disorder in individuals aged 18 years and older. English language full guidelines on adults published from 2008 through the present were included.

Of the 18 guidelines preliminarily identified as meeting the search parameters, seven did not meet the preliminary inclusion criteria. One reason for exclusion included narrow population, specifically focusing only on ante- or post-natal individuals. Other reasons were the limited forms of therapy (i.e., medications only) and interventions (i.e., somatic only) recommended. The Sowerby Centre for Health Informatics at Newcastle (SCHIN) (2010) Guideline, which showed a "Clinical Knowledge Spot" (CKS) topic, was not found. The Clinical Practice

Guidelines: Depression in Adolescents and Young Adults by the National Health and Medical Research Council (NHMRC) were approved on February 11, 2011.

Ten remaining full guidelines were then assessed, first for rigor of development. After evaluating the level of rigor, three assessors determined that five of the ten guidelines were rigorous enough to proceed with the rest of the Appraisal of Guidelines for Research and Evaluation (AGREE) II evaluation. All five guidelines - two published by the National Institute for Health and Clinical Excellence (NICE), one by Veteran Affairs (VA), one by the U.S. Preventive Services Task Force (USPSTF), and the last by the Scottish Intercollegiate Guidelines Network (SIGN) - were deemed acceptable after the three raters assessed the rest of the AGREE II domains: scope and purpose, stakeholder involvement, clarity of presentation, applicability, and editorial independence. The 2010 Kaiser Permanente (KP) Depression guideline was accepted by the Guideline Development Team (GDT) as a foundation for the update, and was not appraised using AGREE II.

Number of Source Documents

This guideline is based on the 2010 Kaiser Permanente (KP) National Depression guideline and five external guidelines.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Refer to Appendix A of the original guideline document for the criteria for grading the evidence.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

After the Guideline Development Team (GDT) and other content experts were solicited for their external guideline suggestions, Care Management Institute (CMI) consultants proceeded with the ADAPTE* process by defining the guideline scope and clinical questions. A systematic literature search was conducted to identify guidelines that satisfied the search parameters. To conduct an initial screening, three independent guideline development leaders evaluated and subsequently reconciled the rigor of development using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument for each identified guideline. Only guidelines that receive a rigor score greater than the scaled final score of 60% ADAPTE - were fully evaluated using the AGREE II instrument. These guidelines were then used to create a recommendation matrix to align the selected clinical questions within the defined scope in the Kaiser Permanente (KP) guideline with those in the identified external guidelines. Once the most rigorous guidelines had been selected, each evaluator examined and independently rated the other five AGREE II domains: scope and purpose, stakeholder involvement, clarity of presentation, applicability, and editorial independence.

The evaluators then reconciled their scores and comments by domain, which allowed for a calculation of domain-specific final scaled scores. All external guidelines that received scores of 60% and above were considered rigorous and used to adopt/adapt recommendations for the updated guideline.

*The ADAPTE process calls for the identification of external guidelines, the determination of congruency with identified clinical questions, analysis of appropriate guidelines for quality, and the rendering of adaptations as needed to fit KP practices and populations.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

To develop this guideline, consultants of the Care Management Institute (CMI) worked with a multidisciplinary Guideline Development Team (GDT). The GDT consisted of a core group of physicians, representing primary care and the specialties most affected by the guideline topic, and, as appropriate, other content experts from disciplines such as pharmacy, nursing, and health education. The members of the GDT were nominated by the respective National Guideline Directors to represent their regions.

To develop the Depression guideline, a multidisciplinary, interregional GDT met in March 2011 to define the scope of the guideline. The Project Management Team then performed systematic reviews of the medical literature for each clinical question identified by the GDT, assembled and presented the evidence, and developed draft recommendations for review by the GDT. The GDT then carefully reviewed the recommendations and supporting evidence in a series of meetings from August 2011 through November 2011. The Guideline Quality (GQ) Committee examined and approved the guideline in June 2012.

The GDT evaluated factors from four GRADE appraisal domains to determine recommendation strength. For more information on this process, see the "Rating Scheme for the Strength of the Recommendations" field.

1. Quality of Evidence: The higher the quality of evidence, the more likely a strong recommendation is warranted.
2. Balance of Benefits versus Harms and Burdens: The larger the difference between the desirable and undesirable consequences of an intervention, the more likely a strong recommendation is warranted. The smaller the net benefit and the lower certainty for that benefit, the more likely a weak recommendation is warranted.
3. Patient Values and Preferences: The greater the variability or uncertainty in patient values and preferences regarding an intervention, the more likely a weak recommendation is warranted.
4. Whether the Net Benefits are Worth the Costs: The higher the costs of an intervention, or the more resources consumed, the higher likelihood a weak recommendation is warranted.

Rating Scheme for the Strength of the Recommendations

Determinants of the Recommendation Strength

Factor	Comment
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted.
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted.
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted.
Costs (resource allocation)	The higher the costs of an intervention--that is, the greater the resources consumed--the lower the likelihood that a strong recommendation is warranted.

