DEPRESSION IN CHILDREN AND ADOLESCENTS

2015 Edition

Joseph M Rey, Tolulope T Bella-Awusah & Jing Liu

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Major depression is an episodic, recurring disorder characterized by persistent and pervasive sadness or unhappiness, loss of enjoyment of everyday activities, irritability, and associated symptoms such as negative thinking, lack of energy, difficulty concentrating, and appetite and sleep disturbances. Manifestations can vary according to age, gender, educational and cultural background. The various subtypes of depression are identified on the basis of symptom severity, pervasiveness, functional impairment, or the presence or absence of manic episodes or psychotic phenomena. There is still much argument about whether depression is a dimensional illness—the difference between having and not having depression is quantitative, a matter of degree, such as in the case of hypertension—or categorical (i.e., difference is qualitative), and whether there are several etiologically different types of depression (e.g., melancholic and non-melancholic).

The terms “depression,” “depressive episode,” “depressive disorder” and “clinical depression” will be used throughout the chapter to mean what DSM-5 defines as “major depressive episode” or “major depressive disorder,” and ICD-10 “depressive episode” and “recurrent depressive disorder.” Unless otherwise specified, all the information in this chapter refers to unipolar depression.

**Epidemiology**

Prevalence varies depending on the population (e.g., country), the period considered (e.g., last three months, last year, lifetime), informant (e.g., parent, child, both), and criteria used for diagnosis. Most studies concur that about 1% to 2% of pre-pubertal children and about 5% of adolescents suffer from clinically significant depression at any one time. The cumulative prevalence (accumulation of new cases in previously unaffected individuals, also known as lifetime prevalence) is higher. For example, by the age of 16 years 12% of girls and 7% of boys would have had a depressive disorder at some time in their lives (Costello et al. 2003). Prevalence of dysthymic disorder is less well known but studies suggest a point prevalence ranging from 1% to 2% in children and 2% to 8% in adolescents. A further 5% to 10% of young persons have been estimated to exhibit sub-syndromal depression (or minor depression). Youth with minor depression show some functional impairment, increased risk of suicide and of developing major depression.

**Gender and culture**

The ratio of depression in males and females is similar in pre-pubertal children but becomes about twice as common among females compared with males during adolescence. Although information is limited, the data available suggest that rates of depression are higher among patients who suffer from chronic medical conditions and in particular groups, such as developmentally disabled or indigenous minority children (e.g., Native Americans, Eskimos, Australian Aborigines).

**Burden of illness**

Depression poses a substantial burden to the individual suffering from this disorder and to the society at large. Interpersonal relationships are particularly likely to suffer when someone is depressed—few families and friends are likely to be untouched by depression. Further, depression is likely to progress into a chronic, recurring disease if not treated. The burden of depression is increased because it appears to be associated with behaviours linked to other chronic diseases.
such as smoking, alcohol consumption, physical inactivity and sleep disturbance among others, although the nature of the association is still unclear (CDC, 2013).

Some researchers have suggested there has been a secular increase in the prevalence of depression with higher rates among those born later in the 20th century. This is not definite for the quality of the studies supporting this finding is suboptimal and more often than not retrospective. It is possible that the perceived increase may be due to greater awareness of children’s symptoms by their parents or an earlier age of onset.

Is youth depression increasing?
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AGE OF ONSET AND COURSE

Depressed patients can display symptoms of depression at any age; however, the pattern varies slightly according to developmental stage, resulting in differences in the way depression manifests itself through the lifespan, as highlighted in Table E.1.1.

Age at onset does not seem to define separate depressive subgroups, but earlier onset is associated with multiple indicators of greater illness burden in adulthood across a wide range of domains such as never being married, more impaired social and occupational functioning, poorer quality of life, greater medical and psychiatric comorbidity, more lifetime depressive episodes and suicide attempts, and greater symptom severity (Berndt et al, 2000).

Although to diagnose clinical depression it is required that symptoms be present every day, most of the day for at least two weeks, adolescents, particularly those who suffer from mild or moderate depression, often have a reactive affect and can, with effort, hide their symptoms.

<table>
<thead>
<tr>
<th>Pre-pubertal children</th>
<th>Adolescents</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Irritability (temper tantrums, non-compliance)</td>
<td>• Irritability (grumpy, hostile, easily frustrated, angry outbursts)</td>
<td>• Anhedonia</td>
</tr>
<tr>
<td>• Affect is reactive*</td>
<td>• Affect is reactive*</td>
<td>• Lack of affective reactivity</td>
</tr>
<tr>
<td>• Frequently comorbid with anxiety, behavior problems, and ADHD</td>
<td>• Hypersomnia</td>
<td>• Psychomotor agitation or retardation</td>
</tr>
<tr>
<td>• Somatic complaints</td>
<td>• Increased appetite and weight gain</td>
<td>• Diurnal variation of mood (worse in the morning)</td>
</tr>
<tr>
<td></td>
<td>• Somatic complaints</td>
<td>• Early morning waking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Extreme sensitivity to rejection (e.g., falsely perceived putdown or criticism) resulting, for example, in difficulties maintaining relationships.</td>
</tr>
</tbody>
</table>

*Ability to be momentarily cheered up in response to positive events (e.g., visit by peers).
Similar to what happens in adults, clinical depression in youth follows a recurring course. An episode of depression in clinically referred patients lasts 7 to 9 months on average, but it can be shorter in non-referred community samples. That is, depressive episodes are, on average, a spontaneously remitting illness. Conversely, there is a 40% probability of recurrence within 2 years. Recurrence is high even after treatment. For example, participants in the 5-year follow up of the Treatment of Adolescent Depression Study (TADS) showed that although the immense majority (96%) of patients recovered from the index episode, after five years almost half (46%) had a recurrence (Curry et al, 2010).

The likelihood of further episodes in adulthood is up to 60% (Birmaher et al, 1996). Thus, depressive illness should optimally be conceptualized as a chronic condition with remissions and recurrences. This has important implications for management, which should seek not only to reduce the duration of the current depressive episode and lessen its consequences but also to prevent recurrences. Predictors of recurrence include poorer response to treatment, greater severity, chronicity, previous episodes, comorbidity, hopelessness, negative cognitive style, family problems, low socioeconomic status, and exposure to abuse or family conflict (Curry et al, 2010).

**SUBTYPES OF DEPRESSION**

Subtyping depressive illness is relevant because different types of depression may have implications for treatment and prognosis. For example, seasonal mood disorder may specifically respond to light therapy, and treatment of bipolar depression is different from that of unipolar depression. With the exception of the unipolar/bipolar distinction, many other subtypes (e.g., primary and secondary, endogenous and reactive, neurotic and psychotic) have been proposed over the years, usually without convincing empirical data or evidence of clinical value. There are currently differences of opinion about the usefulness of the melancholic vs. non-melancholic dichotomy. Some of these concepts are still popular in some countries or settings. The most widely used subtypes of depression, irrespective of their scientific validity, are summarized in Table E.1.2.

**ETIOLOGY AND RISK FACTORS**

The etiology of depression is complex, multifactorial, and the object of much academic argument. As a result, it is not discussed here in detail. Interested readers may wish to consult the summary by Krishnan and Nestler (2010). Research has uncovered a multitude of factors associated with the onset, maintenance or recurrence of depression. This can be confusing or lead to false expectations (e.g., that dealing with the risk factor may in itself be enough to resolve the depression). Risk factors that have implications for prevention, detection or treatment are listed in Table E.1.3.

In summary, depression in youth appears to be the result of complex interactions between biological vulnerabilities and environmental influences. Biological vulnerabilities may result from children's genetic endowment and from prenatal factors. Environmental influences include children's family relationships, cognitive style—most depressed adolescents experience negative thoughts about themselves, the world or the future that seem to arise spontaneously (automatic thoughts), which contribute to a negative cognitive style—stressful life events,

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**Affect reactivity in depressed adolescents**

“This morning I will get out of bed. This morning I will go to school. Today I will finish my maths test. I will hand in my English project and during the lunch break I will socialize with my friends. I will laugh, joke and talk with my friends. I will tell witty stories about my weekend and before I know it the school day will be over and no one will know how I am feeling on the inside. Then when I get home I can go back to bed and not have to pretend for anyone anymore.”

The words above are from a journal entry I wrote on April 20, 2000. At the time I was 14 years old.”


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**Course**

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### Table E.1.2. Subtypes of depression relevant to clinical practice.

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unipolar depression</td>
<td>Depression without history of a manic, mixed or hypomanic episode.</td>
</tr>
<tr>
<td>Bipolar depression</td>
<td>When there is history of at least one non drug-induced manic, hypomanic or mixed episode.</td>
</tr>
<tr>
<td>Psychotic depression</td>
<td>The young person displays hallucinations or delusions in addition to symptoms of major depression in the absence of other psychotic disorder.</td>
</tr>
<tr>
<td>Melancholic depression, major depression with melancholic features, or melancholia</td>
<td>Episodes are characterized by prominent neurovegetative changes such as weight loss, psychomotor retardation, marked sleep disturbance, diurnal mood variation, early morning waking and lack of reactivity. Melancholic depression is largely equivalent to &quot;endogenous&quot; depression.</td>
</tr>
<tr>
<td>Dysthymic disorder or dysthymia</td>
<td>A chronically depressed mood for at least one year but not severe enough to qualify for a diagnosis of depression; symptom-free intervals last less than two months.</td>
</tr>
<tr>
<td>Double depression</td>
<td>The depressive episode occurs in a patient already suffering from dysthymia.</td>
</tr>
<tr>
<td>Catatonic depression</td>
<td>When the mood disorder presents with symptoms of stupor.</td>
</tr>
<tr>
<td>Post-psychotic depression</td>
<td>When it occurs in the course of schizophrenia, often after resolution of the florid psychotic symptoms.</td>
</tr>
<tr>
<td>Premenstrual dysphoric disorder</td>
<td>Premenstrual mood changes—dysphoria, tension, irritability, hostility, and labile mood—that mimic depression. Its nature and validity are still being argued.</td>
</tr>
<tr>
<td>Seasonal depression, major depression with seasonal pattern, seasonal affective disorder</td>
<td>The beginning and remission of major depression follow a pattern (for at least two years) related to specific times of the year, usually onset during autumn or winter and remission in spring.</td>
</tr>
<tr>
<td>Mood disorder not otherwise specified (NOS)</td>
<td>Significant mood symptoms and impairment that do not meet criteria for a specific mood disorder often due to mixed presentations (e.g., depressive and manic symptoms).</td>
</tr>
<tr>
<td>Adjustment disorder with depressed mood</td>
<td>Clinically significant depressive symptoms or impairment occur within three months of identifiable stressors and do not meet criteria for major depression or bereavement. It is expected that symptoms will disappear within six months once stressors have ceased.</td>
</tr>
<tr>
<td>Minor depression, subsyndromal depression, subclinical depression</td>
<td>Depressive symptoms fall short of meeting the criteria for depression (e.g., one core symptom, and one to three associated symptoms, and very mild disability).</td>
</tr>
</tbody>
</table>

and school and neighborhood characteristics. Parental depression is the most consistently replicated risk factor for depression in the offspring. Stressful life events—especially losses—may increase the risk for depression; this risk is higher if children process loss events (or other stressful life events) using negative attributions. Parental lack of care and rejection may also be relevant.

