Depressive Disorders

Patterns of excessive depressed or irritable moods, with associated neurovegetative symptoms (sleep, appetite, concentration), guilty feelings, suicidality, guilt, and functional impairment or significant distress

Primary reference source: AACAP. Practice parameter for the assessment and treatment of children and adolescents with depressive disorders *J Amer Acad Child Adolescent Psychiatry.* 2007; 46(11): 1506-1523

History:
- From parent and child
- review all symptoms of depressive disorders, including suicidality
- Review domains of impairment (family, peers, academic, extracurricular)
-Assess for recent or chronic stressors

Suggestive of depressive disorder?

Safety assessment
- Suicidal or homicidal thoughts/plans
- Adolescent substance abuse
- Rule out maltreatment and family violence
- Weapons and access to other lethal medicines

As needed:
ER emergency referral for safety
Substance abuse referral
Advise firearm safety

Differential Diagnosis (details below)
- Transient,developmentally appropriate reaction to stressor
- Adjustment disorder with disturbance of mood (or mood and conduct)
- Anxiety disorders
- Externalizing disorders (ADHD, ODD)
- Bipolar disorder
- Substance abuse disorder

Treat primary disorder

Primary Care Universal Interventions
- Psychoeducation about depressive disorders and safety
- Develop plan to address remediable stressors
- Ensure household safety
- Follow closely and provide child and family support

Mild depression, minimal impairment

Refer for therapy (CBT, supportive therapy, or interpersonal therapy)

Symptoms/impairment resolved?

Yes

No

Return to primary care with regular monitoring of mood

Moderate depression, low/moderate safety risk, age < 12

Refer for specialized depression therapy (CBT, or interpersonal therapy) and monitor closely until referral well established

Symptoms/impairment resolved?

Yes

Severe depressive disorder, high safety risk, adolescent age group

Refer for specialized mental health assessment and treatment

Monitor closely until referral well established

SSRI Trial x 4-6 weeks
Child: fluoxetine,
Adolescent: Fluoextine,sertraline escitalopram

Monitor symptoms with structured measure

Symptoms/impairment resolved?

No

SSRI Trial # 2 x 4-6 weeks (medication not previously used)

Monitor symptoms with structured measure

Symptoms/impairment resolved?

Yes

No

Yes

Depressive disorders

Hallmark symptoms: Patterns of excessive depressed or irritable moods, with associated neurovegetative symptoms (sleep, appetite, concentration), guilty feelings, suicidality, guilt, and functional impairment or significant distress

	Major depressive disorder	**Dysthymia**	**Adjustment disorder with depressed mood**
Description	Significant depressive disorder	Chronic, debilitating, but less intense form of depressive disorder	Mood symptoms in response to identified stressor which occurred within 3 months of onset of symptoms
Duration of symptoms	At least 2 weeks duration	At least 1 year of symptoms more days than not (no break greater than 2 months)	Symptoms do not last more than 6 months after the stressor has terminated
Core required symptoms	At least one of the following 1) Depressed or irritable mood 2) Decreased interest in activities that were pleasurable	Depressed or irritable mood	Marked distress that is in excess of what would be expected from exposure to the stressor
Additional symptoms	At least 4 of the following 1) Change in appetite or weight (or failure to gain weight appropriately) 2) Sleep disturbances 3) Observable change in psychomotor activity (increased or decreased) 4) Decreased energy 5) Decreased concentration or decisiveness 6) Increased feelings of guilt or worthlessness 7) Recurrent thoughts of death/dying	1) Change in appetite or weight 2) Sleep disturbances 3) Decreased energy/fatigue 4) Decreased self esteem 5) Poor concentration/difficulty with decisions 6) hopelessness	
Must cause significant Impairment and/or distress?	Yes	Yes	Yes
Exclusionary criteria	Never had a manic episode Not caused by substance use	Never had a manic or hypomanic episode Not caused by substance use	Does not meet criteria for MDD, dysthymia, and is not exclusively in the context of bereavement

APA. *Diagnostic and Statistical manual of mental disorders IV-TR*. 4 ed. Washington, D.C.: American Psychiatric Association; 2000.

