

## Pediatric Depression in Primary Care: Assessment and Management

### I. BACKGROUND

**Epidemiology.** Depression is surprisingly common in the pediatric population, and the risk of depression increases with age into adolescence and young adulthood. Major depressive disorder (MDD) affects approximately 3% of prepubertal children and 4 to 8% of adolescents at any one time. Prepubertal girls and boys are affected equally, but female adolescents are almost twice as likely to be depressed as adolescent boys. By age 18 years, approximately 20% of youth will have experienced a MDD, very close to its lifetime prevalence. Dysthymic disorder, a chronic form of depression lasting at least one year, is found in approximately 1% of prepubertal children and between 2 and 8% of adolescents. Persistently depressed or irritable mood does not reflect “normal adolescence”.

**Relevance.** There is growing consensus that primary care providers can and should work to identify children and adolescents under their care who are suffering from depression. This reflects the public health relevance of this disorder. Depressed children and adolescents are functionally impaired relative to their peers (i.e., interpersonally, socially, and academically, with poorer school attendance and performance on average), and are at greater risk for:

- *Suicide* – the 3rd leading cause of death in adolescents and young adults; depression is the most important remediable risk factor for youth suicide.
- *Alcohol, drug, and tobacco use* – these problems may be both cause and consequence of depressed mood and vice versa.
- *Persistence* – median duration of a MDD is approximately 8 months in clinical settings, and 10% of episodes will last longer than one year. Dysthymic Disorder typically persists for an average of 3 to 4 years in children and adolescents.
- *Recurrence* – even after a depressive episode resolves completely, approximately 70% of affected youth will experience another MDD within 5 years. Youth with dysthymic disorder are also at greater risk for MDD, with 70% developing a MDD within 5 years.
- *Other “comorbid” psychiatric disorders* – up to two thirds will suffer from at least one other psychiatric disorder at the same time, typically an anxiety disorder or disruptive behavioral disorder. Some depressed patients develop psychotic symptoms such as hallucinations or delusions.
- *Future psychiatric disorders* – a significant minority will go on to meet criteria for bipolar disorder or manic-depressive illness later in life; predictors include family history of bipolar disorder, psychosis, and manic or hypomanic “switch” during antidepressant treatment.

### II. IDENTIFICATION

The Guidelines for Adolescent Depression in Primary Care (GLAD-PC) are clinical practice guidelines developed to aid primary care clinicians in the identification, assessment, and management of pediatric depressive disorders. The premise underlying GLAD-PC is that primary care clinicians can and should identify depressed youth and coordinate their care. (The GLAD-PC website and its associated toolkit for primary care clinicians can be accessed at <http://www.glad-pc.org>.)

1. GLAD-PC recommends that primary care clinicians identify patients at risk for depression and systematically monitor them over time for the development of a depressive disorder. This is essentially a case finding approach.

Risk factors for depressive disorders include:

- Patient history of depression, bipolar disorder, and/or suicidal behavior
- Family history of depression, bipolar disorder, and/or suicidal behavior
- Patient history of other psychiatric disorders (e.g., anxiety, substance abuse)
- Patient exposure to negative life events, loss, trauma, and/or maltreatment
- Shy temperament or negative attributional style (e.g., neuroticism)
- Patient general medical conditions (e.g., epilepsy, cerebral palsy, diabetes)
- Patient medications (e.g., anticonvulsants, oral contraceptives)
- Family or peer relationship problems

Common presentations of pediatric depressive disorders in primary care include:

- Declining school performance and/or attendance
- Increasing temper outbursts and arguing
- “Medically unexplained” or “functional” somatic symptoms
- Frequent ambulatory visits and minor illnesses
- Alcohol and/or substance abuse
- Withdrawal from friends and/or family
- Nonsuicidal self-injury (e.g., “cutting”)
- Suicidal statements, threats, or behavior

To screen or not to screen?

- In its most recent determination, the U.S. Preventive Services Task Force (2009) only recommends screening for depression in adolescents in primary care when systems to ensure accurate diagnosis, treatment, and follow-up are in place and well established. This is currently not the case in most primary care practices serving children and adolescents, making universal screening difficult to recommend to Ohio primary care providers at this time.