## COMORBIDITY

Comorbidity, the simultaneous occurrence of two or more distinct illnesses in the one individual, is a common and complex issue across all child and adolescent mental disorders that has great theoretical and practical implications—for example for treatment—and is still not well understood.

Data from community surveys suggest that depression comorbid with other disorders is frequent in children and adolescents. This is particularly the case in clinic settings because the likelihood of referral is a function of the combined
Psychiatric disorders often comorbid with depression include anxiety disorders, conduct problems, attention deficit hyperactivity disorder (ADHD), obsessive compulsive disorder, and learning difficulties. An epidemiological study (Costello et al, 2003) showed that in a three-month period, 28% of the young people diagnosed with a depressive disorder also had an anxiety disorder, 7% ADHD, 3% conduct disorder, 3% oppositional defiant disorder, and 1% substance use disorder. The practical implication is that establishing whether a child shows symptoms of one condition (e.g., depressive illness) is only a first step in the evaluation; clinicians ought to enquire for symptoms of other conditions as well.

The link between depression and anxiety is well-known because depressive and anxiety symptoms often coexist and individuals frequently experience depressive and anxiety episodes at different times in their lives. Suffering from a depressive episode not only increases the risk of further depressive episodes (homotypic continuity) but also of anxiety disorders (heterotypic continuity).

Depression is frequently comorbid with post-traumatic stress disorder (see chapter F.5). In particular, adolescents are vulnerable to depression and suicidality in the year following a traumatic event. Mechanisms include so-called survivor guilt (that others died or were severely injured), complicated bereavement, problems in carrying out tasks of daily living owing to impaired concentration or intrusive memories, and distress arising from chronic anxiety symptoms. Other psychiatric complications of traumatic stress that may interact with depression include panic disorder, other anxiety disorders, disruptive behaviors, dissociative disorder, and substance misuse.

**Depression and personality style**

Personality traits become progressively established during adolescence and early adulthood and personality styles can influence the presentation and likelihood of referral for each disorder separately—the so called Berkson effect. Patients with comorbid disorders show greater impairment than those with a single diagnosis. Comorbidity is also associated with worse adult outcomes. For example, childhood depression comorbid with conduct disorder or substance abuse is associated with a higher likelihood of severe or violent offending by age 24 than when depression, conduct disorder or substance misuse occur alone (Copeland et al, 2007).

Gene-enviroment interaction: the serotonin transporter gene, childhood maltreatment and depression.

New Zealand's Dunedin Health and Development Study followed a cohort of 1,037 children from 3 to 26 years of age carefully tracking the development of psychiatric disorders, serious life events and other factors such as childhood mistreatment. A report based on these data concluded that a functional polymorphism of the serotonin transporter gene (5-HTT) moderated the influence of stressful life events on the development of depression. That is, individuals with the short allele of this gene were more likely to develop depression in response to severe stressors or maltreatment during childhood, compared to those with the long allele exposed to the same experiences (Caspi et al, 2003).

This finding caused much excitement because it seemed to finally prove a plausible gene-environment interaction in the causation of depression. However, a subsequent meta-analysis concluded that alterations in the serotonin transporter gene alone or in combination with stressful life events were not associated with an elevated risk of depression (Risch et al, 2009). Another meta-analysis published not long after (Karg et al, 2011) reached the opposite conclusion, while an additional prospective study—also from New Zealand—failed to confirm such an association (Fergusson et al, 2011). Clearly more research is needed to resolve this tantalizing issue, which highlights the importance of replication before findings are accepted, let alone used in clinical practice (e.g., to detect vulnerability for depression).

**“Masked” depression**

Until the second half of the 20th century childhood depression was largely believed not to exist. In the 1950s new theories emerged postulating that depression in this age group did exist but did not express itself as such but through “depressive equivalents”. These included conduct problems, hyperactivity, somatic complaints, enuresis, and school problems. That is, children could be depressed but expressed their depression differently from adults—“masked depression”.

The concept of masked depression was heavily criticized and subsequently largely abandoned. By the 1970’s researchers began to show that childhood depression did exist and by and large has similar symptoms as in adults. While depressed children may initially present with a variety of symptoms that conceal the depression (e.g., tantrums, headaches, tiredness, problems concentrating) a competent clinician should be able to uncover the depression (Carlson & Cantwell, 1980).
### TABLE E.1.3. Risk factors and their implications for prevention, detection or treatment

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Implications for prevention, detection or treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biological</strong></td>
<td></td>
</tr>
<tr>
<td>Family history of depression</td>
<td>Increase suspicion of depression when there is a positive family history of depression or suicide.</td>
</tr>
<tr>
<td>Parental substance use or alcohol misuse</td>
<td>Detect and treat parental substance use.</td>
</tr>
<tr>
<td>Family history of bipolar disorder</td>
<td>Increase suspicion that depression might be bipolar. Implications for pharmacological management.</td>
</tr>
<tr>
<td>Female gender</td>
<td>Female adolescents who attend family doctors should be screened for depression.</td>
</tr>
<tr>
<td>Puberty</td>
<td>Depression is much more common in post-pubertal adolescents, particularly females. Early menarche (&lt;11.5 years) increases the risk. Screen adolescents for depression.</td>
</tr>
<tr>
<td>Chronic medical illness</td>
<td>Exclude depression in patient with chronic physical illness or disability.</td>
</tr>
<tr>
<td>Previous history of depression</td>
<td>Relapse-prevention strategies integral part of treatment.</td>
</tr>
<tr>
<td><strong>Psychological</strong></td>
<td></td>
</tr>
<tr>
<td>Comorbid psychiatric disorder, particularly anxiety</td>
<td>Detection and treatment of comorbid psychiatric disorders.</td>
</tr>
<tr>
<td>Neurotic or highly emotional temperamental style</td>
<td>Detection of individuals at risk and targeted preventive interventions.</td>
</tr>
<tr>
<td>Negative cognitive styles, low self-esteem</td>
<td>Detection of individuals at risk and targeted preventive interventions.</td>
</tr>
<tr>
<td>Trauma</td>
<td>Detection of individuals at risk and targeted preventive interventions.</td>
</tr>
<tr>
<td>Bereavement and losses</td>
<td>Detection of individuals at risk and targeted preventive interventions.</td>
</tr>
<tr>
<td><strong>Family</strong></td>
<td></td>
</tr>
<tr>
<td>Abuse, neglect</td>
<td>Targeted preventive interventions such as parenting and abuse prevention programs.</td>
</tr>
<tr>
<td>Negative parenting styles: rejection, lack of care</td>
<td>Targeted preventive interventions such as parenting programs.</td>
</tr>
<tr>
<td>Parental mental disorder</td>
<td>Detection and treatment of mental disorder in parents. Targeted preventive interventions such as parenting programs and support.</td>
</tr>
<tr>
<td>Parent-child conflict</td>
<td>Parent education and parenting programs.</td>
</tr>
<tr>
<td><strong>Social</strong></td>
<td></td>
</tr>
<tr>
<td>Bullying</td>
<td>Bullying prevention programs at school.</td>
</tr>
<tr>
<td>Child and adolescent offenders</td>
<td>Detection of individuals at risk and targeted preventive interventions.</td>
</tr>
<tr>
<td>Institutionalised or fostered children, refugees, homeless, asylum seekers</td>
<td>Detection of individuals at risk and targeted preventive interventions.</td>
</tr>
</tbody>
</table>
AY, a 14-year old Nigerian female, currently in her fourth year in secondary school, was brought to the hospital about four hours after ingesting a small quantity of a concentrated antiseptic solution with the intention of killing herself. She complained of having felt sad most of the time over the past 6 months and thinking about death a lot. Her decision to drink the poison had come after learning that she would have to repeat a year at school. Prior to this, her grades had been progressively worsening. She felt guilty because her poor school performance was causing a drain in her father’s finances. AY described longstanding difficulties with falling and staying asleep. She still enjoyed watching TV and playing with her friends, but had begun to find it increasingly difficult to carry out her household chores because she felt weak and tired. Her family interpreted this as laziness and she often got scolded or beaten for leaving her chores unfinished. She also felt isolated from her classmates because of her poor school performance.

AY’s mother had suffered episodes of mental illness in the past and was separated from AY’s father, who had since re-married. AY and her four siblings were living with a paternal aunt because the extended family were afraid that they would contract mental illness from their mother. Although the mother now lived and worked successfully in another town, AY only saw her briefly once or twice a year. Her father lived even farther away and she almost never saw him.

manifestation of a depressive illness. This is clearer in adults but it occurs also in the young. Adolescents’ underlying personality features are amplified when they are depressed. For example, those who are anxious tend to show higher levels of anxiety, avoidance and somatic symptoms when depressed (anxious depression), those who are externalizers are likely to show more hostility and irritability.

Borderline personality styles (see Chapter H.5) are particularly relevant to depression as individuals with these traits are dysphoric and extremely sensitive to rejection. Their fears of abandonment can be accompanied by intense but usually brief episodes of sadness, anger, or irritability, which sometimes culminate in incidents of self-harm. Both a depressive disorder and borderline personality traits or disorder can coexist. Depression may, on the one hand, be misdiagnosed when adolescents with borderline personality traits present with sadness, irritability, and self-loading. On the other hand, a depressive episode can exaggerate personality characteristics suggesting that a personality disorder may exist when that is not the case. In the latter situation, the symptoms of personality disorder would remit once the individual has recovered from the depressive episode. Diagnosis of personality disorder should be provisional in a depressed adolescent and made on the bases of symptoms and functioning outside of the depressive episode.

Depression and suicidal behavior

Suicide is one of the leading causes of death in adolescents worldwide. For each completed suicide in adolescents, there are about 100 reported suicide attempts. Suicidal thoughts are common among the young; about one in six girls aged 12 to 16 reports having them in the previous six months (one in ten for boys) but rates in clinic samples are much higher. While suicide is the result of complex interactions in which individual and psychosocial factors as well as mental health problems play a role, there is considerable evidence that depression is the strongest individual risk factor (although there are exceptions; in some countries such as China, impulsivity seems to be the strongest risk factor).

About 60% of depressed young people report having thought about suicide and 30% actually attempt suicide. The risk increases if:

- There have been suicides in the family
- The young person has attempted suicide previously
- There are other comorbid psychiatric disorders (e.g., substance abuse), impulsivity, and aggression
Symptoms of depression

Core symptoms:
- Persistent and pervasive sadness or unhappiness
- Loss of enjoyment of everyday activities
- Irritability

Associated symptoms:
- Negative thinking and low self-esteem
- Hopelessness
- Unwarranted ideas of guilt, remorse or worthlessness
- Suicidal thoughts or thoughts of death
- Lack of energy, increased fatigability, diminished activity
- Difficulty concentrating
- Appetite disturbance (decrease or increase)
- Sleep problems (insomnia or hypersomnia)

Suicidal behaviors and risk need to be carefully evaluated in every depressed young person (see chapter E.4).

