Major Depressive Disorder (MDD) in Children under Age 6

Level 0

Comprehensive assessment. Refer to *Principles of Practice* on page 3.

Level 1

Psychotherapeutic intervention (e.g., dyadic therapy) for 6 to 9 months; assessment of parent/guardian depression and referral for treatment if present.

Level 2

If poor response to psychosocial treatment after 6 to 9 months, re-assess diagnosis, primary care giver response to treatment, and/or consider switching to a different or more intensive psychosocial treatment. Consider child psychiatric consultation or second opinion.

Under 3 years, refer to *Principles of Practice* on page 3.

Level 3

If depression is severe, and there is continued poor response to psychosocial treatment alone, consider combination treatment with fluoxetine and concurrent psychosocial treatment.

- Fluoxetine — 4 to 5 years old
  - Maximum dose: 5 mg/day
  - Discontinuation trial after 6 months of any effective medication treatment with gradual downward taper.
  - **Monitor for behavioral disinhibition and suicidality.** Behavioral disinhibition is defined as impulsive, sensation seeking behaviors and lack of self-regulation.

Not Recommended:

- The use of medication without psychosocial treatment.
- Use of tricyclic antidepressants (TCAs) or paroxetine.

Note: In preschool children, MDD is very rare (point prevalence is thought to be 0.5%).

Major Depressive Disorder (MDD) in Children and Adolescents Ages 6 to 17 Years Old

Level 0

Assessment

- Screening using multi-informant, validated rating scales that include depression and screening for comorbidity (other psychiatric and medical conditions):
  - Patient Health Questionnaire-9 (PHQ-9)
  - Short Mood and Feelings Questionnaire (SMFQ)
  - Pediatric Symptom Checklist (PSC)

  Note: The above scales are available at ***https://floridabhcenter.org/.***
- Perform risk assessment: Specific screen for harm to self or others and access to firearms, knives/sharps, and other lethal means such as alcohol, prescription and non-prescription medications.
- Evaluate sleep hygiene, diet, and exercise.
- Address environmental stressors such as abuse, bullying, conflict, functioning at school, peer relationships, family dysfunction, and caregiver depression.
- **Establish a safety plan:**
  - Removal of firearms, knives/sharps, and other lethal means such as alcohol, prescription and non-prescription medications.
  - **Develop an emergency action plan:**
    - Provide adolescents with mutually agreeable and available emergency numbers and contacts.
    - Engage a concerned third party familiar with the adolescent.
- Positive screen: DSM based interview evaluation.
- Consider medical reason for depression [e.g., hypothyroidism, B12/folate deficiency, anemia, malnutrition (with or without eating disorder), chronic disorder (diabetes, asthma, inflammatory bowel disease, juvenile rheumatoid disease, infectious mononucleosis, etc.)].
- Rule out iatrogenic etiology of depression (i.e., medication side effects/interactions).
- Evaluate past psychiatric and medical history, previous treatment, family conflict and current depression of family and caregivers, bullying, abuse, peer conflict, school issues, and substance use.
- Consider and rule out presence of bipolar depression. Assess for: Prior (hypo) mania, family history of bipolar disorder, atypical depression with reverse neurovegetative signs, seasonal affective component, brief and recurrent episodes, and melancholic depression in a prepubertal child.
- Track outcomes using empirically validated tools. Refer to DSM-5 Severity Measure for Depression, Child Age 11-17 and Child Depression Inventory (CDI) available at ***https://floridabhcenter.org/.***

  Note: The Child Depression Inventory is not available in the public domain.

Level 0 (continued)

Always monitor for:

- Emergence or exacerbation of suicidality and balance the risk-benefit profile of antidepressants during the acute treatment phase.
- Behavioral activation (e.g., difficulty falling asleep, increased motor activity, increased talkativeness)
- Adverse events
- Treatment adherence
- Treatment or inherently emergent comorbidity
- Potential development of (hypo)mania

Level 1

Initial treatment plan

- Active support: 6 week trial (if mild symptoms).
  - Components of active support must include psychosocial interventions and psychoeducation and may include: Self-help materials, active listening/relationship building, school involvement, mood monitoring, pleasant activities, cognitive restructuring, family conflict reduction, sleep hygiene, and exercise.

Level 2

Reassess diagnosis first (e.g., bipolar disorder), rule out psychostimulant or substance use related psychosis. Targeted treatments if symptoms are moderate to severe, impairment continues, and/or no response to active support. Start with Cognitive Behavioral Therapy (CBT), Interpersonal Therapy (IPT), depression-specific behavioral family therapy.

- **2a.** Fluoxetine or combination of CBT or IPT psychotherapy with fluoxetine.
- **2b.** May consider use of escitalopram for age 12 years and above.