### III. ASSESSMENT AND DIAGNOSIS

Quality assessment establishes the foundation necessary for subsequent management. Patients and families should be treated as partners in the assessment process, and multiple sources of information should be used when possible (e.g., patient, family/caregivers, teachers, school nurses, other health care providers). We recommend the following in keeping with the [GLAD-PC Assessment/Diagnosis Guidelines \(PDF\)](#):

1. Primary care clinicians should evaluate high risk youth for depression, as well as those presenting with emotional problems as a chief complaint. Standardized tools are suggested as aids to assessment. Potentially useful and no-cost tools include:
  - [Patient Health Questionnaire 9 \(PHQ-9\) \(PDF\)](#) for Adolescents and [PHQ-9 Modified for Teens \(PDF\)](#) – The PHQ-9 is useful not only as an assessment tool, but also as a tool to gauge response to treatment. We recommend it as the standard depression tool for Ohio primary care clinicians. To learn more, read [Evaluation of the PHQ-2 as a Brief Screen for Detecting Major Depression Among Adolescents \(PDF\)](#).
  - [Center Epidemiologic Studies Depression Scale \(CES-D\) \(PDF\)](#)
  - [Columbia DISC Depression Scale \(PDF\)](#)
  - [Kutcher Adolescent Depression Scale \(KADS\) \(PDF\)](#)
  - [Mood and Feeling Questionnaire Child \(MFQ\) \(PDF\)](#)
  - [Mood and Feeling Questionnaire Parent \(MFQP\) \(PDF\)](#)
2. Assessment should include direct interviews with the patient and family. Family involvement is critical. Ideally, the patient should be interviewed separately at some point in the assessment process. Specific areas requiring assessment include:
  - Patient functioning across domains (e.g., home, school, with peers)
  - Other psychiatric symptoms and disorders – particularly anxiety, mania/hypomania, psychosis, bipolar disorder, and substance abuse
  - Suicidal thinking, plans, and behavior – safety assessment is a critical aspect of any assessment in a patient with suspected depression (see [Suicide Risk: Assessment and Management](#)).
  - Psychosocial adversity, including any current or past history of maltreatment or other psychological trauma
  - Physical health – special consideration should be given to diseases and medications associated with depression
  - Family psychiatric history – most notably family history of depression, bipolar disorder, and completed suicide

Depressive Symptoms. Symptoms relevant to the diagnosis of a depressive disorder are listed below, and should reflect a change from a previous level of functioning. The diagnosis of a depressive disorder can only be made if the symptoms are associated with significant distress or impairment. A depressive disorder cannot be diagnosed unless at least one of the following 2 symptoms is present:

- (1) *Depressed mood* – Persistent dysphoria - sad and/or irritable mood – that is present most of day and nearly every day. Depressed mood may be judged to be present based on subjective child report or by parent or examiner observation (e.g., often tearful). Children may need to be asked about depressed mood a variety of ways, with questions not just about sadness, but also about feeling “bad”, “down”, “blue”, “hopeless”, “overwhelmed”, etc. When in doubt, it can be useful to ask the child to rate their mood on a scale of 1 to 10, with 1 representing

“really bad” or “the worst you ever felt” and 10 representing “really good” or “the best you ever felt”.

- (2) *Loss of interest or pleasure (anhedonia)* – referring to diminished interest or pleasure in all or nearly all activities, most of the day and nearly every day. Like depressed mood, the presence of anhedonia may be judged based on subjective child report or by parent or examiner observation.