**DIAGNOSIS**

While diagnosis is not usually difficult, depression in children and adolescents is often not detected or treated. Young people tend to present initially with behavioral or physical complaints which may obscure the typical depressive symptoms seen in adults. Complaints which should alert clinicians to the possibility of depression include:

- Irritability or cranky mood
- Chronic boredom or loss of interest in previously enjoyed leisure activities (for example, dropping out of sporting activities, or dance and music lessons)
- Social withdrawal or no longer wanting to "hang out" with friends
- Avoiding school
- Decline in academic performance
- Change in sleep-wake pattern (for example, sleeping in and refusing to go to school)
- Frequent unexplained complaints of feeling sick, headaches, stomach-aches
- Development of behavioral problems (such as becoming more defiant, running away from home, bullying others)
- Abusing alcohol or other substances.

It is important to ascertain if the current problems represent a change from the teenager's previous level of functioning or character. For example, depression should be considered in the differential diagnosis in a 14-year-old boy with a six-month history of oppositional and conduct symptoms but no previous behavior problems. Similarly, depression may account for the recent academic failure of a 15-year-old girl who had previously topped her class.

Although definitions are similar, in this section we largely follow the DSM-5 because ICD-10 criteria are more ambiguous. To make a diagnosis of depression in practice requires the presence of:

- Core symptoms
- Some associated symptoms (usually four should be present)
- Pervasiveness (symptoms must be present every day, most of the day)
- Duration (for at least two weeks)
- Symptoms must cause impairment in functioning or significant subjective distress, and
- Symptoms are not the manifestation of the effects of a substance or another medical condition.

The core symptoms are sadness, unhappiness or irritability, and anhedonia. Irritability is the most ambiguous because it can be present in a wide range of psychiatric conditions (e.g., oppositional defiant disorder, obsessive compulsive disorder, bipolar illness).
Associated symptoms include:

- Significant weight or appetite change (when not dieting)
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness or excessive or inappropriate guilt
- Diminished ability to think or concentrate or indecisiveness, and
- Recurrent thoughts of death or suicide.

A key aspect in the assessment of any depressed youth is the evaluation of risk, particularly of suicide and homicide (see Chapter E.4). The outcome of the risk assessment will have an important bearing on management, for example in deciding the best setting (e.g., inpatient, outpatient) in which to treat the patient.

### Informant

Parents and teachers tend to under-estimate depressive feelings in children while young persons may overestimate them. Additionally, reports and questionnaire data from different informants often disagree. This does not necessarily imply untruthfulness—it often reflects observers’ difficulty interpreting children’s emotions and behavior, and their limited knowledge of the child (e.g., teachers observe the young person’s behavior and emotions in the classroom but not at home or in social situations). Hence, it is essential to interview the child, often on several occasions, to obtain an accurate picture of how the young person is feeling. Integrating information from several sources, a key clinical skill, is often difficult in this context. However, contrary to what happens with other conditions such as conduct disorder or ADHD, clinicians should give more weight to the young person’s report when diagnosing depression, though information from parents and teachers should also be considered.

### Severity

Evaluating the severity of a depressive episode is important because treatment guidelines use severity as one of the yardsticks to indicate what treatment should

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>
| - Five depressive symptoms (at least one core symptom)  
- Mild impairment in functioning (distressed by the symptoms, some difficulty in continuing with ordinary work and social activities, which can be done with extra effort). | - Six or seven symptoms (at least one core symptom)  
- Considerable difficulty in continuing with school work, social and family activities. | - More than seven depressive symptoms  
- Hallucinations or delusions can be present (psychotic depression)  
- Severe impairment in most aspects of functioning (home, school, social)  
- Significant risk of suicide is often present. |

To make a diagnosis of depression in practice requires:
- the presence of core symptoms
- some associated symptoms
- pervasiveness (symptoms must be present every day, most of the day)
- duration (for at least two weeks)
- functional impairment or significant subjective distress.
be administered first. However, current definitions of severity are inadequate; assessment of severity is largely based on clinical consensus and largely relies on the skills and experience of the clinician. Table E.1.4 provides guidance about assessing severity. Depression rating scales can also assist in this assessment (see Table E.1.6).

Apart from depressive symptoms and impairment, other factors (e.g., risk to self or others) influence decisions about treatment, particularly about which treatment setting is more appropriate. For example, an adolescent with high suicide risk may require hospitalization while another with an otherwise similarly severe depression but with low risk of suicide may not.

**DIFFERENTIAL DIAGNOSIS**

Sadness and unhappiness are components of normal human experience, particularly following losses and disappointments. Sometimes, however, these feelings are so intense and persistent that individuals are unable to function at the level to which they are accustomed. It is in these situations that the labels

<table>
<thead>
<tr>
<th>Normal adolescent</th>
<th>Adolescent with clinical depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>In spite of some “angst”*, moodiness and other difficulties, they show no significant and enduring change in behavior.</td>
<td>There is a change from previous behavior (e.g., became sad, irritable, lost interest in everyday activities, dramatic response to perceived slights or rejections, frequent complaints of boredom)</td>
</tr>
<tr>
<td>Although they can be sad and tearful at times, this usually occurs in response to life events and is short-lived.</td>
<td>Core depressive symptoms (sadness or anhedonia) are present every day, most of the day for at least two weeks</td>
</tr>
<tr>
<td>No significant change in functioning.</td>
<td>Deterioration from previous functioning (e.g., not coping at school, drop in marks, stopping previously enjoyed activities). They take longer to complete homework and class work than before and it takes more effort; school performance may decline. Withdraw into themselves, their room or the Internet at the expense of previously enjoyed friendships and other social activities.</td>
</tr>
<tr>
<td>Thoughts of death and suicide are infrequent.</td>
<td>Suicidal thoughts (“life is not worth living,” “I may be better off dead”) and attempts are common.</td>
</tr>
<tr>
<td>Risk behaviors, such as reckless driving, drinking, and experimentation with sex are common but usually contained within reasonable limits for that adolescent’s character.</td>
<td>May start engaging in uncharacteristic, dangerous or high-risk behaviors, such as reckless driving, out-of-control drinking, and thoughtless, unsafe sex.</td>
</tr>
</tbody>
</table>

*Anguish, fear, anxiety. “Angst” is often used to describe the intense feelings of apprehension, anxiety or inner turmoil that adolescents experience.
Detecting depression

Depression in adolescents is often not identified by parents, teachers and medical practitioners, sometimes with tragic consequences. Hannah Modra, a 17-year-old bright and successful student confided her recently developed depressive symptoms to her diary. Although her caring and well-educated family realized that something was wrong, they did not understand what, and how serious it potentially was. In her mother’s words: “I still could see that there was something not completely right about Hannah but I had no clue. I didn’t know what it was or what I could do about it or what I should do about it. And so on the 29th of January I said, ‘Look, why don’t I just take you to the doctor?’ The doctor didn’t really know her. Hannah wasn’t saying much, she was just sitting there. And the doctor thought probably a girl of this age, you know, it’s often something to do with, you know, iron deficiency or anemia. So we went off and had her blood taken and then we were coming back home and Hannah said, ‘Mum, I know it’s not anything to do with my blood.’ But I didn’t think anything more of it. You know maybe I could have said to her, ‘Well what is it Hannah?’ You know, but I didn’t say that. I didn’t ask that question, you know, and she didn’t give me an answer. And I thought she was just saying ‘I’m okay.’”

Hannah, who in retrospect had clear symptoms of depression, killed herself the following day (Australian Broadcasting Corporation, 2008).

One of the most common concerns voiced by clinicians when diagnosing depression is: how can we distinguish normal adolescent behavior from that of a depressed youth? This is because teenagers are often perceived as normally being moody, irritable, anhedonic, and bored. Table E.1.5 lists some of the differences.

Physical illness or medication

A variety of medical conditions, treatments and substances can mimic depression in children and adolescents. These include (the list is not exhaustive):

- Medications: isotretinoin, corticosteroids and stimulants (e.g., amphetamines, methylphenidate)
- Substances of abuse: amphetamines, cocaine, marijuana, solvents
- Infections: acquired immunodeficiency syndrome (AIDS), mononucleosis, influenza
- Neurologic disorders: epilepsy, migraine, traumatic brain injury
- Endocrine: Addison’s disease, Cushing’s disease, hypopituitarism, thyroid disorders.

Unipolar or bipolar?

One of the key diagnostic issues when dealing with a depressive episode is to ascertain whether it is unipolar or bipolar because of its implications for treatment. Although the clinical picture can be exactly the same in both, there are characteristics that increase suspicion that a depressive episode may be bipolar, such as a family history of bipolar disorder and the presence of psychotic symptoms or catatonia. However, a bipolar disorder diagnosis should not be made unless there is history of at least one non-drug-induced manic, hypomanic or mixed episode.

of “clinical depression”, “major depression”, “depressive illness” or “melancholia” are applied. People in everyday life speak about being “depressed”, meaning that they feel unhappy, down or sad. The issue therefore is how to distinguish clinical depression on the one hand, from the normal ups and downs of adolescents’ lives and, on the other hand, from conditions that may mimic depression.
Suspicion will encourage conducting a more thorough history looking for manic or hypomanic symptoms in the past. The unipolar-bipolar distinction is made more difficult because bipolar illnesses often start with an episode of depression in childhood or adolescence without previous history of manic symptoms.

**Substance use disorders**

Given the frequency of substance use among adolescents it is always important to clarify whether depressive symptoms are etiologically related to the ingestion of substances such as amphetamines, cocaine, marijuana, and solvents. For example, amphetamine withdrawal can present (particularly after episodes of intense use—“speed run”) with a picture of dysphoria, fatigue, sleep disturbance and psychomotor retardation (“crash”) that can be very similar to depression. It is expected that symptoms would disappear after a few days of abstinence when they are substance-induced. If depressive symptoms persist or precede the onset of substance use, one would suspect that a depressive disorder is present and comorbid with substance use.

**Schizophrenia**

When adolescents present with depressive symptoms as well as hallucinations or delusions it is important to clarify whether schizophrenia or psychotic depression is the appropriate diagnosis. Features suggestive of psychotic depression include a family history of depression or bipolar disorder, relatively rapid onset without a prodromal period, the presence of mood congruent hallucinations (e.g., a voice telling the patient he is bad or that he should kill himself) or delusions (e.g., of sin, poverty, imminent disaster, the belief that she is a witch and has caused harm to others). In spite of these differences, distinguishing between the two conditions can be difficult in practice. For example, it is not uncommon for the dysphoria and self-neglect of a prodromal stage of schizophrenia to be misdiagnosed as depression. Often, only the passage of time (course) helps to solve the diagnostic problem. In circumstances in which there is some doubt, rather than making a diagnosis of psychotic depression or schizophrenia, it may be preferable to diagnose “first episode psychosis” and leave making a final diagnosis for later, when the course of the illness is clearer or more information becomes available.