Qualifiers:

- **Mild:** Begin with Psychosocial interventions only.
- **Moderate/Severe:** Combination of CBT or IPT psychotherapy with fluoxetine.
- **Psychosis:** SSRIs (fluoxetine, escitalopram) plus consider antipsychotics (adult data only). Careful evaluation of symptoms to determine the degree of psychosis to warrant the use of antipsychotics.
- **Comorbidity:** Combination of CBT or IPT psychotherapy combined with fluoxetine for depression; treat the comorbid disorder.
- **Suicidality:** Intensify surveillance and follow-up; combination therapy with CBT or IPT psychotherapy if on antidepressant only or remove antidepressant if otherwise ineffective; if chronic, consider lithium augmentation.

Level 3

Inadequate response

- If no clinical response to the medication utilized in Level 2, switch to monotherapy with another medication listed above.

Level 4

Poor or non-response

- Refer to mental health specialist.
- Re-assess diagnosis (bipolar disorder, substance use disorder, anxiety disorders, PTSD), rule out medical condition (e.g., hypothyroidism), or medication side effects.
- Increase psychosocial intervention and medication dose if tolerated.
- Augment with alternate psychosocial intervention (either CBT or IPT).
- Consider change in level of care (treatment setting and interventions based on severity of illness).
- For milder form and/or seasonal affective symptoms with light sensitivity, consider bright light therapy.

Level 5

If poor or non-response to Level 4 interventions

- **5a.**
  - Switch previously used SSRIs to sertraline, citalopram, bupropion or venlafaxine, especially in those who do not have access to psychotherapy or have not responded to non-pharmacological interventions.
  - Consider augmentation of SSRI with bupropion, thyroxine, lithium, buspirone, mirtazapine, aripiprazole, quetiapine, or risperidone (adult data only).
- **5b.**
  - If psychotic/severe: ECT (for adolescents).

Notes:

- Factors favoring maintenance treatment (at any Level):
  - Partial response
  - Prior relapse
  - Suicidality
  - Comorbidity risk for relapse
  - Environmental risk for relapse
  - Family history of relapsing/recurrent major depression
  - Lack of return to full premorbid functioning
- **Maintenance treatment:** 9 to 12 months.
- **After maintenance treatment:** If stable, at level of premorbid functioning, and no anticipated increase in stressors, consider discontinuation trial over 3 to 4 months.
- **Transcranial Magnetic Stimulation (rTMS):** Research in children and adolescents is lacking. One randomized controlled trial comparing active TMS with sham TMS did not show statistically significant benefit. Several case reports and open-label studies suggest that rTMS could reduce adolescent depressive symptoms. The current evidence does not support use of rTMS in routine psychiatric clinical practice.

	Level 5 (continued) ***Notes:*** ✦ **Esketamine:** Emerging evidence suggests that esketamine may be beneficial, but randomized controlled trials are needed. Insufficient long-term efficacy and safety evidence is available to support the use of esketamine currently. ✦ **Ketamine:** Few studies utilizing ketamine in youth populations exist. One small, randomized placebo-controlled trial of intravenous ketamine in adolescents suggests significant short-term efficacy. Insufficient long-term efficacy and safety evidence is currently available to support the use of ketamine. ✦ **Cannabadiol (CBD):** Currently, there are no studies to support use of CBD in clinical practice for MDD. ✦ **Pharmacogenomic testing:** The current evidence does not support pharmacogenomic testing in routine psychiatric clinical practice. For a full list of references, visit ***https://floridabhcenter.org/***

Additional Clinical Information

- ✦ May titrate to lowest therapeutic dose once weekly.
- ✦ After reaching the lowest therapeutic dose, can increase dose after three weeks if well tolerated and significant symptoms remain.
- ✦ If switching medications, in the absence of side effects, it is preferable to cross-titrate with an overlap of the two medications rather than titrating off one medication before starting the next medication.

Persistent Depressive Disorder

- ✦ Few studies are available to inform the use of antidepressant medication in children and adolescents with persistent depressive disorder.
- ✦ Consider fluoxetine or escitalopram as first-line medications.

Major Depressive Disorder comorbid with Anxiety Disorder(s)

- ✦ Co-occurring depression and anxiety are common in clinical populations of children and adolescents.
- ✦ Children and adolescents with MDD and comorbid anxiety disorder tend to have greater symptom severity and less robust medication response compared with those who have either alone.
- ✦ Consider fluoxetine as first-line medication.

Medications for the Treatment of Major Depressive Disorder

Clinicians should realize that data below age 6 for treating major depressive disorder is extremely limited. Caution in using pharmacological treatment below age 6 is warranted.

Table 12.

