Clinical Guidelines:

Treatment of Adults with Major Depressive Disorder

Updated September 1, 2023





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1. BACKGROUND

Major Depressive Disorder (MDD) is one of the most common and debilitating illnesses in the United States. According to the National Institute of Mental Health, 21 million adults 18 years or older (8.4% of all U.S. adults) and 4.1 million adolescents ages 12 to 17 (17.0% of U.S. adolescents) had at least one major depressive episode in 2020. Of those, only 66% of U.S. adults and 41.6% of U.S. adolescents received treatment for depression (and this may be an overestimate), indicating a clear need to connect more patients to mental health care. Adults ages 18-25, females, and those who identified as two or more races had the highest reports of major depressive episodes in 2020. In addition to the mental health burden, depression is also a risk factor for physical health concerns such as cardiovascular disease and those with depression have a higher risk of dying from suicide. A 2015 study found that the total economic burden of MDD was \$210.5 billion per year, representing a 21.5% increase from \$173.2 billion in 2005. Nearly half (48-50%) of these impacts were attributed to the workplace, including absenteeism and reduced productivity while at work, whereas 45-47% were related to direct medical costs (e.g., psychological, pharmacy, medical costs) which are shared by employers, employees, and society. About 5% of the costs were related to completed suicide, although the financial impact of suicide is dwarfed by the human cost.

Community Behavioral Health (CBH) has adopted Clinical Practice Guidelines (CPGs) to outline best practices for the treatment of specific disorders or certain populations. These guidelines will be used as one tool for CBH to assess the quality of care provided to CBH members. As such, providers are advised to review and, where appropriate, implement these practices in their care. CPGs apply to all clinical settings where members are seen with these disorders. CPGs should be used in conjunction with any level of care (LOC) specific performance standards, as well as all other required CBH, NIAC, state, and federal regulations and standards.

2. PURPOSE

The aim of this CPG is to articulate best practices and quality monitoring standards for providers who treat MDD for adults. These guidelines will be maintained and updated with ongoing scientific literature reviews and collaboratively with providers and system stakeholders to reflect evolving evidence-based practices or changes in national guidelines. Appendices acknowledge that potential approaches to certain populations (children/adolescents, peripartum, and geriatric) may require more specialized approaches to care. Specific guidelines for post-partum depression, bipolar depression, or other syndromes that carry separate DSM-5 diagnoses are not covered here. CBH recognizes that there are other possible sub-groups where modifications to these guidelines can be clinically justified by evidence.

CBH and DBHIDS encourage a biopsychosocial and recovery-based approach to treatment; in each case these guidelines for treatment should be part of a multidisciplinary treatment approach that also involves collaboration between physical health and behavioral health providers and inclusion of families and other supports whenever appropriate and possible.



3. PRACTICE GUIDELINES

3.1. Screening and Referral

The U.S. Preventive Services Task Force recommends screening for depression in the general adult population, including pregnant and postpartum women. Screening should be implemented with adequate systems in place to directly provide care or make a referral to a qualified provider to ensure accurate diagnosis, effective treatment, and appropriate follow-up.

Standardized and validated instruments may be used to offer efficient and accurate screening. Selfadministered questionnaires are often useful for busy practitioners. However, reading proficiency and primary language should be considered when employing these instruments. These tools should be considered for screening purposes only, not as a method for definitive diagnosis. Providers are advised to use measures that are psychometrically sound. While some measures must be purchased, other free, brief, and validated screening measures of depression are available.

Examples of commonly used screening instruments include, but are not limited to, the Patient Health Questionnaire (PHQ-2 and PHQ-9) and Beck Depression Inventory (BDI). Age-appropriate measures should be used, and use of screening instruments should be differentiated from assessment and treatment monitoring instruments.

3.2. Safety/Risk Assessment

Suicide risk, which is not exclusively associated with a diagnosis of MDD, should be monitored regularly for ongoing care and suicide assessment should always be documented. There are also specific instances that warrant immediate safety assessment:

- Crisis evaluation
- Evaluation during either an initial inpatient or outpatient intake assessment
- Before a change in observation status or treatment setting (e.g., discontinuing one-to-one observation, discharge from inpatient setting, etc.)
- When there is a lack of improvement or worsening symptoms despite treatment
- Acute decompensation, expressing suicidal thoughts, engaging in self-harming behaviors, or not properly caring for oneself
- Anticipation or experience of a significant interpersonal loss or psychosocial stressor

If a person is determined to be of imminent suicide risk, this must be addressed emergently. Appropriate clinical interventions could include (but are not limited to): supervision, team/physician consultation and input, interdisciplinary meeting, safety planning, treatment plan revision, medication adjustment, referral to a higher LOC, or involuntary commitment.



