Evidence-based treatments for Depression in Children and Youth

Christopher Bellonci, M.D.
Vice President of Policy and Practice
Chief Medical Office
Judge Baker Children’s Center
Overview

Depressive disorders significantly impact functioning and are characterized by sad, empty or irritable mood and somatic and cognitive changes (APA, 2013).

This presentation will focus on two common depressive disorders in children: Major Depressive Disorder and DMDD. The clinical presentation, etiology and treatment differ and so they will be taken on in two parts.
Changes since DSM-IV

• Depressive disorders are given their own chapter in the DSM-5. Previously, they were combined with “Bipolar and Related Disorders” (APA, 2013).

• Two new disorders in the DSM-5 chapter on Depressive Disorders
  – 1) Premenstrual Dysphoric disorder and
  – 2) Disruptive mood dysregulation disorder (DMDD).

• Dysthymia is now called Persistent Depressive Disorder
Depression is categorized by the following disorders:

- Disruptive Mood Dysregulation Disorder (DMDD)
- Major Depressive Disorder
- Persistent Depressive Disorder (Dysthymia)
- Premenstrual Dysphoric Disorder
- Substance/Medication-Induced Depressive Disorder
- Depressive Disorder Due to Another Medical Condition
- Other Specified Depressive Disorder
- Unspecified Depressive Disorder
Major Depressive Disorder (MDD)

- MDD is characterized by **five or more symptoms** of depression present during the **same two-week period** that causes **clinically significant distress or functional impairment**.

- These symptoms must include either depressed mood or loss of interest or pleasure in all or almost all activities (in children mood can be irritable instead of sad).
Other symptoms can include:

• Significant weight loss or weight gain/decreased or increased appetite nearly every day
• Insomnia or hypersomnia nearly every day
• Psychomotor agitation or retardation nearly every day
• Fatigue or loss of energy nearly every day
• Feelings of worthlessness or excessive guilt nearly every day
• Difficulty thinking, concentrating or making decisions nearly every day
• Recurrent thoughts of death, suicidal ideation or suicide attempt
SIGECAPS

S = Sleep
I = Interest
G = Guilt
E = Energy
C = Concentration
A = Appetite
P = Psychomotor
S = Suicidal
There are many specifiers to consider in MDD

• Major depressive disorder:
  – single episode
  – recurrent episode
  – Severity (mild, moderate, severe)
  – With Psychotic features
  – remission specifiers,
  – followed by additional specifiers (such as with seasonal pattern, with anxious distress, etc.)
Other considerations

• Many bipolar illnesses begin as a depressive episode (sometimes more than one depressive episode)

• Depression with psychotic or mixed features increases later risk for bipolar disorder.

• Psychotic features can also indicate the possible future development of schizophrenia

(APA, 2013)
Differentiating from developmentally appropriate sadness

• Sadness is a commonly experienced emotion. Even periods of being down can be developmentally normal. A key diagnostic feature is that symptoms need to last most of the day, nearly every day for a two-week period.

• What is sadness over a loss, such as death or a divorce, versus depression?

• APA notes that the predominant effect of grief is feelings of emptiness or loss while in major depression symptoms are more consistent with persistent depressed mood or inability to anticipate happiness.
Grief

• Grief is often tied to thoughts of the deceased and people with grief can experience humor or positive emotions and whereas those with major depression often cannot.

• Another distinguishing feature is that with grief self-esteem is preserved, but not so with major depression.