**ADHD and disruptive behavior disorders**

Irritability and demoralization are very common symptoms in children—particularly pre-pubertal children—who suffer from ADHD, oppositional defiant disorder or conduct problems, often in a context of significant family dysfunction, poverty, neglect, foster care, or institutionalization. In these cases it is difficult to establish whether demoralization is the result of the child’s plight or a manifestation of clinical depression. If symptoms meet criteria for depression, a comorbid diagnosis of depression (i.e., two diagnoses) is encouraged by the DSM system. The ICD system, on the other hand, recommends making only one diagnosis: mixed disorder of conduct and emotions or depressive conduct disorder. At this point, the advantages of one approach over the other are unclear, although research shows that children with both conduct problems and depression grow up resembling more closely children with conduct disorder than those with depression.

**Adjustment disorder with depressed mood and bereavement**

Clinicians often diagnose adjustment disorder when the onset of symptoms occurs following a significant life event. This is correct only if clinically significant

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**Stigma**

“Fear of embarrassment and pride are keeping me both from the medication and counsellors. However I could be a great help to others if I tried out these things and reported things that worked and things that didn’t work to the public. Everyone would know I have a depression weakness but I would be helping myself and others” (Australian Broadcasting Corporation, 2008).

Adolescents are self-conscious about their mental health and often consider depression a sign of weakness or a character flaw. Stigma makes diagnosis and treatment more difficult.
depressive symptoms or impairment occur within three months of identifiable stressors and do not meet criteria for major depression or bereavement. In the case of adjustment disorder, it is also expected that symptoms will disappear within six months once stressors have ceased.

Bereavement can present with a clinical picture very similar to a depressive episode but depression should not be diagnosed unless symptoms are severe, persistent, and incapacitating (e.g., inappropriate and persistent guilt, morbid preoccupation with worthlessness, significant impairment of functioning). Symptoms of grief tend to decrease over days or weeks, are often associated with thoughts or reminders of the deceased, are not as pervasive as in the case of major depression, may be accompanied by periods of positive emotions and even humor, and—contrary to what happens in major depression in which feelings of worthlessness are common—self-esteem is generally preserved.

**RATING SCALES**

There are numerous rating scales for child and adolescent depression. The clinician-administered Hamilton Rating Scale for Depression is the most widely used to rate adult depression but its usage in children and adolescents has not been extensive. The Children's Depression Rating Scale (CDRS) (Poznanski & Mokros, 1996) is also clinician-administered and was specifically developed for the young. This proprietary scale has been used in major treatment trials such as the TADS (Curry et al, 2010). There are also interview-based diagnostic instruments, such as The Child and Adolescent Psychiatric Assessment (CAPA) (Angold & Costello, 2000) which are mostly used in research.

The most widely used rating scales are self-rating, most having child, parent, and teacher versions. Since rating scales cannot validly be used to make a diagnosis—which requires an assessment interview by a competent clinician and, optimally, interviewing key informants—these instruments are mostly used for screening purposes (e.g., in schools or among people considered at risk) or to assess response to treatment over time (outcome). Increasingly, they are being modified to be completed by the young person using computers, smart phones, and tablets (Stevens et al, 2008).

Overall, self-report scales seem to be of limited use in pre-pubertal children but more helpful in adolescents. The impact of new technologies, such as smart phones, has not been fully exploited and may increase their utility. The majority of these scales are proprietary and costly but none has demonstrated a clear superiority over the others. Table E.1.6 lists some of the scales that are free of charge for clinical use; some are available in several languages.

**TREATMENT**

It is necessary to aim high, that is, seeking to achieve full remission of symptoms and a return to the premorbid level of functioning (recovery). Anything less is a suboptimal outcome because persistence of depressive symptoms increases the likelihood of poorer psychosocial functioning, suicide and other problems (e.g., substance abuse), as well as relapse and recurrence.

In most cases it is good practice to involve the young person's parents in the evaluation and treatment process (for example, in discussions about the treatment options available and their relative risks and benefits) but the degree
<table>
<thead>
<tr>
<th>Scale</th>
<th>Rater</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>CES-DC:</td>
<td>Self, parent (Children, adolescents)</td>
<td>• There are questions about its specificity measuring depressive symptoms (as opposed to distress).</td>
</tr>
<tr>
<td>MFQ:</td>
<td>Self, parent, teacher (Children, adolescents)</td>
<td>• Free for clinical or research use, with permission.</td>
</tr>
<tr>
<td>DSRS:</td>
<td>Self (Children, adolescents)</td>
<td>• Available in several languages</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Few studies</td>
</tr>
<tr>
<td>KADS:</td>
<td></td>
<td>• Two versions with 6 and 11 items respectively.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The 6-item KADS is designed for use in institutional settings (such as schools or primary care settings) where it can be used as a screening tool to identify young people at risk for depression or by trained health care providers (such as public health nurses, primary care physicians) or educators (such as guidance counselors) to help evaluate young people who are in distress or who have been identified as possibly having a mental health problem. It is currently available in English, French, Chinese, German, Spanish, Portuguese, Korean, and Polish.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The 11-ITEM KADS is available in English, Portuguese, and Turkish.</td>
</tr>
<tr>
<td>PHQ-A:</td>
<td>Self (adolescent)</td>
<td>• A short questionnaire developed as part of the PRIME-MD package funded by Pfizer.</td>
</tr>
<tr>
<td>SDQ:</td>
<td>Self (adolescent), parent, teacher</td>
<td>• Measures overall psychopathology but a subscale can be used to screen for depression risk.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Reasonably sensitive and specific when screening “probable” depressive illness.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Can be completed by the young person on-line and get immediate feedback at <a href="http://www.youthmind.info/UK/sdqonline/StartSelf.php">http://www.youthmind.info/UK/sdqonline/StartSelf.php</a></td>
</tr>
</tbody>
</table>

Click on the picture to access the National Institute for Health and Clinical Excellence (NICE) (2005) guideline.
of involvement will depend on the young person’s age, stage of development, their wishes and circumstances, and the culture of the country. Taking time to do this will strengthen the therapeutic relationship, improve adherence to treatment and outcome. It is always recommended to monitor regularly the severity of the depression using a rating scale (e.g., one of those listed in Table E.1.6). Suicide risk should also be evaluated regularly and not just at the first assessment interview because suicide risk fluctuates.

**Watchful waiting** is an approach to managing illnesses in which time is allowed to pass before further treatment is considered. Watchful waiting is often used in conditions with a high likelihood of self-resolution or where the risks of treatment may outweigh the benefits (e.g., prostate cancer). A key component of watchful waiting is the use of explicit rules to ensure a timely transition to another form of management, if necessary. The National Institute for Health and Clinical Excellence (NICE) (2005) guideline introduced watchful waiting as a strategy “for children and young people with diagnosed mild depression who do not want an intervention or who, in the opinion of the healthcare professional, may recover with no intervention, a further assessment should be arranged, normally within 2 weeks”. It is important to note that watchful waiting does not mean no-treatment. During the watchful waiting period, treatment should take place as described in the supportive management section below.

**Supportive management**

The American Academy of Child and Adolescent Psychiatry (AACAP) practice parameter (Birmaher et al, 2007) indicates that instead of medication “it is reasonable, in a patient with a mild or brief depression, mild psychosocial impairment, and the absence of clinically significant suicidality or psychosis, to begin treatment with education, support, and case management related to environmental stressors in the family and school. It is expected to observe response after 4 to 6 weeks of supportive therapy.” That is, education, support, and case management—supportive management—is a valid, widely used but poorly researched treatment option.

Many patients seek help following a crisis (e.g., a suicide attempt); in these emotionally-charged circumstances symptoms tend to be exacerbated. Dealing with the crisis itself may be enough to settle the perceived depression, particularly in primary care settings. As part of the supportive management, seeing the adolescent—and parents, if appropriate—on two or three occasions allows for a more thorough assessment of the illness and of factors maintaining it, and to discuss treatment options, risks and side effects in more detail. Thus, supportive management/watchful waiting are useful strategies when suicide risk is low and depression not severe.

**Psychosocial interventions**

Psychosocial interventions (summarized in Table E.1.7), in particular cognitive behavior therapy (CBT) and interpersonal psychotherapy (IPT), appear to be effective in the treatment of mild to moderate depression although the number and quality of studies examining specific therapies is limited. The optimal number of CBT and IPT sessions is not known. Most studies report using weekly one-hour sessions for 8 to 16 weeks, though booster sessions may improve outcomes and reduce recurrence. In practice the number of sessions can be tailored to patients’ needs, severity of the illness and other relevant factors.
Though antidepressants achieve better results in the short term, differences in outcome between the various psychosocial interventions and with antidepressant medication tend to disappear after 24-36 weeks (TADS Team, 2007). The quality of the therapist (trained therapists vs. paraprofessionals) as well as the strength of the patient-therapist alliance seem to be relevant factors for response in all the psychotherapies.

**Cognitive behavior therapy (CBT)**

CBT is based on the assumption that depressed mood is associated with an individual’s behavior and thoughts, and that changing behavioral and cognitive patterns will lead to a reduction in depressive feelings and improved functioning. Individuals are exposed to a range of stressors and respond automatically to them with feelings; in depressed adolescents these automatic responses are unrealistically negative — often cataclysmic: “no one likes me”; “I am good for nothing”. These depressed thoughts and subsequent actions make them feel worse, often generating a downward spiral: unhappy feelings leading to unrealistically negative thoughts and behaviors. The aim of treatment is to turn back this vicious cycle by learning (a) that one’s feelings, thoughts, and actions are interconnected, and (b) by developing strategies for more positive patterns of thinking and behaving, which in turn lead to more positive feelings (Langer et al, 2009).

The *first goal* of CBT is to help patients identify links between mood, thoughts and activities in their lives (e.g., speaking to a friend on the phone resulting in an improvement in mood) and challenge some of their negative beliefs; at the same time the number of activities is increased using strategies such as scheduling enjoyable activities. Optimally, this requires using a mood diary (see Figure E.1.1). *Another goal* is to help the patient discriminate between helpful and unhelpful thoughts, to develop strategies for generating more helpful thoughts, and to practice using helpful thought patterns in response to stressful situations (cognitive restructuring). The *third goal* is to equip the young person with skills to build and maintain relationships, undermined by the adolescent’s depression, by training in social skills, communication and assertiveness.

**Interpersonal psychotherapy (IPT)**

Interpersonal psychotherapy stresses the importance of interpersonal relationships and that people experience distress when disruptions occur in their significant attachments. This results in a loss of social support that causes or maintains depressive feelings. IPT therapists do not probe into the adolescent’s past, focusing instead on current interpersonal conflicts, targeting depressed adolescents’ interpersonal skills to improve their relationships (Mufson et al, 2009).