Other symptoms relevant to the diagnosis of depressive disorders are:

- (3) *Change in appetite or weight* – decreased or increased appetite nearly every day and/or a significant gain or loss of weight (a 5% change in body weight in a month or failure to make expected weight gain in children).
- (4) *Sleep disturbance* – insomnia or hypersomnia nearly every day. In children and adolescents, a rule of thumb is that difficulty falling asleep of at least 1 hour is significant. Similarly, sleep continuity disturbance is likely significant when a child awakens during the night and typically takes 30 minutes or longer to return to sleep. Persistent early morning awakening, as well as marked difficulty “getting up and going”, may also reflect significant sleep disturbance.
- (5) *Psychomotor slowing or agitation* – perceived slowed thinking, speech, and/or movement nearly every day, or evidence of agitation, marked restlessness.
- (6) *Fatigue or perceived loss of energy* – nearly every day.
- (7) *Feelings of worthlessness or inappropriate/excessive guilt* – nearly every day. The child may evidence very low self-esteem and low perceived competence.
- (8) *Poor concentration/indecision* – diminished ability to think or concentrate, or indecisiveness, nearly every day.
- (9) *Recurrent thoughts of death and/or suicide* – a range of symptoms may be considered significant, from preoccupation with death through passive death wish, nonspecific suicidal thinking, suicidal ideation with plan, and suicidal behavior.

Clinicians may find the [Brief MDD Screening Form of the American Academy of Pediatrics \(AAP\) \(PDF\)](#) a useful tool in guiding recall of clinically relevant symptoms of depression.

### **Specific Psychiatric Disorders Characterized by Depression:**

- Major Depressive Disorder (MDD) is the paradigmatic depressive disorder. In order for a child or adolescent to meet criteria for MDD, at least 5 of the 9 possible depressive symptoms must be present over a 2 week period, with at least one symptom being a core depressive symptom (i.e., depressed mood or anhedonia).
- Dysthymic Disorder is characterized by depressed or irritable mood in a child or adolescent that is present for most of the day, more days than not, for at least 1 year (2 years in adults). At least 2 of the following symptoms must also be present:
  - (1) Change in appetite or weight
  - (2) Sleep disturbance
  - (3) Fatigue or low energy
  - (4) Low self-esteem
  - (5) Poor concentration/indecision
  - (6) Feelings of hopelessness
- Bipolar Depression may be diagnosed when the patient has a past or current history of mania or hypomania and meets criteria for MDD. Bipolar depression is particularly important to recognize since management is somewhat different from “unipolar” depression. The ongoing treatment of youth suffering from bipolar depression is likely best initiated in the specialty care setting by a child and adolescent psychiatrist. The core symptom necessary to define a manic or hypomanic episode is:
  - (1) Persistent elevated, expansive, or irritable mood lasting at least one week (in the case of mania) or 4 days (in the case of hypomania).At least 3 of the following symptoms must also be present (4 if the core mood symptom is irritability alone):
  - (2) Inflated self-esteem or grandiosity – uncritical self-confidence.
  - (3) Decreased need for sleep – this symptom may be the single best specific symptom in determining the presence of mania or hypomania. A history of the patient not needing to sleep for over 48 hours, particularly in the absence of substance use or an isolated event such as a sleep over, or of feeling rested after only 2 or 3 hours of sleep per night for several days supports the diagnosis. A useful question may be: “What is the longest you have stayed awake without any sleep and still felt pretty good?”
  - (4) Talkativeness or pressured speech – the patient may speak loud, rapid, and be difficult to interrupt, perhaps joking, punning, or rhyming

- (5) Flight of ideas or the subjective experience that thoughts are racing
- (6) Distractibility – with attention drawn to unimportant or irrelevant stimuli
- (7) Increased goal directed activity or psychomotor agitation – which may include excessive planning of social or work related activities, increased sociability or interpersonal intrusiveness, and increased sexual drive and behaviors
- (8) Reckless behaviors – excessive involvement with high risk pleasurable activities (e.g., unrestrained buying sprees, reckless driving, gambling, sexual indiscretions)
- Mood Disorder due to a General Medical Condition is diagnosed when a depressive disorder is present and the symptoms are judged to be a primary consequence of a general medical condition. The possibility that depression may be the consequence of a general medical condition, a medication, or an illicit substance should always be considered.