The Grading of Recommendations Assessments, Development and Evaluation (GRADE) system offers two grades of recommendations: strong and weak. When the desirable effects of an intervention clearly outweigh the undesirable effects, or clearly do not, guideline panels offer strong recommendations. On the other hand, when the trade-offs are less certain--either because of low quality evidence or because evidence suggests that desirable and undesirable effects closely balance, weak recommendations become mandatory.

To determine the overall strength of the recommendations, the Guideline Development Team (GDT) assigned equal weight to the four GRADE domains. For example, when less uncertainty (in balance of harms to risks, differences in values and preferences, and net benefits and costs) and higher quality evidence were identified in 3 or 4 of the 4 domains, the GDT assigned a strong recommendation. Otherwise, the GDT considered the recommendation as weak.

Cost Analysis

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

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Each regional representative presented the draft guideline recommendations to key experts and champions in their regions for critical review and approval to improve the likelihood of implementation once the guideline was finalized.

The Guideline Quality (GQ) Committee examined and approved the guideline in June 2012. The guideline was approved by the National Guideline Directors in June 2012.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The updated recommendations are based on the 2010 Kaiser-Permanente National Depression guideline and five external guidelines relating to major depressive disorder in individuals aged 18 years and older (see the "Adaptations" field for a list of these guidelines).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Accurate screening for major depressive disorder (MDD)
- Appropriate treatment and management of adult patients with MDD

Potential Harms

- Adverse effects of medication, including suicidal ideation
- Risk of injury with vigorous or competitive exercise/sports
- Potential adverse effects of prenatal antidepressant exposure includes increased risk of fetal malformations (for paroxetine), transient pulmonary complications, and transient neonatal behavioral syndromes

Contraindications

Contraindications

Avoidance of new starts of paroxetine during early pregnancy seems wise due to the increased risk in cardiac malformations compared with other antidepressants especially in light of a U. S. Food and Drug Administration (FDA) black box warning on paroxetine for use in pregnancy. If the mother is already using paroxetine when pregnancy is detected, the risk of teratogenicity due

to exposure may have already occurred; hence increased fetal surveillance for malformations seems clinically indicated.

Qualifying Statements

Qualifying Statements

- This guideline is informational only. It is not intended or designed as a substitute for the reasonable exercise of independent clinical judgment by practitioners, considering each patient's needs on an individual basis.
- Guideline recommendations apply to populations of patients. Clinical judgment is necessary to design treatment plans for individual patients.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Kaiser Permanente Care Management Institute. Diagnosis and treatment of depression in adults: 2012 clinical practice guideline. Oakland (CA): Kaiser Permanente Care Management Institute; 2012 Jun. 73 p. [32 references]

Adaptation

This guideline is adapted from the following sources:

1. The 2010 Kaiser Permanente (KP) National Depression guideline
2. Management of Major Depressive Disorder (MDD) by the Department of Veteran Affairs (VA) 2009
3. Depression in Adults with a Chronic Physical Health Problem: Treatment and Management by National Institute for Health and Clinical Excellence (NICE) 2009
4. Depression: The NICE Guideline on the Treatment and Management of Depression in Adults by National Institute for Health and Clinical Excellence (NICE) 2010

5. Non-pharmaceutical Management of Depression in Adults by the Scottish Intercollegiate Guidelines Network (SIGN) 2010
6. Screening for Depression in Adults: U.S. Preventive Services Task Force (USPSTF) Recommendation Statement (2009)

Date Released

2004 Apr (revised 2012 Jun)

Guideline Developer(s)

Kaiser Permanente Care Management Institute - Managed Care Organization

Source(s) of Funding

Kaiser Permanente Care Management Institute

Guideline Committee

Kaiser Permanente Depression Guideline Project Management Team

Kaiser Permanente Guideline Development Team

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Financial Disclosures/Conflicts of Interest

There were no conflicts of interests for any member of the Guideline Development Team (GDT).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Kaiser Permanente Care Management Institute. Depression clinical practice guidelines. Oakland (CA): Kaiser Permanente Care Management Institute; 2006 Mar. 196 p. [157 references]

To keep current with changing medical practices, all guidelines are reviewed and, if appropriate, revised at least every two years.

Guideline Availability

Electronic copies: None available

Print copies: Available from the Kaiser Permanente Care Management Institute, One Kaiser Plaza, 16th Floor, Oakland, CA 94612

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on December 6, 2004. The information was verified by the guideline developer on January 20, 2005. This summary was updated by ECRI on August 15, 2005, following the U.S. Food and Drug Administration advisory on antidepressant medications. This NGC summary was updated by ECRI on September 28, 2006. The updated information was verified by the guideline developer on October 3, 2006. This summary was updated by ECRI on November 22, 2006, following the FDA advisory on Effexor (venlafaxine HCl). This summary was updated by ECRI Institute on November 9, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs. This summary was updated by ECRI Institute on January 8, 2010 following the U.S. Food and Drug Administration advisory on Norpramin. This summary was updated by ECRI Institute on March 8, 2013. This summary was updated by ECRI Institute on May 24, 2016 following the U.S. Food and Drug Administration advisory on Olanzapine.

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