• A bereaved person can have thoughts of dying in order to join the deceased – these aren’t necessarily symptomatic of depression because in depression thoughts of death are related to feelings of worthless or inability to cope. (APA, 2013)
Clinical Presentation

• Differences based on age
  – **Preschool age** - “Nothing is fun.” “I’m bored.” These children aren’t engaging the play-based interactions that you’d expect. Their outlook is gloomy. They lack self-esteem – “I can’t draw.”
  – **School age** – A child who used to love sports may find reasons to not go to practice. Children with depression may fail to meet expected weight gain.
  – **Adolescent** – Mood swings in adolescents are normal, but persistent depressive feelings and functional impairment are markers for MDD.
Prevalence

- **Preschool**
  - Depression has been validated in children as young as age 3 (Luby, 2009)
  - 40-60% have comorbid disorders including ADHD and oppositional defiant disorder (Luby, 2009).
  - Epidemiologic study of 2-5 year olds in pediatrics practices in NC showed a rate of 2.1% (Egger & Arnold, 2006)

- **School-age**
  - In children 7 to 15 years old, 2% of boys and 4% of girls reported MDD in the past year (Siu, AL, U.S. Preventive Services Task Force, 2016)
Adolescent Prevalence

- Adolescents
  - In 2014, **11.4%** of the population aged 12 to 17 years experienced at least one depressive episode (12-month prevalence) (NIMH).

- **Females lifetime prevalence 15.9%, more than twice that of males** (NCS-A).

- Can appear at any point, but likelihood of onset increases with puberty and incidence peaks in the 20’s.

- Comorbidity: frequent co-occurrence with panic disorder, OCD, eating disorders and substance use disorder. (APA, 2013)
Risk and Prognostic Factors

• **Temperament** – negative affectivity (APA, 2013)

• **Environmental** – adverse childhood experiences represent both a risk factor for and precipitant of major depression (though there need not be specific precipitant for a major depressive episode)

• **Genetic and physiological** – first-degree family relatives with MDD are two to four times more likely to experience MDD than the general population, but the risk may be greater for early-onset and recurrent depression. (APA, 2013)
Assessment

• Diagnostic interview
• Collateral information
• Screening tools
  – Patient Health Questionnaire for Adolescents (PHQ-A), designed for children 11 – 17 years old and is well-validated. It is available for free. US Preventive Services Task Force
  – Beck Depression Inventory and Children’s Depression Inventory are both widely used in research, but they are costly to purchase.
  – US Preventive Services Task Force found inadequate evidence for depression screening tools in children 11 years old and younger (2016)
Treatment

• Treatment is difficult and requires partnership between the clinician, child and family.

• 30-50% of youth are non-responsive to the first treatment approach, including SSRIs, CBT and the combination of CBT and SSRI (McMakin, et al., 2012).

• Choosing your treatment approach, First-line options differ by age and development
Preschool age

- Dyadic developmental approaches (focusing on both the child and parent together)
- Parent-Child Interaction Therapy – Emotional Development (PCIT-ED)
  - Long-established and effective treatment for disruptive behavior in childhood adapted to treat depression.
  - Short-term (14-session) manualized program whereby a trained therapist helps parents engage their child in ways that increase emotional regulation, coping skills, and combats negative thoughts.
  - Uses a one-way mirror and ear-bud to microphone communication system whereby the therapist can coach the parent.
  - The child learns the skills and the parents learn how to reinforce the skills (Luby, 2009).
Preschool Age (cont’d)

Child FIRST (Child and Family Interagency, Resource, Support, and Training)

• Home-based, psychotherapeutic program for families with children from birth to six years (also can include pregnant women)

• Lasts between six and 12 months.

• The program seeks to prevent or reduce children’s emotional, behavioral, developmental, and learning problems, and prevent or reduce abuse and neglect by their caregivers (SAMHSA, 2016).
Child FIRST (cont’d)

- Two-member team consisting of a care coordinator and clinician.
  - Care coordinator links the family to local activities and providers.
  - Clinician is trained to provide trauma-informed, child–parent psychotherapy to build parenting skills and improve the parent child relationship.
  - Team meets with the family weekly, or more if needed.
- The program has strong evidence for reducing maternal depression, but not for reducing child internalizing behavior problems. ([www.childfirst.com](http://www.childfirst.com)). (SAMHSA, 2016).
School Age