3.3. Harm Reduction

The National Suicide Prevention Lifeline provides 24/7, free and confidential support to people across the U.S. in suicidal crisis or any type of emotional distress. As of July 16, 2022, the three-digit dialing code 988 routes callers to the Lifeline. While the old number (1-800-273-8255) remains operational, the shorter dialing code aims to improve access to the lifeline's network of trained counselors and over 200 crisis centers.

3.4. Assessment

A complete evaluation of depression should address the following:

- History of present illness and current symptoms
- Medical history focused on medical causes of mood disorders
- Past psychiatric history including onset, periodicity, and chronicity of symptoms of depression; prior treatment (e.g., medication trials, interventions, hospitalizations), side effects, and response; presence of symptoms relevant for differential diagnosis, including mania and psychosis
- Current medications, including prescribed and over-the-counter agents and supplements
- History of substance use and treatment for substance use disorders
- Personal, social, and occupational history (e.g., response to life transitions, major life events)
- Family history of major depression and other psychiatric disorders
- Mental status examination
- Diagnostic tests as indicated to rule out general medical causes of depressive symptoms
- Suicide risk assessment

Assessors should evaluate severity of symptoms, immediate safety concerns, and treatment needs. Determination of appropriate level of care intervention should follow the assessment with preference given to the level of care most likely to be effective for improvement and stabilization of symptoms while respecting rights and supporting the individual's preferences. Most individuals with MDD will be effectively treated with outpatient treatment. However, when impaired activities of daily living or safety risks are identified, providers may consider a higher level of care, including partial hospitalization, subacute inpatient psychiatric, or acute inpatient psychiatric level of care. For imminent safety concerns, providers should ensure transfer to a secure treatment location with appropriate monitoring.

3.5. Cultural and Social Determinants of Health

There is widespread evidence to support screening for various aspects of social risk within clinical care. As part of assessment and recovery planning, providers should identify relevant social determinants of health.

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Modifiable factors should be noted, and attempts should be made to support or link members to resources to address those factors as part of a comprehensive recovery plan. Loss of job, housing insecurity, past trauma, divorce, and substance use can increase the risk of becoming depressed. Additionally, LGBTQ youth are more likely to experience depression. The Trevor Project's 2021 National Survey on LGBTQ Youth Mental Health, which includes data from 35,000 LGBTQ U.S. youth ages 13-24, found that within the past year, 62% of LGBTQ youth reported having symptoms of major depressive disorder and 42% reported serious considerations of attempted suicide. Furthermore, only half of LGBTQ youth who sought counseling from mental health professionals received those services. Racial, cultural, social, linguistic, and other factors that may impact the success of the therapeutic alliance for the individual should be considered in treatment. Efforts should be made to reduce barriers to engagement (e.g., transportation difficulties) when feasible.

3.6. Diagnosis

Diagnosis of MDD should be made in accordance with DSM-5-TR criteria. Specifiers of severity and other features of illness (presence of psychosis, mixed features) should inform evidence-based treatment decisions. Alternative diagnoses, like bipolar disorder, where depressed mood presents as a symptom, should be screened for. Comorbid psychiatric conditions, like trauma-related disorders, anxiety disorders, substance use disorders, and personality disorders should be appropriately treated concurrently. Selection of treatment should consider the full diagnostic picture inclusive of comorbidities.

3.7. Laboratory Testing

Relevant labs to characterize thyroid functioning (e.g., TSH) may be necessary to rule out depressive symptoms related to an underlying thyroid condition. Other medical conditions, endocrine disturbances, and nutritional deficiencies may also contribute to depressive symptoms; laboratory evaluation should be considered as clinically indicated.

3.8. Treatment

Major components of MDD treatment include psychotherapy, behavioral approaches, enhancing psychosocial supports, and pharmacotherapy. In addition, in the case of severe illness or treatment resistance, neuromodulation treatments such as Transcranial Magnetic Stimulation (TMS) and electroconvulsive therapy (ECT) may be considered.

Behavioral activation may be considered for virtually all patients with MDD. Behavioral activation protocols (including structured exercise therapy) have been demonstrated to be safe, effective, and tolerable in individuals with MDD. However, some people with severe illness or substantial medical comorbidities may find it difficult to adhere to prescribed exercise; goals should be tailored to the capabilities of the individual. Due to its negligible adverse effects and broad health benefit, behavioral activation should be considered as an element of treatment for most people and is usually recommended in concert with psychotherapy and/or psychopharmacology.