IPT has many commonalities with CBT. For example, the goals are to link mood with interpersonal events happening at the time, to provide psychoeducation about depression, and to encourage participation in enjoyable activities (especially at school) as a means to feeling better. However, the focus is on interpersonal issues (e.g., examining and modifying maladaptive communication patterns and interpersonal interactions) and on teaching the adolescent how to deal with them constructively.

In recent years *mindfulness* techniques are often added to CBT and IPT programs with growing evidence of effectiveness in the treatment of depression and to prevent recurrences. Mindfulness is a technique in which individuals

**Medication**

Antidepressant drugs and their efficacy are summarized in Table E.1.8. Antidepressants are an important weapon for treating depression in the young, however several antidepressants that are effective in adults are not effective in youth (e.g., tricyclic antidepressants) or too risky to use in this age group (e.g., MAOIs)—highlighting the issue that empirical data obtained in adult treatment trials cannot necessarily be generalized to children and adolescents. The placebo effect, if anything, is stronger among children and adolescents than in adults, severity of the depressive episode being an important consideration: antidepressants are not more effective than placebo in mild depression but appear to be more effective when depression is severe.

A key aspect of prescribing and obtaining informed consent is to discuss with the patient, and family if appropriate the:

- Reasons for the medication
- Possible adverse effects (including emerging or escalating suicidal thinking, nervousness, agitation, irritability, and mood instability)
- Need to take medication as prescribed, and
- Delayed action of antidepressants (to dampen expectations of immediate benefit).

### Table E.1.7. Summary of evidence of effectiveness of psychosocial therapies for unipolar depression.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Cognitive behavior therapy (CBT)               | • Some evidence showing that individual CBT (8 to 16 one-hour weekly sessions) is effective in the short term.  
|                                                | • Differences between CBT and medication usually disappear by 12 months.                      |
| Interpersonal psychotherapy (IPT)              | • Some evidence showing that IPT is effective in the short term.                             |
| Psychodynamic (psychoanalytic) psychotherapy   | • Very few studies but some evidence that it might be effective.                              
|                                                | • Requires longer duration of treatment (e.g., one year)                                     |
| Family therapy                                 | • More effective than no treatment. Unclear how effective it is in comparison to other treatments.  
|                                                | • May be particularly useful in cases with family conflict or disharmony.                    |
| Group therapies (mostly CBT-based)             | • Evidence is limited and results conflicting.                                               
|                                                | • Mostly used as a preventive intervention for at-risk individuals.                          |
| Self-help (e.g., relaxation, educational leaflets or books, support groups) | • Data are limited and with conflicting results.                                               
|                                                | • Growing interest in CBT-based internet-delivered self-help but little evidence of effectiveness as yet.  
|                                                | • Psycho-education is usually included as part of clinical treatment.                        |
A typical CBT session begins by collaboratively setting an agenda for the session, reviewing homework from the previous week, teaching and practicing the current cognitive-behavioral skill, addressing crises and issues that have arisen in the youth’s life over the previous week, helping the youth to summarize the skills that have been learned during the session, and allocating practice/homework assignments (Langer et al, 2009).

Write down the relevant activities in each day (morning and afternoon) and rate your mood from 0 (very unhappy), to 5 (neither happy nor unhappy), to 10 (very happy). Use all the range of ratings.

<table>
<thead>
<tr>
<th>MOOD</th>
<th>MONDAY</th>
<th>TUESDAY</th>
<th>WEDNESDAY</th>
<th>THURSDAY</th>
<th>FRIDAY</th>
<th>SATURDAY</th>
<th>SUNDAY</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>PM</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

Figure E.1.1. Example of a completed mood chart.

Good practice also recommends reviewing the patient at weekly intervals (personally or, when this is not possible, over the phone) for the first month once medication is prescribed. These reviews allow further supportive management and monitoring of side effects and response (by the administration at each visit of a depression rating scale).

Under-treatment—not enough medication or not for long enough—is a common error in clinical practice. Although it is important to start with a low dose, the amount of medication should be gradually increased until symptoms lessen or side effects appear, keeping in mind that there is wide individual variation in the dose of medication required.

Side effects of medication

Since antidepressants other than SSRIs will rarely be used in youth, only side effects of SSRIs are discussed in detail. In the case of TCAs, anticholinergic side effects and cardiac toxicity are the main ones, while hypertensive crises are the main risk for MAOIs.

Suicidality

It has been suggested that, paradoxically, SSRIs may induce suicidal behavior in the young. Ascertaining whether this is true is not easy because depression also increases suicide risk. So far, data are contradictory. On the one hand, pharmaco-epidemiological and ecological studies suggest that increased use of SSRIs may have resulted not on an increase but on a lessening in youth suicide. On the other hand, a review by the FDA of controlled trials with more than 4400 children and adolescents showed a robust if small (2%) short-term increase in the incidence of suicidality (suicidal thoughts, attempts) in those receiving antidepressants, mostly SSRIs, compared with placebo. There were no suicides. This resulted in the FDA and regulatory bodies in other countries warning of this risk. The mechanisms underlying this phenomenon are unclear. SSRIs can induce akathisia, agitation,
Helping adolescents solve problems in a structured way

1. “What’s the problem?” — ask the teenager to write it down.
2. List all possible solutions — brainstorm and list all possible solutions. The teenager should write down all the solutions they can think of without evaluating them (i.e., both good and bad solutions).
3. Take each possible solution on the list and think about the pros and cons.
4. Ask the teenager to choose the best or most practical solution.
5. Work out how to implement the best solution and the resources needed. You may need to rehearse the difficult steps with the teenager.
6. After the teenager has carried out the chosen solution, review and praise all efforts. If the solution did not work, go through the steps again and identify an alternative solution.

Placebo response and severity of depression

One of the most puzzling aspects of the treatment of depression is the high rate of placebo response, estimated at 50% to 60% in RCTs examining the pharmacological treatment of clinical depression in youth. A review of RCTs found that placebo response was higher in children than adolescents, among those with milder depression, and increased with the number of centers participating in the study (Bridge et al., 2009).

Effectiveness of antidepressants does not seem to increase with growing severity but placebo response decreases. That is, placebo response is similar to that of medication in cases of mild depression, while placebo response is clearly inferior to medication in severe depression. For example in TADS, in which participants were severely depressed, at 12 weeks, 35% of those taking placebo had responded compared with 61% of those treated with fluoxetine. Similar results have been reported in adults. This is one of the reasons why antidepressants are not usually recommended as a first line of treatment in mild depression.

irritability and disinhibition. Like other antidepressants, SSRIs can also trigger a manic switch.

The implications of these findings are that patients need to be warned of this risk and clinicians ought to put in place strategies to manage it such as weekly reviews during the first month of treatment, and educating patient and family about detecting changes in behavior (e.g., agitation, thoughts of self-harm) once medication is started.

Other side effects

SSRIs are also associated with higher rates of agitation, akathisia, nightmares and sleep problems, weight gain, sexual dysfunction (reduced sexual desire, difficulty reaching orgasm, inability to maintain an erection) and increased risk of bleeding. Most of these side effects are dose-related and can be controlled by reducing the dose.

Depending on the half-life of the specific SSRI, stopping treatment abruptly or missing several doses can cause withdrawal symptoms, also called discontinuation syndrome, including: nausea, headaches, dizziness, and flu-like symptoms (infrequent with fluoxetine, very common with paroxetine). Abrupt cessation may also increase the likelihood of relapse or recurrence.

Antidepressant use in pregnancy

The use of SSRIs (the other antidepressants are not usually recommended in the young) during pregnancy is an important issue due to reports of SSRIs being associated with teratogenicity, spontaneous abortion and premature labor, low birth weight, and pulmonary hypertension. The evidence is conflicting but the weight of it suggests that properly used SSRIs are safe. Thus, most treatment guidelines state that these concerns should not prevent prescription of SSRIs (with the exception of paroxetine) for the treatment of major depression in pregnancy once the potential benefits outweigh the risks, taking into account that depression during pregnancy carries its own dangers. Paroxetine should not be used because of an association with both major malformations and cardiac abnormalities (Bellantuono et al, 2007). Bellantuono C, Migliarese G, Gentile S (2007). Serotonin reuptake inhibitors in pregnancy and the risk of major malformations: A systematic review. Human Psychopharmacology, 22:121–128.
Table E.1.8. Summary of evidence of effectiveness of antidepressant drugs for unipolar depression.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Tricyclic antidepressant (TCAs):</td>
<td>• No evidence of superiority vs. placebo for any of them, particularly in pre-pubertal children</td>
</tr>
<tr>
<td>Amitriptyline, clomipramine, desipramine,</td>
<td>• Significant side effects (anticholinergic, QT prolongation)</td>
</tr>
<tr>
<td>dosulepin, doxepin, imipramine, lofepramine,</td>
<td>• Toxic (cardiotoxic) in overdose (with the exception of mirtazapine)</td>
</tr>
<tr>
<td>nortriptyline, protriptyline, trimipramine</td>
<td>• To be avoided in children and adolescents</td>
</tr>
<tr>
<td>• Tetracyclic antidepressants (TeCAs):</td>
<td>• As a group, SSRIs are more effective than placebo, particularly in adolescents with severe depression</td>
</tr>
<tr>
<td>Amoxapine, maprotiline, mianserin, mirtazapine</td>
<td>• Few side effects but may increase suicidality</td>
</tr>
<tr>
<td>• Selective serotonin reuptake inhibitors (SSRIs):</td>
<td>• Fluoxetine is the best studied and has the best evidence of effectiveness. Approved by the FDA and EMEA* for those aged 8 years or older.</td>
</tr>
<tr>
<td>citalopram</td>
<td>• Sertraline, citalopram, escitalopram: less robust evidence of effectiveness, though they may be effective in patients who did not respond to fluoxetine (Brent et al, 2008). Escitalopram has been approved by the FDA for adolescent depression</td>
</tr>
<tr>
<td>escitalopram</td>
<td>• Paroxetine: appears not to be effective in youth and shows more side effects than the other SSRIs. Short half-life easily resulting in withdrawal symptoms; use not recommended.</td>
</tr>
<tr>
<td>fluoxetine</td>
<td>• One study showed that venlafaxine is as effective as SSRIs in patients with treatment-resistant depression but has a worse side-effect profile (Brent et al, 2008). Not recommended in youth.</td>
</tr>
<tr>
<td>fluvoxamine</td>
<td>• No consistent evidence about the others.</td>
</tr>
<tr>
<td>paroxetine</td>
<td>• Evidence of effectiveness in this age group is lacking.</td>
</tr>
<tr>
<td>sertraline</td>
<td>• No evidence of effectiveness in the young</td>
</tr>
<tr>
<td>• Serotonin-norepinephrine reuptake inhibitors (SNRIs):</td>
<td>• Significant risk of side effects due to non-compliance with dietary restrictions</td>
</tr>
<tr>
<td>Venlafaxine, desvenlafaxine, duloxetine,</td>
<td>• To be avoided in children and adolescents</td>
</tr>
<tr>
<td>milnacipran, Levomilnacipran</td>
<td></td>
</tr>
<tr>
<td>• Monoamine oxidase inhibitors (MAOIs):</td>
<td></td>
</tr>
<tr>
<td>Isocarboxazid, moclobemide, phenelzine,</td>
<td></td>
</tr>
<tr>
<td>selegiline, tranylcypromine, pirlindole</td>
<td></td>
</tr>
<tr>
<td>• Other antidepressants:</td>
<td></td>
</tr>
<tr>
<td>agomelatin, buspirone, nefazodone,</td>
<td></td>
</tr>
<tr>
<td>vilazodone, vortioxetine.</td>
<td></td>
</tr>
</tbody>
</table>

*EMEA: European Medicines Agency

Antidepressant benefit and risk of suicidality

Across antidepressants, mainly SSRIs, a meta-analysis including 15 depression RCTs reported numbers needed to treat (NNT) that ranged from 4 (for fluoxetine) to 20 (for nefazodone) and a pooled average of 10 (Bridge et al, 2007). That is, four depressed youth will need to be treated with fluoxetine for one to get better due to treatment (as opposed to other factors such as the placebo effect or natural course of the illness).