### **“Subthreshold” Depression**

Some patients with clinically significant depression and associated impairment may not meet criteria for MDD or Dysthymic Disorder. Such patients with are typically diagnosed with:

- Depressive Disorder, Not Otherwise Specified – when the patient suffers from at least one core depressive symptom (i.e., depressed mood or anhedonia) and experiences significant distress or impairment, but does not meet criteria for MDD, Dysthymic Disorder, or an Adjustment Disorder with Depressed Mood.
- Adjustment Disorder with Depressed Mood – when the depressed mood is present for less than 6 months, a psychosocial stressor occurred within 3 months of onset, and criteria for MDD or Dysthymic Disorder are not met. Interestingly, Adjustment Disorder with Depressed Mood does not appear to confer an increased risk of subsequent MDD, unlike both MDD, Dysthymic Disorder, and Bipolar Depression.

### **Making the Diagnosis**

Prior to offering a diagnosis of depressive disorder, it is often wise for the clinician to meet with patient and parents/ caregivers together in order to review the symptoms that have been reported and confirm their presence. This ensures clarity of communication and helps avoid unhelpful “back tracking” by patients and families related to concerns about stigma when a depressive disorder does appear to be present. The diagnosis should be discussed clearly and frankly, without embarrassment. This is often the ideal time to offer education about the disorder and its management, frame the treatment process as a partnership, and instill hope and positive expectations.

## **IV. INITIAL MANAGEMENT**

There is good news – evidence based, effective treatments are available for children and adolescents suffering from depressive disorders. Unfortunately, there is also bad news – most depressed youth do not receive any treatment, and most who do fail to receive treatment in keeping with best practices. Many patients who initiated treatment fail to adhere fully to the recommended treatment regimen.

The GLAD-PC suggests the following with regard to initial management:

1. Educate the patient and family about depression and known management options – the goal is to create informed consumers of care, determine patient and family treatment preferences, and delineate patient, family, and provider roles and responsibilities in the management process.

#### What Do Patients and Families Need to Know?

- Depression is both common and serious – reviewing the epidemiologic data about pediatric depression and its impact can help put the patient’s disorder into context provide the rationale necessary for treatment.
- Depression is an illness – it is best understood as the consequence of an interaction between individual vulnerability and exposure, not unlike asthma. Consequently, the presence of depression does not imply patient weakness, willfulness, or spite. The patient and family are not “at fault”.
- Depression is most often a recurrent condition – in contrast to uncomplicated grief or mourning, between 60 and 80% of children and adolescents with MDD or Dysthymic Disorder will experience another episode of MDD within the next 5 years. Again, the analogy to asthma is apt. Treatment is not only of values in making the symptoms go away, but also in preventing relapse and recurrence.
- Symptoms and common presentations of depressive disorders – a better understanding the patient’s depressive symptoms and other potential symptoms increases the capability of patient and family to monitor treatment response and detect relapse or recurrence.