A wealth of research demonstrates the effectiveness of psychotherapy for the treatment of MDD. For many individuals, psychotherapy alone is a viable treatment option. While a diverse array of psychotherapies can be used, and the choice of therapy should be tailored to personal preference and accessibility, therapies with

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a large evidence base (such as cognitive behavioral therapy or interpersonal therapy) are preferred. Evidence-based treatments typically offer clear guidelines or a manual to facilitate clinicians being able to deliver it as intended. However, there is also empirical support for using these practices in a way that is flexible and responsive to the needs of the individual while maintaining fidelity to the treatment. Effective treatment also rests upon a strong therapeutic relationship, regardless of modality. A review of psychotherapy options for MDD can be found in the Clinical Practice Guideline for the Treatment of Depression Across Three Age Cohorts, the American Psychological Association Guideline Development Panel for the Treatment of Depressive Disorders, adopted as Policy in February 2019.

Psychopharmacology remains a central component in the treatment of MDD. There are many effective FDA approved medications for MDD; most are detailed in full in the American Psychiatric Association 2019 Guidelines. For the initial treatment of MDD, selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs) remain the standard first line pharmacotherapy. However, due to the diverse array of effective pharmacotherapy options available, clinicians should select treatment after a thorough informed consent process. At present there are not well-established differences in the efficacy of pharmacotherapies for MDD, so treatment is usually tailored based on the success of past trials, family history of response to treatment, and the desire to avoid or leverage specific types of adverse effects (e.g., increased appetite, weight gain, sedation, etc.).

People who present with MDD may present for care after prior trials of treatment, but they may not achieve remission with their first treatment trial, or they may report adverse effects that limit adherence. As such, it is common to switch between therapies or augment treatment with a second agent or modality of treatment. For pharmacotherapy, after one (or no more than two) full therapeutic trial(s) at adequate dosing for adequate duration of one type of antidepressant (like an SSRI), switching to another antidepressant with distinct mechanism is often recommended. For those who experience a partial response but not remission, optimization of dosage may be appropriate followed by consideration of augmentation with an agent that has a different pharmacological profile such as an antipsychotic medication. Spravato® (esketamine) nasal spray may be considered for adults with treatment-resistant depression or those with major depressive disorder with acute suicidal ideation, in conjunction with an oral antidepressant. While Spravato has displayed promising efficacy in randomized trials, there are serious warnings and considerations, resulting in the strict monitoring of side effects and limited access only through REMS approved providers. Augmentation of pharmacotherapy may also include the addition of psychotherapy and vice versa.

If combined treatment with pharmacotherapy and psychotherapy fails, TMS or ECT may be considered in those with severe and enduring symptoms such as failure to thrive (i.e., not eating). ECT may also be considered earlier in treatment where a rapid response is essential due to particularly grave severity (e.g., catatonia).

There is an abundance of additional research on interventions for MDD including other somatic therapies. Some interventions have been validated and approved for treatment of MDD in the United States and may be used as clinically indicated. Several others are being studied and have shown promise as well, including those with novel mechanisms of action. Additional treatments will be incorporated into practice guidelines as more clinical experience and guidance for populations emerge.



3.9. Monitoring of Treatment

In all phases, careful and objective monitoring of treatment response is essential for guiding adjustments to treatment and maximizing the likelihood of achieving recovery. Monitoring should occur on a regular basis to assess response to psychotherapy, pharmacotherapy, or both. Measurement-based care is helpful to employ for efficient and consistent reassessments of response to treatment. Examples of validated and standardized tools used for monitoring of treatment include, but are not limited to, the Hamilton Depression Scale (HAM-D) and the BDI. Side effects of medications require monitoring. Safety concerns should receive regular attention.

Frequency of monitoring should be determined by:

- Severity of symptom (e.g., suicidal ideation)
- Co-occurring mental and physical health conditions
- Adherence to treatment
- Social support
- Frequency and severity of side effects

If improvements are not seen within four to eight weeks of treatment initiation:

- Reappraise diagnosis
- Assess side effects
- Assess and address co-occurring conditions that may be complicating therapy
- Review psychosocial factors
- Assess adherence
- Adjust treatment plan

3.10. Coordination and Care/Linkages

A 2012 Cochrane review showed that collaborative care results in better medication adherence, improved quality of life, and satisfaction with depression treatment. Providers are required to have a system in place that supports integrated care and collaboration with social supports and other treatment providers including, but not limited to, the physical health provider, psychotherapist, prescriber, and case manager.