Differential Diagnosis of Depressive Disorders

Diagnosis	How the diagnosis can be differentiated from depressive disorders
Normal development	*Sadness or irritability is not pervasive, responds appropriately to comfort or resolution of stressors, and does not cause functional impairment*
ADHD	*Fidgeting ("psychomotor agitation") is present, and mood symptoms may accompany repeated limit setting or consequences, but child shows full range of affect in situations that do not challenge the ADHD behaviors*
Anxiety Disorders (Including generalized anxiety, separation anxiety, specific phobias, obsessive compulsive disorder)	*Anxiety disorders are often co-morbid with depressive disorders, but isolated anxiety disorders do not cause sadness or irritability, although they can cause distress. Children and adolescents are usually able to describe the triggers for their anxiety.*
Bipolar disorder	*Patient has experienced at least 1 episode of mania or hypomania characterized by euphoria/extreme irritability associated with decreased need for sleep, psychomotor agitation, high risk taking behaviors, goal directed activities, grandiosity.*
Eating Disorders	*Although physical symptoms of starvation may mimic depression (weight loss, decreased energy, concentration), patients with an eating disorder without co-morbid depressive symptoms are less likely to endorse depressed mood or identify distress.*
Frustration associated with **Developmental Delays or learning problems**	*Mood symptoms are more likely to be limited to learning domains but not present when the child is participating in a developmentally appropriate activity*
Hypothyroidism	*Weight gain, bradycardia, GI symptoms, thyromegaly may be present. Patients with hypothyroid-drive mood changes are less likely to be suicidal or to be able to identify recent stressors.*
Substance abuse disorder	*May endorse substance use (or gateway drugs). Mood and behavior changes are more erratic (may be "himself" for a few days, then substantial change for period of time), less persistent. Patient may be spending more money or stealing from family. Physical findings related to substance use may be present.*

Assessment Strategies

Universal screening- Pediatric Symptom Checklist or other broad-band screener. Attend to "2"'s on items related to mood symptoms.

Symptom-Specific Structured measures

- Center for Epidemiologic Studies- Depression Scale
  - Scores ≥15 are positive- higher likelihood of depressive disorder

History

- Include history from child and parent
- Review any major life events or stressors including violence exposure and (in adolescent girls) potential pregnancy
- Review changes in functioning in family, school, with peers, or in extracurricular activities including more arguments at home, declines in grades, withdrawal from social activities or other enjoyable activities
- With child alone, explore suicidal and homicidal thoughts and behaviors including
    - Self-injurious behaviors without intent to kill self (e.g. cutting)
    - Passive suicidal ideation- not wanting to be alive
    - Active suicidal ideation- wanting to kill self
    - Active suicidal ideation with plan- wanting to kill self and having developed a plan
    - How close the child has come to acting on the thoughts
    - What has stopped him or her from acting on such thoughts
    - Ability to "contract for safety" – commit to MD and parent that he/she would follow an identified safety plan to alert a responsible adult if thoughts of harming self became more intense
    - Presence of lethal means in home or environment (guns, insulin, other potentially lethal medications)
- Review family history, especially for first degree relatives with mood disorders (depression or bipolar disorder) and household members with mood disorders

Physical Examination/observations

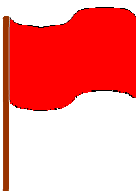
- Physical exam unlikely contributory
- Examine for signs of self injurious behaviors including
    - Cutting- forarms, inner thighs, ankles, underside of breasts, under arms
    - Self-induced vomiting- abrasions on metacarpals
- Signs of substance use (track marks on arms or ankles, nasal septal Thyromegaly

Labs to consider

- Pregnancy test if adolescent girl, especially if considering medication treatment
- TFT's to assess for hypothyroidism

Referrals to consider

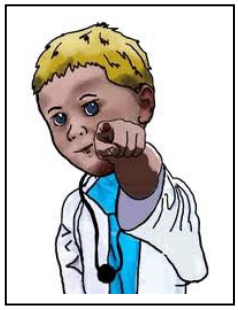
- Cognitive testing or developmental testing (r/o specific learning disability, developmental delay)



Safety issues in Depressive Disorders

- Confirm any firearms or other weapons or lethal means of self-harm in home are secured
- Consider substance abuse and consider urine screen

Primary Care Interventions for DBDs



Prevention

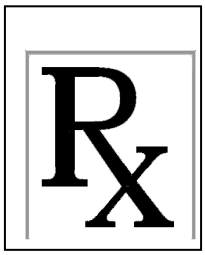
- Mention mood/stress management at every visit
- Monitor high risk children (e.g. those with family histories of depression or bipolar disorder) closely

Prevention and early intervention

- Provide safe "listening" place where child's negative mood is not perceived as a burden or something to be punished
- Schedule frequent follow-ups if concerned
- Provide handouts on mood management and relaxation skills
- Encourage parental self-care if appropriate