The same meta-analysis reported number needed to treat to harm (NNH) — defined as emerging suicidal behavior — that ranged from 112 (across 13 depression trials) to 200 (across 6 OCD trials) and to 143 (across 6 non-OCD anxiety disorder trials), with a pooled average of 143. That is, 112 depressed adolescents will need to be treated with antidepressants for one to develop suicidal behavior attributable to the treatment. In summary, across indications, benefits of antidepressants appear to be much greater than risks from suicidal ideation/suicide attempt.
Pharmacogenomics and individualized treatment

Antidepressants are of moderate effectiveness overall but there is wide variation between patients in their response to individual antidepressants. Clinical characteristics (e.g., whether there is melancholia or not) have not been helpful indicators of antidepressant response. The only option currently available is trial and error (i.e., try an antidepressant, if it does not work, try another), which is time consuming and cumbersome.

It is well known that when parents respond well to one antidepressant drug, children are also likely to respond to the same drug. As a result there is growing interest in detecting gene variants (e.g., serotonin transporter, norepinephrine transporter) that may be associated with response to antidepressants. This situation is further compounded because antidepressants are metabolized by enzymes that vary considerably from person to person. For example, cytochrome P450 (CYP) 2D6 is instrumental in the metabolism of many antidepressants but more than 74 allelic variants of the CYP2D6 gene have been found, and the number is still growing. This results in CYP2D6 activity varying considerably within a population from ‘ultra-rapid’, to ‘extensive’, to “intermediate’, to “poor” metabolizers. Distribution of these alleles also varies between ethnic groups. Clinical consequences of CYP2D6 polymorphism can be either the occurrence of adverse drug effects or lack of response. There is an expectation that genetic testing may in the future help choosing the right antidepressant for a given individual. Thus far this is not possible.

Physical treatments

Physical treatments are summarized in Table E.1.9. Besides medication, several physical treatments are used in the management of depression in children and adolescents. Of these, electroconvulsive therapy (ECT) has been administered to the young for about 60 years—described as “lifesaving” in some cases—and has a place in the armamentarium to treat depression. However, there are no controlled trials in youth (they pose significant ethical challenges) and there is no wide agreement on when ECT should be used, whether reasonably early in the course of treatment (e.g., if antidepressants are not tolerated), as a last resort, or never. This largely reflects individual countries’ attitude towards ECT, which has been severely stigmatized due to ECT having been used occasionally as a means of political control, negative media portrayals, or misuse by some psychiatrists. As a result, many states place legal restrictions on its use—some countries (e.g., Slovenia) have even outlawed its use.

More recently, transcranial magnetic stimulation (TMS) has been used in young people but it can only be considered an experimental treatment at this time. For more details see Walter and Ghaziuddin (2009). Light therapy has been used for seasonal mood disorders with some success.

Complementary and alternative medicine treatments

Use of complementary and alternative medicine treatments (CAM) is widespread (see Chapter J.2). For example, St John’s wort is one of the most commonly prescribed antidepressants for children in Germany. A host of CAM interventions have been recommended or used for the treatment of depression but hardly any are supported by credible evidence of effectiveness, particularly in children and adolescents. This is compounded by the fact that CAM remedies have to satisfy less rigorous efficacy and safety criteria than prescription drugs. For example, they lack standardized preparation and are more prone to contamination, adulteration and inaccurate dosage, among other problems. While clinicians recognize patients’ and families’ interest in CAM therapies, often do not feel comfortable asking about, discussing, or recommending them. Nevertheless a competent clinical evaluation should include routine questioning about CAM usage. An open, informed stance by the treating clinician often leads to disclosure, acknowledgement of patients’ dislikes and beliefs, and better patient education and outcomes. Alternative medicine treatments are summarized in Table E.1.10.

Toxicity

Toxicity—death due to acute poisoning by a single drug, with or without ingestion of alcohol—is much lower among the SSRIs (1.3 deaths per million prescriptions) than with TCAs (34.8), and MAOIs (20.0). That is, toxicity is 27 times higher for TCAs than SSRIs. Toxicity of venlafaxine is quite high (13.2) (Buckley & McManus, 2002).
MANAGING ACUTE DEPRESSIVE EPISODES

Unipolar depressive episode

Currently treatment of unipolar depressive episodes in youth is largely guided by their severity. Following initial assessment clinicians should contact children and young people with depression who do not attend follow-up appointments.

- **Mild severity**: supportive management or psychosocial treatment, if available. If no response after 4 to 6 weeks: CBT, IPT or medication
- **Moderate severity**: supportive management or psychosocial treatment, if available; in some cases (e.g., patient preference, non-availability of psychosocial treatment), medication. Medication should be used also if patients do not benefit from 4 to 6 weeks of supportive management or psychosocial treatment
- **Severe**: psychosocial treatment and antidepressant medication
- **Psychotic depression**: as per severe depression but adding a second generation antipsychotic.

Bipolar depressive episode (see also Chapter E.2)

There is little evidence available to guide treatment in young people. Recommendations are therefore extrapolated from adult data (Frye, 2011):

- Initial treatment (first line) would usually be lithium carbonate or quetiapine

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Electroconvulsive Therapy (ECT)    | • ECT is rarely used in this age group. It would appear to be of comparable efficacy as in adults  
                                         • Used in severe depression when other treatments have failed or are not tolerated  
                                         • ECT should not be used in pre-pubertal children except in the most extreme circumstances  
                                         • Few side effects, retrograde amnesia being the main one  
                                         • Use subject to legal restrictions in some countries |
| Transcranial magnetic stimulation (TMS) | • Few studies, but early results promising  
                                          • Experimental treatment at this stage  
                                          • Side effects are generally mild and transient, mostly headache and scalp pain |
| Light therapy                      | • Data limited, but includes controlled trials reporting positive results  
                                          • Used for seasonal mood disorder. Suggestions that it may also be effective in non-seasonal mood disorder (e.g., in older patients)  
                                          • Few adverse effects |

Serotonin syndrome

Serotonin syndrome is a potentially serious toxic effect resulting from too much serotonin. It has been observed in overdose of (a) a single agent (usually an SSRI), (b) with the simultaneous use of two drugs that increase serotonin levels or serotonergic transmission (e.g., monoamine oxidase inhibitors or moclobemide used with any drug that inhibits re-uptake of serotonin such as SSRIs and some tricyclic antidepressants), or (c) by failing to observe an adequate washout period when switching antidepressants. Risky situations include polypharmacy, use of over-the-counter or alternative medicine substances such as St John’s wort, or of illicit drugs such as ecstasy.

Clinical features of serotonin syndrome include:

- **Mental**: confusion, agitation, hypomania, hyperactivity, restlessness
- **Neuromuscular**: clonus (spontaneous, inducible or ocular), hypertonia, hyperreflexia, ataxia, tremor (hypertonia and clonus are symmetrical and more obvious in lower limbs to begin with). Clonus is the most important distinguishing feature in diagnosis.
- **Autonomic**: hyperthermia, sweating, tachycardia, hypertension, mydriasis, flushing, shivering

MANAGING ACUTE DEPRESSIVE EPISODES

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- **Severe**: psychosocial treatment and antidepressant medication
- **Psychotic depression**: as per severe depression but adding a second generation antipsychotic.

Bipolar depressive episode (see also Chapter E.2)

There is little evidence available to guide treatment in young people. Recommendations are therefore extrapolated from adult data (Frye, 2011):

- Initial treatment (first line) would usually be lithium carbonate or quetiapine
Table E.1.10. Summary of evidence of effectiveness of alternative treatments for unipolar depression.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comments</th>
</tr>
</thead>
</table>
| St John’s wort (*hypericum*)    | • Many RCTs in adult patients, mostly with mild depression. Results inconsistent—larger, better designed studies with more severely depressed patients show negative results more often than smaller ones with mildly depressed patients. Very limited data for children.  
  • *Hypericum* might be as beneficial as antidepressants in mild depression.  
  • Few adverse effects  
  • Significant risk of interaction with a wide range of prescribed medications due to activation of the cytochrome P450 system |
| Omega-3 fatty acids             | • Several RCTs in adults of heterogeneous quality but few in young people  
  • Not clear yet whether they are effective  
  • Few, minor side effects |
| S-Adenosyl Methionine (SAMe)    | • Trials of inconsistent quality show that SAMe might be as effective as TCAs in adults. No evidence for children.                             |
| Exercise                        | • Some evidence of a specific benefit in mildly depressed older patients. No definite evidence in youth                                      |

- Second line treatments would be:
  (a) A combination of lithium or valproate with an SSRI  
  (b) Olanzapine and an SSRI, or  
  (c) Lamotrigine.

- There is no evidence that antidepressants alone (without a mood stabilizer) are helpful and are not recommended due to risk of a manic switch or of induction of rapid cycling.

- Lithium and valproate should be avoided in women of childbearing age (teratogenic).

**Which antidepressant?**

- Choice of antidepressant should be guided by two considerations: effectiveness and safety. As a group, SSRIs are the safest antidepressants; of these, fluoxetine has the best evidence of effectiveness in this age group.

- Response or non-response or adverse effects of treatment during a previous episode will influence the choice of medication for the current episode.

- Start with 10mg of fluoxetine. If well tolerated, increase dose to 20mg after one week; 20mg is usually sufficient for pre-pubertal children. In adolescents, dose may need to be increased to 30 or 40mg if they do not respond adequately to 20mg and is well tolerated, although 20mg would suffice in most cases.

- If fluoxetine is not well tolerated or there are other reasons for not using it, try another SSRI (e.g., sertraline or escitalopram).

**Duration of treatment**

It is widely accepted that stopping treatment early (e.g., after 8 to 12 weeks), when the patient is getting better, often results in relapse. Clinical wisdom suggests
that treatment should continue for at least six months after recovery. When ceasing antidepressants, it should be done gradually and not abruptly to avoid withdrawal or cessation phenomena, common in all antidepressants but particularly in SSRIs with short half-life.