3.11. Aftercare Planning/Discharge

The aftercare planning process should begin in the initial stages of treatment. Below are factors that should be considered:

- Members should be involved in aftercare planning, and the plan should reflect the individual's goals and preferences
- Planning should include a crisis plan
- Planning should include a clear and specific plan for follow-up at the next recommended level of
- Whenever feasible, an appointment should be scheduled and there should be a warm handoff
- There should be a clearly stated plan regarding provision of medications until the member is able to engage with the next provider, including prior authorization paperwork if needed

4. MONITORING

CBH encourages its providers to maintain internal quality management programs to ensure treatment adheres to these and other applicable guidelines. CBH will continue to develop systematized strategies to support high quality care within the network, including tracking of valid quality of care metrics for various elements of treatment. In certain instances, CBH may request medical records to be reviewed for quality-of-care concerns. In addition, CBH will be tracking and sharing the following performance metrics with relevant providers:

The HEDIS AMM Measure for Antidepressant Medication Management is used to assess the percentage of members 18 years of age and older who were effectively treated with antidepressant medication during the acute and continuation phases.

CBH monitors performance for both numerators that are part of this measure, as follows:

- Effective acute phase treatment is defined as percentage of members 18 years of age and older who had a diagnosis of MDD and who were treated with and remained on an antidepressant medication for at least 84 days (12 weeks).
- Effective continuation phase treatment is defined as percentage of members 18 years of age and older who had a diagnosis of MDD and who were treated with and remained on an antidepressant medication for at least 180 days (6 months).
- The HEDIS FUH Measure for Follow-up After Hospitalization for Mental Illness will be adapted to capture follow-up after hospitalization due to severe symptoms of MDD including suicidal ideation or attempted suicide. The FUH measure is 2-part and includes:

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- » 7-day follow-up: An outpatient visit, intensive outpatient visit, or partial hospitalization with a mental health practitioner, within seven days of discharge.
- » 30-day follow-up: An outpatient visit, intensive outpatient visit, or partial hospitalization with a mental health practitioner, within thirty days of discharge

In addition, providers should maintain documentation of evaluations and interventions described in these guidelines, whether delivered by the provider or for relevant information from an outside practitioner. CBH and the <u>DBHIDS Network Improvement and Accountability Collaborative (NIAC)</u> will continue to monitor treatment provided to ensure that care is consistent with the <u>DBHIDS Network Inclusion Criteria (NIC) Standards of Excellence</u>.

APPENDIX A: REFERENCES

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- ➤ Kendall, P. C., & Frank, H. E. (2018). Implementing evidence-based treatment protocols: Flexibility within fidelity. Clinical Psychology: Science and Practice, 25(4). doi:10.1111/cpsp.12271
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APPENDIX B: COMMUNITY RESOURCES

- **CBH Provider Directory**
- **EPIC Evidence-Based Practice (EBP) Program Designation**
- **Healthy Minds Philly Mental Health Screening Tools**
- **CBH Depression Screening Program**
- The City of Philadelphia, through DBHIDS, operates a 24-hour telephone hotline to assist people and their families dealing with behavioral health emergencies: 215-685-6440
- Philadelphia Warm line: 1-855-507-9276

APPENDIX C: ADHERENCE RESOURCES

- Medication Adherence Rating Scale Live Link
- → CBH Antidepressant Medication Guide (English) (Spanish)
- CBH Member Medication Wallet Card (English) (Spanish)

APPENDIX D: GUIDELINES FOR PRIMARY CARE **PROVIDERS**

Often, those presenting with symptoms of depression will seek guidance from their primary care physician. Relevant guidelines for those treating depression in primary care are provided below:

Adults

Nonpharmacologic and Pharmacologic Treatments of Adults in the Acute Phase of Major Depressive Disorder: A Living Clinical Guideline From the American College of Physicians

Adolescents

- **→** Guidelines for adolescent depression in primary care (GLAD-PC): Part I. Practice preparation, identification, assessment, and initial management
- Guidelines for adolescent depression in primary care (GLAD-PC): Part II. Treatment and ongoing management



APPENDIX E: PERIPARTUM

Special consideration should be given to depression in the peripartum period. A summary of key points from the APA Practice Guidelines for the treatment of patients with MDD includes the following:

- Major depression in the peripartum period is common and providers should strive to be familiar with the management of depression in the peripartum period.
- The most commonly used screening questionnaire for postpartum depression is the Edinburgh Postnatal Depression Scale (EPDS). Screening does not replace clinical diagnosis.
- Safety assessment should include screening for any suicidal ideation, homicidal ideation (including thoughts to harm the child/children) and psychotic symptoms. Consideration should be given to the welfare of any children in the person's care.
- For individuals who are pregnant or breastfeeding, informed consent discussions about medication are essential and should highlight possible risks to mother and unborn child, as well as benefits and alternatives. Also included in these discussions should be any risks associated with untreated depression. Providers should consider the reproductive status of the individuals that they treat and should aim to have these discussions prior to pregnancy if possible.