Indicators of need for specialty referral

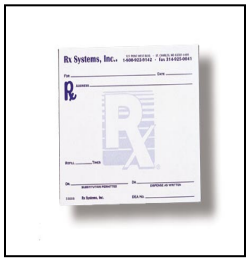
- No improvement with supportive interventions for mild-moderate depression
- Severe depression
- High risk suicidality (active suicidal ideations with plan)
- Multiple co-morbid conditions beyond generalized anxiety disorder or panic disorder



Evidence based treatments for depression

Program name	**Age Range**	**Brief Overview**
Cognitive Behavioral Therapy	4-adult	Focuses on the thoughts, feelings and behaviors in depression. • Learn to identify feeling states accurately and be aware of them • Identify and learn to analyze negative, automatic thoughts that occur in the context of depression (e.g. "I am a complete failure" when making a small mistake) • Develop coping skills and relaxation skills to fight maladaptive reactions (thoughts and behaviors) to stressors Includes homework exercises and in-session practicing of the skills.
Interpersonal Therapy	12-adult	-Focuses interactions with others and perceptions of those interactions as important factors in the development and perpetuation of depressive symptoms. - Includes in-session role plays of difficult or stressful interactions
Supportive psychotherapy (effective for mild depression only)	all	-Focuses on providing support, coping strategies and providing some reflections to allow the patient to understand interpersonal patterns -less formally structured
Family therapy	all	Focuses on enhancing family interactions that may reduce depression and on identifying problematic interactions that may have triggered/perpetuated depressive symptoms

Adapted from AACAP (2009) ODD: A guide for families from the American Academy of Child and Adolescent Psychiatry. Washington DC. www.aacap.org



Psychopharmacology in depressive disorders

Principles of psychopharmacology in treating Depressive Disorders

- Follow guidelines in parentsmedguide.org physician information
- May be first line treatment for moderate-severe depression, especially in adolescents
- Should be second line treatment for younger children and those with milder depression
- Informed consent includes black box warning re: suicidality as well as risks of mania in children with bipolar disorder that has not yet presented
- Start low go slow
    - Children and adolescents may have higher rates of adverse events than adults
    - Careful monitoring warranted in children with family history of bipolar disorder
    - Generally, start children on ¼ of the adult starting dose and adolescents on ½ of adult starting dose (see table below)
    - Slow titration (increasing dose every 4-6 weeks) is appropriate due to slow onset of action
- Monitor closely with initiation and each dose increase
    - Risk of increased suicidality highest in first 2 months after dose changes
- If no substantial adverse effects, maximize dose before discontinuing an SSRI and starting a new trial
- Avoid multiple serotonerigic medications (especially multiple anti-depressants and or anti-migraine medications) concurrently because of risk of serotonin syndrome (hyperthermia, tachycardia, hypertension, and mental status changes)

First line treatment choice

- Children < 12: fluoxetine has best efficacy:risk ratio. Consider it first line unless very high risk of bipolar disorder or other reason that long half life would be problematic.
- Adolescents: fluoxetine, sertraline, escitalopram have strongest evidence and should be considered first line treatments. Half life, potential for "activation", and family history of response to specific SSRI's should guide recommendation.
- Advise parents that there is approximately a 60% chance of response to first line medication.

Second line treatment

- If treatment is ineffective after 4-6 weeks on a dose expected to be therapeutic (at least one increase after initial starting dose) or if patient develops intolerable adverse effects, select one of the medications among fluoxetine, sertraline, escitalopram for second trial. Of treatment resistant adolescents, would expect 60% to respond to second SSRI.
- Non-SSRI medications, such as the SNRI's (venlafaxine, duloxetine) should be selected only in consultation with a psychiatrist. Venlafaxine has more side effects than an SSRI and does not improve the outcome in treatment resistant depression.
- Serotonin agonists (mirtazapine) are not supported by randomized controlled trials and would not be considered appropriate second line treatment without consultation.

- Buproprion also has not been demonstrated to be effective in randomized clinical trials and generally should not be used as second line treatment except in consultation.
- Tricyclic antidepressants have no efficacy in treating pediatric depression and should not be used.

Length of treatment

- Because of the high risk of relapse in first 6-9 months after a depressive episode, it is recommended that patients continue effective SSRI for at least that period before planned weaning off the medication with close monitoring of symptoms. Weaning may be most safely done during school vacations or other low stress periods.