**The patient does not improve**

The majority of patients recover; with ongoing treatment, improvement continuing after 12 weeks. For example, in the TADS follow up study, 88% had recovered by two years and 96% by five years (Curry et al, 2010). However, this also shows that a small minority of patients do not recover (see Figure E.2.2). Before considering a patient *partial-responder, non-responder* or *treatment-resistant* it is imperative to review all potential factors that may have contributed to the patient’s poor response; these are listed in Table E.1.11. For example, a child’s depression was not improving; further assessment showed the mother to be depressed; treating the mother’s depression resulted in an improvement in the child as well. A clinical review in an adolescent who was not getting better showed short periods of hypomanic symptoms and a grandfather who suffered from bipolar disorder; treatment with lithium carbonate resulted in an improvement of symptoms.

One of the key issues is to ascertain whether the patient has been treated with an effective antidepressant at the appropriate dose (e.g., 40mg of fluoxetine) and for long enough (e.g., 12 weeks). Inadequate dosage can also be due to poor adherence to treatment, willful or accidental.

**Treatment resistance**

Despite the importance of this matter there is very limited empirical data on treatment-resistant depression in youth and no agreed definition. Birmaher and colleagues (2009) proposed the following definition of treatment resistance: a youth whose symptoms of depression and functional impairment persist after 8-12 weeks of optimal pharmacological treatment or 8-16 sessions of IPT or CBT and a further 8-12 weeks of an alternative antidepressant or augmentation therapy with other medications or evidence-based psychotherapy. That is, treatment resistance should be diagnosed only after two trials of evidence-based treatment at an adequate dose and for an appropriate duration (e.g., 12 weeks).
Once treatment resistance has been confirmed, several options are available (following clinical wisdom and extrapolation of adult data, although none is backed by evidence). These include optimization, switching, augmentation, and ECT. An important practical aspect is that changes to treatment should be made one at a time; otherwise it will be difficult to ascertain which change resulted in the improvement.

There is little empirical data to guide us on the advantages of switching versus augmentation, although it would appear that switching from fluoxetine to another SSRI or to venlafaxine results in response in about one third of the patients, consistent with data from adults (Brent et al, 2008). However, those treated with venlafaxine showed more side effects. This suggests that if switching is the chosen option, the initial switch should be to another SSRI rather than venlafaxine.

### Treatment setting

Most depressed young people should optimally receive ambulatory treatment, which minimizes disruption to school attendance, family and social relationships and stigma. Inpatient care may be justified when patients’ safety cannot be guaranteed (e.g., high suicide risk), depression is very severe (e.g., severe psychotic symptoms), or there is a lack of response. In the last case, admission to hospital may allow for a more accurate assessment of the reasons for non-response and to monitor adherence and changes in treatment more closely.

### RECURRENT DEPRESSION

It has already been highlighted that depression in the young is an illness that tends to recur. In the TADS follow up, for example, almost half (47%) of those who recovered had a recurrence by 5 years. Adolescents who had responded poorly in the short term, females and those with comorbid anxiety disorder were more likely to have a new episode. However, recurrence rates were the same irrespective of the treatment provided (e.g., those who received fluoxetine combined with CBT did not seem to obtain an extra benefit) (Curry et al, 2010). Treatment of a

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**Table E.1.11. Factors associated with partial or no response to treatment.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Family</th>
<th>Environment</th>
<th>Clinician</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger age</td>
<td>Maternal depression</td>
<td>Bullying</td>
<td>Misdagnosis</td>
</tr>
<tr>
<td>Severe depression</td>
<td>Lack of cooperation</td>
<td>Stressors</td>
<td>Inappropriate treatment</td>
</tr>
<tr>
<td>Poor short-term response</td>
<td>Unreliability</td>
<td>Dysfunctional school or neighborhood</td>
<td>(non-evidence-based treatment, inadequate dose or not for long enough)</td>
</tr>
<tr>
<td>Poorer functioning</td>
<td>Mistreatment, conflict</td>
<td>Antisocial peer group</td>
<td>Non-recognition of side effects</td>
</tr>
<tr>
<td>Appetite or weight disturbance</td>
<td>Psychopathology (e.g., drug and alcohol)</td>
<td>Cultural/ethnic issues</td>
<td>Poor doctor-patient therapeutic relationship</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor adherence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comorbid psychiatric or medical conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Side effects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medications (e.g. steroids)</td>
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</table>
recurrence should be the same as for the acute episode. Frequent recurrences may require ongoing treatment with an antidepressant.

**TREATING DEPRESSION COMORBID WITH OTHER DISORDERS**

Treating depression in youth comorbid with other psychiatric disorders (e.g., anxiety, ADHD) requires particular skill. One would seek to alleviate symptoms of the most severe disorder first and symptom change should be monitored with specific rating scales and not by assessing global functioning alone:

- If at all possible, begin with a single medication.
- Make one medication change or addition at a time and allow adequate time for response and dose adjustment.
- A change in medication may be warranted after 4 to 8 weeks of treatment if there is no or minimal response in spite of an adequate dose. If there is some response, continue with the medication making sure the dose is adequate.
- If symptoms persist after the administration of two evidence-based treatments, follow the protocol for treatment-resistant depression.
- If use of multiple medications is clinically warranted (e.g., to treat the comorbidities), you must be aware of and monitor potential interactions.

**Substance use**

Depression comorbid with substance use disorder poses particular challenges and getting parents involved constructively in these efforts is critical. Because of the increased risk of harm, implementing a safety plan when first assessing the adolescent and higher vigilance throughout treatment are very important. This may include education regarding safe sex, sexually transmitted diseases including HIV, contraception and about the additive impact of depression and substance use on these risks. It is necessary to emphasize that drugs and alcohol are not acceptable treatments for depression; they may appear to relieve symptoms in the short term but will make the depression worse in the longer term.

Treatment should be integrated; that is, concurrent rather than sequential. For example, do not wait for abstinence from drugs before starting antidepressant treatment. Psychotherapies such as family therapy, motivation-enhancement therapy and CBT should also be administered concurrently.

Managing a patient with a substance use disorder may require collecting laboratory specimens such as urine drug screens regularly. In that case you should know in advance—usually after discussion with the adolescent—to whom you will inform of the results, under what circumstances, and how you will use that information (see Chapters G.1, G.2 and G.3).

**Depression in the intellectually disabled**

Depression is difficult to diagnose and under-recognized in the intellectually disabled. No reliable data on the prevalence of depression in children with intellectual disability (mental retardation) exists, although there are suggestions that it may be several times more common than in the general population. Depressed, intellectually disabled youth usually show a sad or miserable facial expression, crying and irritability, loss of interest in usual activities or stereotypical interests, and appetite and sleep disturbances in the context of a change from previous

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**Combining antidepressant medication and CBT**

The TADS showed that combining an SSRI (fluoxetine) and CBT was better than fluoxetine or CBT alone. Results in depressed adults also suggest that adding CBT to antidepressant medication results in higher improvement rates. As a consequence, many treatment guidelines recommend the use of an SSRI combined with CBT as the treatment of choice for severe depression in the young.

A meta-analysis (Dubicka B et al, 2010) addressed the question of whether CBT confers additional benefit to antidepressant treatment in adolescents with unipolar depression. Results showed no evidence of an advantage when combining antidepressants and CBT over medication alone for depressive symptoms, suicidality and global improvement after acute treatment or at follow-up. The combined treatment did result in a greater reduction in impairment in the short-term (at 12 weeks). These results, therefore, challenge current wisdom but will need replication. However, some specific groups of young people may benefit from the combination. Evidence is emerging that a combination of an antidepressant with CBT may be more effective than other interventions in adolescents who had failed to respond to an appropriate course of an antidepressant.
behavior. Reduced food intake or food refusal, slowed movements, impaired self-care, and catatonia are suggestive of depression in those more severely disabled. Adolescents with mild intellectual disability are often able to report on their internal world and to describe depressive symptoms such as sadness, hopelessness, and suicidal thinking. Information from parents, caregivers, teachers, and respite workers is important.

Given that there is no empirical evidence referring specifically to the treatment of intellectually disabled children and adolescents with depression, recommended management is the same as for non-intellectually disabled youth with the appropriate adjustments (e.g., cognitive aspects are often inappropriate). Consent to treatment issues, particularly to invasive treatment (such as ECT) pose particular problems in these patients.

**Depression comorbid with physical illness**

Depression is common among young people with chronic physical illness and its impact on their quality of life is considerable. According to Ortiz-Aguayo and Campo (2009) “rather than being just another disorder suffered by a physically ill child, the relationship between physical disease and depression is often complex and bidirectional.” As a result recognition and diagnosis of depression in chronically ill children is often a challenge because there is the risk of misattributing symptoms of the physical disease (e.g., fatigue, poor sleep or appetite) to a mood disorder and vice versa. Evaluation of changes in functioning is essential.

While treatment is as described for depressive episodes in other youth, medication is particularly well suited to the management of depression in medical settings but also has drawbacks, such as increased likelihood of adverse events and drug interactions, requiring careful tailoring. For example, SSRIs may increase the risk of gastrointestinal bleeding in children with coagulation disorders or in combination with non-steroid anti-inflammatory drugs.

**CROSS-CULTURAL PERSPECTIVES**

Do all youth, regardless of their culture, experience depression and its manifestations similarly or does it vary according to cultural background? There are many obstacles to answering this question. The well documented lack of epidemiological data about childhood mental disorders in the developing world is one. Accordingly, research is limited, unreliable and compounded by variations in diagnostic practices. While cultural considerations in the assessment, diagnosis, and treatment of childhood depression are necessary, it is difficult to disentangle what is biological, what is cultural, and what is due to service issues. For example, it has been suggested the reported increase in rates of childhood depression in North America and Europe may only reflect a lowering of the threshold for diagnosis, while the higher rate of suicide among Chinese young women compared with men as well as its weaker association with depression seem to be largely due to easy access to pesticides and poor access to emergency medical care in rural Chinese communities. Though not specifically relating to depressive symptoms but to behavior and emotional symptoms in general, data available suggest that differences within groups in one society can be greater than differences between societies (Achenbach et al, 2008).

There are many case reports about cultural differences in the manifestation of depression. For example, depressive symptoms in Afghanistan are similar to those
in other countries but in Afghanistan the majority of depressed patients express passive death wishes rather than active suicidal thoughts. Despite suggestions that a higher incidence of guilt feelings in Western countries is due to the influence of the Judeo-Christian religion, when different religions are compared, the presence or absence of guilt feelings is associated with the level of education and the degree of depression rather than with religious background (Inal-Emiroglu & Diler, 2009). Japanese patients do not describe depression in the same way as Americans, nor do they express feelings in the same way. For the Japanese, concrete images from nature allow personal emotions to be expressed impersonally; as a result, they often lack a personal reference or connection when expressing emotions. Rather than as feelings of guilt or low mood, depression is frequently experienced in somatic terms in Hispanic populations. Clinicians must be aware that depressed Hispanic youth may present with headaches, gastrointestinal and cardiovascular symptoms, or complaints of “nerves”. Many Chinese people when depressed do not report feeling sad; they complain of boredom, feelings of inner pressure, pain, dizziness, and fatigue and often find a diagnosis of depression morally unacceptable and meaningless.