- **CBT** for school age children (Luby, 2009)
- Modular Approach to Therapy for Children with Anxiety, Depression, Trauma, or Conduct Problems (**MATCH-ADTC**)  
  - Addresses not only *anxiety, depression, trauma-related issues, or conduct problems*, but also related issues or challenges that may emerge during therapy.
  - Developed from a review of meta-analyses of evidence-based treatments and the *commonly used components* in practices for children and adolescents.
  - Modules include components of cognitive behavior therapy, parent training, coping skills, problem solving, and safety planning.
Adolescents

• **CBT for Adolescent Depression** (CBT-AD) has strong evidence to support its efficacy (SAMHSA NREPP, 2006; Luby, 2009).

  – CBT-AD adapts CBT steps and tools to adolescents’ developmental needs. It uses more concrete examples, explores autonomy and trust issues and focuses on cognitive distortions, affective awareness/regulation, problem-solving, and social skills.

  – Typically last 12-16 weeks.
Attachment Based Family Therapy

• The model is based on an **interpersonal theory of depression**.

• Proposes that the quality of family relationships may precipitate, exacerbate, or prevent depression and suicidal ideation.

• Ruptures in family relationships, such as those due to abandonment, neglect, or abuse or a harsh and negative parenting environment, influence the development of adolescent depression.

• Families with these attachment ruptures lack the normative secure base and safe haven context needed for an adolescent's healthy development, including the development of emotion regulation and problem-solving skills.

• Designed for adolescents **ages 12-18**. Involves **semi-structured protocol with clearly defined process and goals**.

• Evidence that it is effective for treating depression and suicidal ideation and reduces anxiety (SAMHSA NREPP)
Interpersonal Psychotherapy (IPT)

- IPT is a *brief, time-limited psychotherapy* that seeks to reduce symptoms of depression and improve social functioning.
- Well established treatment for depression first developed in the 1960’s with roots going back to Bowlby’s attachment theory and focus on the important of relational bonds for mental health.
- Its efficacy in treating adolescent depression was demonstrated in 1996 and has been replicated since (Society of Clinical Child and Adolescent Psychology, 2012)
Other therapies identified as effective (as defined by SAMHSA NREPP)

• Adolescents Coping with Depression (CWD-A)
• Culturally Informed and Flexible Family Based Treatment for Adolescents (CIFFTA), and
• Relapse-Prevention CBT
• Computer-based Cognitive Behavioral Therapy-Beating the Blues
Therapies identified as Promising

- These are therapies that have demonstrated efficacy in a limited number of studies or non-RCT designs.
- The EBP databases (NREPP, CEBC, Blueprints, etc.) are being constantly updated as new interventions are investigated and existing programs are replicated.
Medication Management

• Psychopharmacological interventions aren’t considered first or second-line treatment in preschool age children (Luby, 2009). There are no FDA-approved medications for the treatment of depression in the preschool age-group.
Treatment of Adolescents with Depression Study (TADS)

- Provided evidence for current standard treatment
- Study of 439 adolescents (12-17 years old) with MDD, who were randomized to one of four study arms:
  1. Fluoxetine (Prozac) alone;
  2. CBT alone;
  3. Fluoxetine and CBT; and
  4. Pill placebo

(TADS Team, 2004)
TADS Conclusions:

- Rates of response for fluoxetine with CBT were 71.0% (95% confidence interval [CI], 62%-80%)
- Fluoxetine alone, 60.6% (95% CI, 51%-70%);
- CBT alone, 43.2% (95% CI, 34%-52%);
- Placebo, 34.8% (95% CI, 26%-44%)
- Combination treatment and fluoxetine alone had significantly faster time to response than pill placebo
- Combination treatment had significantly faster time to response than CBT

(TADS Team, 2004)
Treatment of Resistant Depression in Adolescents (TORDIA)

• Large study of 334 adolescents with depression who did not respond to SSRI medications.

• Used randomized assignment to a medication switch alone or a medication switch plus CBT over 24-weeks.