- Effective treatments are available – Patients and families should understand that specific psychotherapeutic treatments such as cognitive-behavioral therapy (CBT) delivered with good fidelity by experienced therapists, as well as certain antidepressant medications (i.e., the selective serotonin reuptake inhibitors or SSRIs) have been shown to be effective treatments for pediatric depression, and that there is reason to believe that the combination of evidence based psychotherapy and antidepressant medications is likely superior to either treatment alone.
  - Risks and benefits of the specific treatment approaches – special attention should be given to discussing what is known about the short and long term safety risks associated with the use of active treatments such as antidepressant medications. If antidepressant medication is being considered, the small, but likely real risk of suicidality with their use must be discussed. Please refer to [AAP Brief MDD Screening Form \(PDF\)](#) for more information on this.
  - Fundamentals of mood hygiene and self-care – The importance of keeping a regular schedule, moderate exercise, working to stay productive and active, and a healthy diet should be emphasized. Patients and families should understand that by working to return to their previous level of function, they are likely to help themselves and reduce depressive symptoms. Waiting for symptoms to resolve prior to returning to functioning is likely to prove counterproductive, suggesting that approaching depression with a rehabilitative mindset is typically wise. The “cure me and then I’ll get better” is less than ideal at best, and to be discouraged. All depressed patients should be encouraged to maintain a regular schedule, obtain moderate exercise, eat a healthy diet, and refrain from the use of alcohol, illicit drugs, tobacco, and excessive caffeine.
  - The importance of identifying and treating parental depressive disorders to child well-being – there is now solid evidence that the successful treatment of parental depression can have a positive impact on the mood of their depressed children. Depressed parents and family members should be encouraged to seek and participate in treatment with competent help.
  - That hope and positive expectations for depressed youth are warranted – it is useful for the patient and family to know that significant improvement is a safe bet with time and attention. It is quite unusual for a persistent patient with a committed family and a resourceful clinician to fail to improve. If the first treatment tried does not seem to work, the likelihood that a positive response will be obtained using a different approach is still excellent.
2. Develop a treatment plan with the patient and family and set specific treatment goals in key areas of patient functioning. Developing a treatment plan in partnership with the patient and family requires informed consumers of care, and allows for patient and family preferences to be expressed. Agreeing on specific treatment goals may improve patient and family adherence.
  3. Establish linkages and collaboration with community based mental health resources as appropriate – A key decision is the degree to which care will be provided directly in primary care or in the community by specialty mental health providers. Encouraging patient and family involvement with other consumer based organizations such as NAMI and Mental Health America is often a helpful strategy.
  4. Establish a safety plan – this is especially important and a necessary part of any treatment planning effort for a depressed patient (See Suicide Risk: Assessment and Management). Key elements of an adequate safety plan include:
    - Ensure adequate adult supervision and support – the stability and security of the home environment must be assessed, and the family must be capable of providing necessary support and containment for the patient as dictated by the determined degree of risk.
    - Restrict patient access to lethal means – encourage family to remove any firearms from the home (or at a minimum secure access if removal is refused) and to secure household medications and take charge of medication administration with at risk patients.
    - Warn patients and family of the disinhibiting effects of drugs and alcohol – encourage abstinence from alcohol and drug use and explain the rationale in relation to how substance use can potentiate suicide risk.
    - Develop an emergency communication mechanism - should the patient deteriorate, become a danger to self or others, or experience a psychosocial crisis, both patient and family need to understand how to proceed. The patient and family should be provided emergency contacts and telephone numbers (including crisis “hot lines”) and understand how to access local crisis services.

## V. TREATMENT

Following the [GLAD-PC Treatment \(PDF\)](#) framework, the following guidelines for the treatment of pediatric depression are suggested:

1. For MILD depression (i.e., minimal impairment or normal functioning that requires unusual effort and no evidence of suicidality) consider active support and monitoring (weekly to biweekly visits for up to 6 weeks) before initiating evidence based treatment.

2. For MODERATE, SEVERE, or depression COMORBID with psychosis, substance abuse, or evidence of mania/hypomania, consultation with a mental health specialist should be considered.

Individual roles and responsibilities of the primary care clinician and specialist should be defined, and the patient and family should be involved in decision making. When there will be a significant wait for specialty consultation or referral, serious consideration should be given to providing active support and treatment for the patient in primary care, ideally after telephone consultation with a child and adolescent psychiatrist.

3. Scientifically tested and proven treatments for pediatric depression should be recommended whenever possible. These include:
  - Cognitive Behavioral Therapy (CBT) – this treatment focuses on the “distortions” in thinking experienced by depressed youth, and aims to interrupt the commonly observed cycle of negative thinking, depressed mood, and maladaptive behaviors. Core features include:
    - Cognitive restructuring – the patient is trained to become aware of negative thinking and how to counteract it.
    - Behavioral activation– the patient is encouraged to return to usual routines, activities, and functioning, including activities they previously found rewarding. This intervention is particularly relevant in primary care, where clinicians can and should encourage patients to adopt a rehabilitative mindset and return to doing things they used to enjoy and find satisfying, even if they no longer do.
    - Other elements – include training in relaxation, problem solving, and assertiveness in social settings.
  - Interpersonal Therapy (IPT) – here the focus is on the interpersonal context of depression, with the target being the reduction of interpersonal stress. Goals include the reduction of interpersonal conflict and the enhancement of fulfilling relationships. Topics commonly addressed in IPT include loss, roles disputes and transitions, and interpersonal skills deficits.