Medications for the Treatment of Major Depressive Disorder				
Drug Name	**Young Child (4-5 Years)**	**Child (6-12 Years)**	**Adolescent**	**Comments**
***Fluoxetine**				
Starting Dose: Maximum Dose:	2.5 mg/day 5 mg/day (limited data)	2.5-5 mg/day 40 mg/day	10-20 mg/day 60 mg/day	May divide daily dose into two doses (e.g., morning and noon) if the dosage is 20 mg/day or more.
***Escitalopram**				
Starting Dose: Maximum Dose:		2.5-5 mg/day 10–20 mg/day	5-10 mg/day 20 mg/day	May titrate by 5mg every three to four weeks as needed.
Sertraline				
Starting Dose: Maximum Dose:		12.5 mg/day 100-150 mg/day	25 mg/day 150-200 mg/day	Titrate gradually by 12.5 to 25 mg/day every four weeks; a more rapid titration by 25 mg to 50 mg/day every one to two weeks has been reported in some studies.
Citalopram				
Starting Dose: Maximum Dose:		5 mg/day 20-40 mg/day	10 mg/day 40 mg/day	Gradual titration by 10 mg/day every four weeks is recommended; however, some studies have reported titration as often as every week. The FDA has issued warnings that citalopram causes dose-dependent QT interval prolongation that can lead to arrhythmias.
Venlafaxine				
Starting Dose: Maximum Dose:		XR: 37.5 mg/day XR: 75-112.5 mg/day (25-39 kg)	XR: 37.5 mg/day XR: 150 mg/day (40-49 kg) 225 mg/day (≥50 kg)	May titrate by 37.5 mg/day weekly Caution due to robust evidence of a significantly increased risk for suicidal behavior or ideation.

Medications for the Treatment of Major Depressive Disorder				
Drug Name	**Young Child (4-5 Years)**	**Child (6-12 Years)**	**Adolescent**	**Comments**
Bupropion				
Starting Dose: Maximum Dose:		IR: 75 mg/day (in divided doses) SR: 100 mg/day XL: 150 mg/day IR: 250-300 mg/day (divided dose) SR: 300-400 mg/day (divided dose) XL: 300 mg/day	IR: 75 mg/day (in divided doses) SR:100 mg/day XL: 150 mg/day IR: 250-300 mg/day (divided doses) SR: 300-400 mg/day (divided dose) XL: 450 mg/day	IR: May titrate every one to two weeks. SR: Age group at least 11 years old. Start 100 mg as a morning dose. Do not exceed 150 mg/dose as a single dose. May titrate every two to three weeks as needed. XL: Age group: At least 12 years of age. Due to dose-related risk of seizures, gradually titrate. When discontinuing treatment, doses of 300 mg/day or more should be tapered to 150 mg/day prior to discontinuation. Dosing conversions between IR, SR, XL products: Convert using same total daily dose (up to the maximum recommended dose for a given dosage form), but adjust frequency: IR (2-3 times/day), SR (twice daily), XL (once daily).

**Indicates FDA approved indication for MDD: fluoxetine 8 years and older; escitalopram 12+ years and older.*

Note: The FDA does not currently provide any dosing guidelines for the treatment of MDD in children under the age of 6 years. The FDA also does not currently provide any dosing guidelines for the treatment of MDD in children 6-11 years old for escitalopram and children and adolescents for sertraline, citalopram, venlafaxine and bupropion.

Major Depressive Disorders (MDD) Resources

Selected Resources

- **Guides for Parents:**
  - If Your Adolescent Has Depression or Bipolar Disorder: An Essential Resource for Parents (Evans, 2005)
  - Adolescent Depression: A Guide for Parents (Mondimore and Kelly, 2015)
  - Depression and Your Child: A Guide for Parents and Caregivers (Serani, 2013)
  - HelpGuide: Parent's Guide to Teen Depression ***https://www.helpguide.org/articles/depression/parents-guide-to-teen-depression.htm***
- **Workbooks for Youth:**
  - Think Good, Feel Good: A Cognitive Behavior Therapy Workbook for Young People (Stallard, 2002)
  - How to Get Unstuck from the Negative Much: A Kid's Guide to Getting Rid of Negative Thinking (Sullivan, 2013)
- **Books for Children:**
  - What to Do When You Grumble Too Much: A Kid's Guide to Overcoming Negativity (Huebner, 2007)
  - The Princess and the Frog: A Story for Children with Depression (Jones, 2015)
- **Relevant Websites:**
  - American Academy of Child and Adolescent Psychiatry (AACAP) Depression Resource Center: ***https://www.aacap.org/aacap/Families_and_Youth/Resource_Centers/Depression_Resource_Center/Depression_Resource_Center.aspx***
  - National Institute of Mental Health—Teen Depression: More Than Just Moodiness: ***https://www.nimh.nih.gov/health/publications/teen-depression***
  - National Alliance of the Mentally Ill (NAMI): National Alliance of the Mentally Ill (NAMI) ***https://www.nami.org/***
  - Depression and Bipolar Support Alliance: Depression and Bipolar Support Alliance: ***https://www.dbsalliance.org/***
  - Teen Mental Health Website: ***http://teenmentalhealth.org/care/parents/***
  - UpToDate–Patient education: Depression in children and adolescents (Beyond the Basics): ***https://www.uptodate.com/contents/depression-in-children-and-adolescents-beyond-the-basics#!***

Note: Above resources and website links were updated at the time of publication.

For a full list of references, visit ***https://floridabhcenter.org/***.