BARRIERS IN THE IMPLEMENTATION OF EVIDENCE-BASED CARE IN LOW-INCOME COUNTRIES

There are numerous barriers to the implementation of evidence-based care for depression in developing countries (for more detail see Inal-Emiroglu & Diler, 2009). This is most concerning because the proportion of the population younger than 18 years is much higher in low income than in affluent nations.

Barriers to care exist in all countries but more so in low-income ones. Besides issues such as transportation and the capacity to pay for services, the dearth of professionals, including allied health, trained in this area is a global problem. Not only are there few child and adolescent psychiatrists but also the profession is not formally recognized as specialty in many countries, even in some developed nations. The number of child psychiatrists per million people was estimated around 2006 to be 21 in the United States, 2.8 in Singapore, 2.5 in Hong Kong and 0.5 in Malaysia. With few exceptions, the number of child and adolescent psychiatrists is negligible in most African, Eastern Mediterranean, Southeast Asian, and Western Pacific countries. This also applies to child psychologists, social workers and nurses trained in this area, and to the services available. Gaps are often filled by religious figures (i.e., priests, imams) and healers (see Chapter J.2). Inpatient facilities for children and adolescents do not exist in many countries even developed ones.

Countries in Central and Eastern Europe deserve special mention. They comprise 30 new democracies with a population of around 400 million that had been under communist regimes for 50 to 70 years and have moved to democratic systems of government towards the end of the 20th century (see Chapter J.10). These Central and Eastern European countries had developed a unique system of mental health care driven by Soviet ideology, which focused in residential institutions reflecting state policies based on the social exclusion of vulnerable groups. The usual solution was to institutionalize children when families were in crisis or if children developed problems. Ignoring psychosocial factors was the consequence of believing that psychosocial problems had been successfully solved by the Soviet political system. These attitudes and structures are gradually changing (Puras, 2009).
Parents’, teachers’ and health professionals’ knowledge of, and attitudes towards depression may lead to delayed or inappropriate help-seeking, or may hamper adherence to clinicians’ recommendations. In general, knowledge about depression in developing countries is limited, emotional problems being viewed as more stigmatizing—a sign of weakness, contagious—in some cultures than others. However, stigma appears to be a more significant barrier to treatment in high income than in low income countries. Perceptions of depression are often inconsistent. For example a survey suggested that Turkish people identified depression as an illness, perceived it as a social problem, believed that depression could be treated with drugs but had little knowledge about medications and treatment and were doubtful about society’s acceptance of depressed patients (Inal-Emiroglu & Diler, 2009). Training primary care doctors on the diagnosis and treatment of depression may be the best way to improve treatment.

Access to psychosocial treatments in developing countries is very poor due to lack of trained professionals, so it is access to medication. The WHO’s (2010) list of essential medicines for pediatric patients only includes fluoxetine, while for adults it only includes fluoxetine and amitriptyline for the treatment of mood disorders, as well as lithium carbonate, carbamazepine, and valproic acid for bipolar disorder. Less than half of the countries in the world provide some form of subsidy for medication. Even if medication is prescribed, follow up is likely to be inadequate.

**PREVENTION**

The goal of prevention is to decrease the likelihood of depressive symptoms and disorders from developing in a population (universal intervention). There are other, more targeted, preventative options that may be more useful, for example early intervention with individuals with subclinical levels of depressive symptoms, seeking to reduce these symptoms and prevent the development of a full blown depressive episode: selective (if the target participants have significant risk factors) or indicated prevention (when individuals already show subclinical levels of depressive symptoms). Table E.1.3 lists key risk factors and implications for prevention.

Overall, outcome of prevention programs has been mixed. Targeted (selective and indicated) programs show small to moderate effect sizes but greater than those of universal programs, which have been found to be largely ineffective. The most efficacious programs focus on cognitive restructuring, social problem-solving, interpersonal communication skills, coping, and assertiveness training individually or in groups. Prevention programs are typically conducted with groups of children or adolescents in school or clinic settings (Garber 2009; US Preventive Services Task Force, 2009). One approach that seems to have achieved more success is the *Coping with Depression Course for Adolescents*. The program consists of eight weekly 90-minute group sessions followed by six continuation sessions. In one study the program showed significant sustained effects compared with usual care in preventing the onset of depressive episodes in youth at risk over a 3-year period (Beardslee et al, 2013).
REFERENCES


Brent D, Emslie G, Clarke G et al. Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy for adolescents with SSRl-resistant depression. The TORDIA randomized controlled trial. *JAMA*, 2008; 299:901-913.


Appendix E.1.1

SELF-DIRECTED LEARNING EXERCISES AND SELF-ASSESSMENT

- Interview a child or adolescent who is complaining of depressive symptoms.
- Write a letter to the family doctor or referring agent summarizing the above case (formulation), including a provisional diagnosis and a management plan (as per Chapter A.10).
- Watch the documentary The Girl Less Likely (30 Minutes) [http://www.abc.net.au/austory/specials/leastlikely/default.htm](http://www.abc.net.au/austory/specials/leastlikely/default.htm) and write a summary (less than one page in length) highlighting the main issues raised.
- What are the important medical causes of depressive symptoms that should be considered before making a diagnosis of major depression? (see page 12)
- Write short summary describing risk factors for depression (see Table E.1.3 on page 7).
- Describe and contrast the appropriate management of mild, moderate and severe unipolar depression (see page 23).
- Describe the difference between the treatment of unipolar depression and bipolar depression and the reasons for it (see Page 23 and 24).

**MCQ E.1.1** What class of medication is the first line treatment for severe depression OR moderate depression unresponsive to psychotherapy in children and adolescents?

- A. Monoamine oxidase inhibitors
- B. Selective serotonin reuptake inhibitors
- C. Serotonin norepinephrine reuptake inhibitors
- D. Tetracyclic antidepressants
- E. Tricyclic antidepressants

**MCQ E.1.2** Fluoxetine in the treatment of depression in children and adolescents:

- A. Is the best studied and has the best evidence of effectiveness
- B. Is a Selective Norepinephrine Reuptake Inhibitor
- C. Shows more side effects than the other SSRIs
- D. Is a Monoamine Oxidase Inhibitor
- E. Is a Tricyclic antidepressant

**MCQ E.1.3** Paroxetine in the treatment of depression in youth:

- A. Has a longer half-life than other selective serotonin reuptake inhibitors
- B. Has been shown to be as effective as other antidepressants
- C. Has more side effects than other selective serotonin reuptake inhibitors
- D. Has no withdrawal symptoms
- E. Is less likely to cause a serotonergic syndrome

**MCQ E.1.4** All of the following substances are known to mimic depression in children and adolescents except:

- A. Corticosteroids
- B. Isotretinoin
- C. Marijuana
- D. Solvents
- E. Tetracyclines
MCQ E.1.5  The prevalence of depression in children and adolescents:
A. Is lower in teenage girls than teenage boys
B. Is higher in patients who suffer from chronic medical conditions
C. Is lower in indigenous minority children
D. Is lower in adolescence than in childhood
E. Is the same from country to country

MCQ E.1.6  The course of depression in children and adolescents:
A. Generally does not have recurring episodes
B. Is likely to be better with earlier onset
C. Is likely to continue in adulthood
D. Is not similar to that of adults
E. On average, episodes do not spontaneously remit.

MCQ E.1.7  Predictors of depression recurrence in children and adolescence do not include which of the following?
A. Comorbidity
B. Greater hopelessness
C. High socioeconomic status
D. Negative cognitive style
E. Previous episodes

MCQ E.1.8  All of the following medical conditions are known to mimic depression in children and adolescents except:
A. Acquired Immunodeficiency Syndrome (AIDS)
B. Pyloric Stenosis
C. Mononucleosis
D. Thyroid Disease
E. Migraine

MCQ E.1.9  All of the following should increase suspicion that a depressive episode is part of a bipolar disorder except:
A. Catatonic symptoms
B. Comorbid thyroid disease
C. Family history of bipolar disorder
D. Manic switch after treatment with antidepressants
E. Psychotic symptoms.

Q E.1.10  Parental depression is the most consistently replicated risk factor for depression in the offspring.
True or false?

Q E.1.11  Diagnosis of personality disorder should be provisional in a depressed adolescent and made on the bases of symptoms and functioning outside of the depressive episode.
True or false?

MCQ E.1.12  Which of the following psychosocial therapies has evidence that it can be effective for mild to moderate depression in as few as 8 to 16 sessions?
A. Cognitive Behavioral Therapy
B. Family therapy
C. Group therapies
D. Psychodynamic (psychoanalytic) psychotherapy
E. Self-help

MCQ E.1.13  While antidepressants tend to achieve better results in the short term, differences between medication and therapy tend to disappear after:
A. 2-5 weeks
B. 6-10 weeks
C. 11-18 weeks
D. 19-23 weeks
E. 24-36 weeks
MCQ E.1.14  The most important distinguishing feature in the diagnosis of serotonin syndrome is:

A. Ataxia  
B. Bradycardia  
C. Clonus  
D. Confusion  
E. Diarrhea  

MCQ E.1.15  In a unipolar depressive episode of mild severity in a 10-year-old, the appropriate first intervention is:

A. Anti-depressants  
B. Electroconvulsive therapy  
C. S-adenosyl methionine  
D. Second generation antipsychotic  
E. Supportive management or psychosocial treatment  

MCQ E.1.16  First line therapy for a bipolar depressive episode in a young teenager usually is:

A. An antidepressant  
B. Lamotrigine  
C. Lithium carbonate or quetiapine  
D. Olanzapine and an antidepressant  
E. Valproate and an antidepressant  

Q E.1.17  Antidepressant treatment in an adolescent for a first episode of unipolar depression should be:

A. Continued for at least 6 months after recovery  
B. Continued indefinitely  
C. Continued until recovery  
D. Stopped after 6 months  
E. Stopped after 8 weeks
ANSWERS

• MCQ E.1.1: B; see page 18,19 & 21.
• MCQ E.1.2: A; see page 21.
• MCQ E.1.3: C; see Table E.1.8 on page 21
• MCQ E.1.4: E; see page 12
• MCQ E.1.5: B; see page 2-3.
• MCQ E.1.6: C; see page 3-4.
• MCQ E.1.7: C; see page 4.
• MCQ E.1.8: B; see page 12
• MCQ E.1.9: B; see page 12
• Q E.1.10: True; see page 5
• Q E.1.11: True; see page 8
• MCQ E.1.12: A; see page 16
• MCQ E.1.13: E; see page 17
• MCQ E.1.14: C; see page 23
• MCQ E.1.15: E; see page 16
• MCQ E.1.16: C; see page 23
• Q E.1.17: A; see page 24-25.