### Applying Psychotherapeutic Principles in Primary Care

*“If we take people as they are, we make them worse. If we treat them as if they were what they ought to be, we help them become what they are capable of becoming.” Goethe*

Accessing high quality, evidence based psychotherapy for pediatric depression may be every bit as difficult, if not more difficult, than obtaining access to competent pharmacologic management, particularly in rural areas. Although the delivery of formal psychotherapy is beyond the skill set of most primary care clinicians, thoughtful support and guidance provided by an informed clinician in primary care cannot be of substantial benefit. Taking a rehabilitative approach and framing the patient’s depression as a challenge to be overcome can be useful. Some key elements of effective psychotherapies for pediatric depression that may be readily applied in primary care include:

- Behavioral activation to increase activity – most patients accept the notion that they are less active because they are depressed, but fail to realize that increasing activity and returning to activities they previously enjoyed can actually improve mood as well. Though counter intuitive, it is nevertheless true and well demonstrated. Be an encourager – support regular school attendance and continued involvement in sports and social activities where appropriate.
- Promotion of patient competence and perceived self-efficacy – acknowledge patient strengths and build upon them. Communicate that the patient “has the stuff” to overcome the burden of depressive symptoms and return to previous function. Model positive expectations for parents and family members.
- Enhancement of interpersonal relationships and communication skills – encourage positive peer activities and other healthy social interactions.

- Selective serotonin re-uptake inhibitor (SSRI) Antidepressants are considered the first line of pharmacological treatment for pediatric depressive disorders. SSRIs have a superior safety, tolerability and effectiveness profile and a stronger knowledge base than is currently available for newer antidepressants. Fluoxetine (Prozac) is the only antidepressant approved by Food and Drug Administration (FDA) for the treatment of depression in children and adolescents, and is the only drug proven efficacious in treating prepubertal depression. Older antidepressants such as the tricyclic antidepressants (TCAs) have not demonstrated efficacy in children and adolescents. An outstanding resource for patients and families considering antidepressant treatment for pediatric depression is provided at [www.parentsmedguide.org](http://www.parentsmedguide.org). You can also refer to the [Parents Med Guide Depression \(PDF\)](#).

### SSRIs Currently Available in the U.S.

- Citalopram (Celexa)
- Escitalopram (Lexapro) – FDA approved for adolescent MDD
- Fluoxetine (Prozac) – FDA approved child and adolescent MDD and OCD
- Fluvoxamine (Luvox) – FDA approved for pediatric OCD
- Paroxetine (Paxil)
- Sertraline (Zoloft) – FDA approved for pediatric OCD

- Combination Evidence Based Psychotherapy and Antidepressant Treatment – a growing body of evidence suggests that the combination of an SSRI antidepressant and CBT is superior to either treatment alone. This is important information for patients and families to understand when they are making treatment decisions.

Refer to the [GLAD-PC Clinical Management Flow Chart \(PDF\)](#)

### Tips for Prescribing SSRIs in Primary Care

“Start low and go slow...”

Begin with suggested starting dose for the first 3 to 7 days.

If tolerated, increase to initial target dose.

Re-evaluate response and increase dose incrementally if partial response.

If no response at target dose or higher at 4 to 6 weeks, consider medication change.

<u>Starting Daily Dose (mg/day)</u>	<u>Target Daily Dose</u>	<u>Max Daily Dose</u>
Citalopram 10 mg	20 to 40 mg	60 mg
Escitalopram 5 mg	10 to 20 mg	30 mg
Fluoxetine 10 mg	20 mg	60 mg
Fluvoxamine 50 mg	100 to 150 mg	300 mg
Paroxetine 10 mg	20 mg	60 mg
Sertraline 25 mg	50 to 100 mg	200 mg

4. Monitor closely for the emergence of adverse events during antidepressant treatment. In general, SSRIs have a relatively high therapeutic index, with low short term toxicity. Adverse effects are generally mild and dose dependent, and can usually be managed by beginning with a low dose and advancing it slowly. Original FDA monitoring guidelines suggesting weekly face-to-face monitoring for the first 4 weeks of treatment, then at 6 and 8 weeks, followed by monthly monitoring thereafter were not empirically based and probably unrealistic in real world settings. Careful monitoring for SSRI adverse effects is nevertheless important, with more frequent monitoring being wise early in treatment. A useful approach may involve weekly telephone calls or “check ins” to ensure patient safety and to monitor response. Please visit the FDA Medication Guide Website at [www.fda.gov/Drugs/DrugSafety/ucm085729.htm](http://www.fda.gov/Drugs/DrugSafety/ucm085729.htm) for specific medication guides.