Monitoring of children and adolescents on SSRI's

- AAP and AACAP have recommended weekly monitoring of suicidality and activation in the first month of treatment and then every two weeks for the second month. Such check-ins may sometimes be performed by phone with patients and families who are assessed to be able to provide reliable information over the phone.
- Emergency planning should be reviewed including phone numbers and appropriate resources for families in area.
- Monitor depressive symptoms with structured measure at least monthly in person.

Medication vs. Therapy: the evidence

- In large study of adolescents with depression (TADS)
    - Adolescents on fluoxetine alone or in combination with CBT showed more rapid response than children receiving CBT alone after 12 weeks of treatment
    - After 9 months of treatment, all 3 groups showed equal response rates (about 80% response)
    - Take home message: children in whom a rapid response to treatment is important (e.g. more severe depression. distress), a combination of therapy and medication or medication alone is recommended
- In children < 12, the data supporting medication is weaker (ONLY found for fluoxetine) and the rates of adverse effects are higher, therefore therapy is preferable
- Children under 6: clinical experience suggests therapy is the appropriate treatment. Because of the complexities of assessing mood disorders in preschoolers, specialty assessment is recommended.

Co-morbid conditions

- Anxiety: follow depression recommendations
- ADHD: treat most impairing disorder first (if equal, start with ADHD because of more rapid response). Then reassess residual symptoms and make decision about appropriate treatment.
- Other disruptive behavior disorders- strongly encourage therapy
- Substance use- refer for specialty treatment. If depression predated the substance abuse, it is appropriate to treat depressive disorder while also addressing substance abuse disorder.
- Eating disorders- SSRIs are unlikely to be effective until not in physiologic starvation state

Summary of Medications used in treatment of depression

Medication (brand name)	Medication class	Usual starting dose (all for children > 6)	Usual titration plan	Maximum pediatric dose	Supported by RCTs?	FDA Approved for depression	Unique characteristics	Common Adverse effects	Potentially dangerous adverse effects
Fluoxetine (Prozac)	SSRI	Child: 5-10 mg Adolescent: 10-20 mg	Increase by 10 mg after 2 weeks and then again after 4 weeks	60 mg (approved in OCD)	Yes	8-18 yo	Long $t_{1/2}$ (4-6 days for fluoxetine, 9 days for active metabolite) May be more activating in first few days	GI distress Head aches Tremor Sleep disturbance Sexual dysfunction Anorexia	Suicidality Mania Serotonin syndrome Abnormal platelet function SIADH Acute angle glaucoma PPHN
Escitalopram (Lexapro)	SSRI	10 mg	Increase after 4 weeks to 20 mg	20 mg	Yes	12-18 yo	Weak CYP450 inhibitor- fewer interactions with other medications than most SSRIs		
Sertraline (Zoloft)	SSRI	Child: 12.5 mg Adol: 12.5-25 mg	May increase by doubling after 2-4 weeks	200 mg (OCD)	Yes	No	May be less activating initially		

Resources for parents:

See parentsmedguide.com.

Brief information about mood disorders for parents: AAP's healthy children.org

Summary of CBT for families: AAP's healthy children

Hamil S (2004) My feeling better workbook: Activities that help kids beat the blues. Available on Amazon.com

Chansky T (2008) Freeing Your Child from Negative Thinking: Powerful, Practical Strategies to Build a Lifetime of Resilience, Flexibility, and Happiness. Da Capo Lifelong Books. Available on Amazon.com

Prescriber reference for black box: parentsmedguide.com.

References for Depressive disorders

AACAP, *Practice Parameter for the Assessment and Treatment of Children and Adolescents With Depressive Disorder.* Journal of the American Academy of Child & Adolescent Psychiatry, 2007. 46(11): p. 1503-1526.

Gunlicks, M. and M.M. Weissman, *Change in Child Psychopathology With Improvement in Parental Depression: A Systematic Review.* Journal of American Academy of Child and Adolescent Psychiatry, 2008. 47(4): p. 379-389.

TADS Study Team, *Fluoxetine, Cognitive-Behavioral Therapy, and Their Combination for Adolescents With Depression: Treatment for Adolescents With Depression Study (TADS) Randomized Controlled Trial.* JAMA: Journal of the American Medical Association, 2004. 292(7): p. 807.

Treatment for Adolescents With Depression Study Team., *The Treatment for Adolescents With Depression Study (TADS): Outcomes Over 1 Year of Naturalistic Follow-Up.* Am J Psychiatry, 2009. 166(10): p. 1141-1149.

Vitiello, B., et al., *Long-term outcome of adolescent depression initially resistant to SSRI treatment.* Journal of clinical Psychiatry, 2010. online ahead of print.