The following are recommended resources for more information related to MDD during pregnancy:

- Yonkers, KA et al. The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists. 2009. (Reaffirmed 2014). 114 (3) 703-713.
- MacQueen, GM et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 6. Special Populations: Youth, Women, and the Elderly. Can J Psychiatry. 2016; 61 (9) 592-595.
- **PubMed Drug and Lactation Database (Lactmed)**
- **CDC's Treating for Two**
- Womensmentalhealth.org
- Ncrptraining.org

Patient Facing Resources:

- Mothertobaby.org
- postpartum.net
- NIH Perinatal Depression Patient Education (English)(Spanish)



APPENDIX F: CHILDREN/ADOLESCENTS

Special consideration should be given to depression in children and adolescents. The clinical presentation for a youth with depression may be informed by their developmental stage and functioning. Externalizing symptoms may be more salient than verbal expressions of emotional distress in youth with MDD and symptoms may overlap with mental health comorbidities. Children with MDD may present with irritability, impaired frustration tolerance, somatic complaints, dysregulated behavior and failure to meet developmental milestones. They may also demonstrate impairment in school performance or difficulties with school attendance. Key recommendations from the American Academy of Child and Adolescent Psychiatry's (AACAP) Practice Parameter for the Assessment and Treatment of Children and Adolescents with Major and Persistent Depressive Disorders include the following:

- The psychiatric assessment of children and adolescents should routinely include screening for depressive symptoms.
- A comprehensive assessment should include collaboration with caregivers and important collateral supports including physical health providers, social service professionals, and school personnel
- The clinician should evaluate for exposure to current or past negative events, including trauma
- Evidence-based psychotherapy such as cognitive behavioral therapy and interpersonal therapy are indicated for children and adolescents with major depressive disorder or persistent depressive disorder. Antidepressants are recommended either alone or with combination psychotherapy, particularly those in the selective serotonin reuptake inhibitor class.
- Treatment should include the management of comorbid conditions.

The following are recommended resources for the management of depression in children and/or adolescents:

- Walter HJ, Abright AR, Bukstein OG, Diamond J, Keable H, Ripperger-Suhler J, Rockhill C. Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents With Major and Persistent Depressive Disorders. J Am Acad Child Adolesc Psychiatry. 2023 May;62(5):479-502. doi: 10.1016/j.jaac.2022.10.001. Epub 2022 Oct 21. PMID: 36273673.
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- National Institute for Health and Care Excellence (NICE). NICE Guideline: Depression in children and young people: identification and management. Published: 25 June 2019



APPENDIX G: OLDER ADULTS

Special consideration should be given to depression in the elderly population. A summary of key points from the APA Clinical Practice Guideline for the Treatment of Depression Across Three Age Cohorts, Older Adults Section, includes the following:

- MDD is common in the older adults, with even higher prevalence in nursing home residents.
- Care must be taken to assess for comorbid or contributing medical problems or side effects of medications causing psychiatric/cognitive symptoms, as it is known that physical or somatic issues can manifest with depressive symptoms and vice versa. Cognitive symptoms of depression can lead to challenges with diagnosing formal cognitive disorders concurrently. Collaborative care is recommended, and providers should make any necessary referrals or connections to other required
- Suicide assessment remains a critical factor in this population, as suicide risk is higher in this population.
- Older adults are more likely to have comorbid conditions requiring medication treatment. Psychotherapy may be the preferred method of treatment to avoid medication interactions.
- Recommendations for initial treatment include group life review treatment or Group Cognitive Behavioral Therapy over no treatment or combination of interpersonal therapy and pharmacotherapy over interpersonal therapy alone. Doses may be lower in the elderly depending on the person's physical health and concurrent medications, and attention should be given to potential medication interactions and polypharmacy.

The following are recommended resources for MDD in older adults:

- American Psychological Association. (2019). Clinical Practice Guideline for the Treatment of **Depression Across Three Age Cohorts.**
- MacQueen, GM et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 6. Special Populations: Youth, Women, and the Elderly. Can J Psychiatry. 2016; 61 (9) 596-603.
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