### Potentially Serious Concerns Associated with SSRI Use:

- *A small, but real risk of new onset suicidal thinking or behavior.* The “black box” warning issued by the FDA in 2004 followed a meta-analysis of short term placebo controlled trials found a small, but statistically significant increased risk of new suicidal thinking or behavior in children and adolescents treated with SSRIs and other second generation antidepressants (4%) compared to placebo (2%). A subsequent meta-analysis that included over 5,000 subjects found an even smaller, but still significant between group risk difference of 0.7%. Contrasting individual risk and population risk, a number of large scale observational studies suggest that antidepressant treatment is associated with a reduced risk of youth suicide. Length of treatment may also matter, with depressed youth treated with an antidepressant for at least 6 months being less likely to attempt suicide than those treated for 2 months or less. It is troubling to note that the first observed increase in the youth suicide rate in over a decade followed the FDA warning and an observed reduction in the prescription of antidepressants to younger patients. Only additional research can determine if an early increased risk of suicidality for selected individuals exposed to antidepressants will prove to be balanced by a protective effect on the population level and with longer treatment.
- *A small, but real risk of precipitating mania/hypomania* – pay special attention to this risk when there is a personal or family history of bipolar disorder. Patients and families should be advised about what to look for that might signal a manic or hypomanic “switch”, as well as to contact the prescriber immediately.

- *Risk of long term adverse effects are unknown* – though there are no well documented serious long term adverse effects associated with pediatric SSRI use, this area is not well studied. It is of little comfort to note that we know as much about the long term effects of SSRIs as we do about other commonly used pediatric medications. Although it is tempting to speculate that pediatric antidepressant treatment may have long term benefits, this has not been demonstrated or well studied.
- *Bleeding predisposition (e.g. easy bruising)* – use SSRIs cautiously in youth with bleeding disorders, low platelet counts, or those taking medications associated with bleeding (e.g., non-steroidal anti-inflammatory drugs or NSAIDs).
- *Serotonin syndrome* – symptoms include restlessness, autonomic instability (HR, BP changes), nausea/vomiting, diarrhea, fever, incoordination, hyperreflexia, and/or hallucinations. Serotonin syndrome has been reported to occur with SSRI treatment alone, but this is quite unusual. This malady is more likely to occur when SSRIs are combined with other serotonergic medications or illicit drugs (e.g., antidepressants-MAOIs, dextromethorphan, linezolid, ondansetron, pain medications such as meperidine and tramadol, triptans, St. John’s wort, ginseng, Ecstasy, LSD).

**Less Serious Adverse Effects of SSRIs:**

- Anxiety, nervousness, panic – typically after medication initiation. Can often be managed by beginning with a low dose and advancing slowly. Despite this potential early side effect, many patients accommodate. SSRIs have demonstrated effectiveness in the treatment of pediatric anxiety disorders.
- Apathy, amotivation
- Change in appetite (↑ or ↓) – typically mild.
- Dizziness or lightheadedness
- Gastrointestinal symptoms (e.g., nausea, diarrhea)
- Headache
- Irritability, agitation, and “behavioral activation”
- Restlessness, akathisia
- Sexual dysfunction
- Sleep disturbance (e.g., ↑ or ↓ sleep, vivid dreams)
- Other (e.g., sweating, tremor)

**VI. ONGOING MANAGEMENT**

Following the GLAD-PC framework, the following guidelines for the ongoing management of pediatric depression are suggested

1. Systematic tracking of treatment goals and outcomes, including assessment of depressive symptoms and key domains of function. Here, the goal is to ↓ depressive symptoms and functional status. The PHQ-9 and other depression tools may be helpful in documenting clinical progress.

## When and How to Stop an SSRI

Patients who have not responded to an adequate dose of an SSRI after 6 to 8 weeks of treatment are unlikely to benefit from longer treatment. Some responders to SSRI treatment will inevitably relapse, and the risk of relapse increases when the SSRI is stopped before at least 6 months of adequate dose treatment. Continuing treatment beyond the acute treatment phase reduces the relapse rate, but the ideal duration of SSRI treatment remains unknown.

The decision to stop or continue medication should be accomplished in partnership with the patient and family, and an effort should be made to create informed consumers of care by reviewing what we know and don't know. Current practice is to continue SSRI treatment for at least one year after a positive treatment response has been achieved, and most clinicians will be reluctant to discontinue the SSRI after less than 6 months of treatment. Some patients and families will nevertheless be reluctant to stop the SSRI, either due to an unwillingness to risk "ever feeling that bad again", a history of recurrent episodes, or a bad experience when a taper was attempted previously. Given that we still know so little about ideal practice, it appears reasonable to respect patient and family preferences to continue SSRI treatment as long as they understand the potential risks and benefits, particularly if the treated disorder has been recurrent, chronic, or particularly severe.

When a decision is made to discontinue medication, most clinicians will initiate a slow taper followed by discontinuation of the SSRI if clinical improvement is maintained. A reasonable approach is to cut the maintenance dose in half, monitor for approximately one month on the reduced dose, then continue the process by halving the dose monthly until it appears reasonable to stop the SSRI. This is typically the case when the daily dose has been reduced to: 5 mg per day for escitalopram (Lexapro); 10 mg per day for citalopram, fluoxetine, and paroxetine; and, 25 mg per day for fluvoxamine and sertraline. Each patient is different, so the taper should be tailored to individual circumstances and needs. Clinicians can feel comfortable reversing the "start low, go slow" approach to initiating SSRIs.

It is critical to monitor for clinical deterioration, which may not manifest as soon as the dose is reduced, so it is important to give enough time to evaluate for recurrence. In addition, some patients may experience an SSRI discontinuation syndrome characterized by dizziness, moodiness, nausea, vomiting, myalgia, and fatigue when SSRIs are rapidly discontinued. Patients being treated with SSRIs that have a relatively short half life (e.g., paroxetine, fluvoxamine) appear to be most vulnerable.

2. Diagnosis and initial treatment should be reassessed if no improvement is noted after 6 to 8 weeks of treatment. In cases where a patient has been treated with only one mode of treatment (e.g., antidepressant medication or evidence based psychotherapy), consideration should be given to begin the absent treatment. Should a patient taking an SSRI antidepressant fail to fully respond to treatment, consultation with a child and adolescent psychiatrists may be helpful. The clinician may consider the following:
  - (1) Encourage evidence based psychotherapy (e.g., CBT)
  - (2) Switch to a different SSRI
  - (3) Switch to a different antidepressant class – options include venlafaxine, desvenlafaxine, duloxetine, bupropion, and mirtazapine
  - (4) Consider SSRI augmentation strategies – options include bupropion, busiprone, lithium, mirtazapine, and atypical antipsychotics (e.g., aripiprazole).
3. Consider specialty mental health consultation for partial responders. The goal is to treat to remission. Subsyndromal depressive symptoms increase the risk of relapse and recurrence of MDD.
4. Depressed youth referred for specialty mental health services should continue to be followed in the medical home.

### Useful References:

1. Birmaher B, Brent DA and AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with depressive disorders. *J Am Acad Child Adolesc Psychiatry* 2007; 46:1503-1526
2. Bridge J et al. Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. *JAMA*. 2007 Apr 18;297(15):1683-96.
3. Zuckerbrot RA et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): Part I. Identification, assessment, and initial management. *Pediatrics* 2007; 120(5):e1299-312.
4. Cheung A et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): Part II. Treatment and ongoing management. *Pediatrics* 2007; 120(5):e1313-26.