• TORDIA had four treatment arms – 1) switch to different SSRI, 2) switch to different SSRI plus CBT, 3) switch to venlafaxine (trade name Effexor), and 4) switch to venlafaxine plus CBT. (Brent, DA, et al., 2008).
TORDIA Conclusions:

• “For adolescents with depression not responding to an adequate initial treatment with an SSRI, the combination of cognitive behavioral therapy and a switch to another antidepressant resulted in a higher rate of clinical response than did a medication switch alone. However, a switch to another SSRI was just as efficacious as a switch to venlafaxine and resulted in fewer adverse effects.” (Brent, DA, et al., 2008).
TORDIA Conclusions (cont’d)

• Likelihood that a treatment will lead to remission is evident fairly early in treatment – in TORDIA, at 6-weeks, the patients whose symptoms would remit versus those whose symptoms would not remit started to show divergent trajectories. At 12 weeks, those with treatment response predicted a threefold higher likelihood of eventual symptoms remission as compared to non-responders (Emslie, GJ, et al., 2010).
TORDIA Conclusions (cont’d)

• Nevertheless, **remission rates at the end of 24-weeks in TORDIA were only 40%** (Emslie, GJ, et al., 2010).

• Anhedonia (the inability to experience pleasure in normally pleasurable acts) is uniquely predictive of longer time to recovery in adolescents in the TORDIA trial (McMakin, et al., 2012).
Additional Combination Trials

- 2015 study of 144 youth (ages 8-17) with MDD, showed CBT following acute medication management (MM) significantly reduces relapse rates as compared to those receiving medication management alone.

- CBT plus MM during treatment period (30 weeks) resulted in relapse rate of 9% versus relapse rate of 26.5% for those receiving MM alone.

- At 78-weeks (long-term assessment following study) MM+CBT maintained relapse prevention gains over MM alone (relapse rate of 36% versus 62%).

- Over a third of precipitants experienced relapse. Remission rate among both groups were similarly high at greater than 90%. (Emslie, et al., 2015)
Recent meta-analysis (34 trials eligible, including 5260 participants and 14 antidepressant treatments) in the Lancet showed only fluoxetine (name brand is Prozac) to be statistically significantly more effective than placebo (Cipriani, et al., 2016).
Suicide Risk Factors

• Adolescence through young adulthood is the peak time for the emergence of suicidal thoughts and behaviors (Goldston, et al 2016).
• Adolescents can be particularly challenging to engage in consistent treatment (Mehlum, et. al., 2016).
• Comorbid borderline personality disorder, smoking, past substance use disorder or alcoholism, family history of suicidal acts, head injury, and child-hood abuse history increase risk for suicide attempt (Mann et al., 1999).
Suicide Risk Factors (cont’d)

• Past attempts and threats, but most completed suicides aren’t preceded by failed attempts (APA, 2013).

• Being male, living alone, access to lethal means (e.g. Guns) and feelings of hopelessness are associated with risk for completed suicides.
Treatment for SI and self-harming behaviors

• Recent study looking at outcomes of dialectical behavioral therapy for adolescents (DBT-A) versus enhanced usual care (EUC) for adolescents with repeated suicidal and self-harming behaviors showed that DBT-A far outperforms EUC during the 19-week treatment period.

• After one year, the outcomes were not significantly different. Adolescents in the DBT-A arm largely maintained their gains in reducing depression and suicidal/self-harming behaviors; notably the clinical status of those in the EUC arm improved significantly (Mehlum, et al., 2016).
Treatment for SI and self-harming behaviors (cont’d)

Two significant conclusions are noted:

– While DBT-A led to a more rapid decline in symptomology, the usual therapy that most in the EUC group where engaged in was also effective over the year-long period.

– Adolescents with repeated suicidal and self-harming behaviors are in fact treatable.

(Mehlum, et al., 2016)
Disruptive Mood Dysregulation Disorder (DMDD)

• DMDD is characterized by 1) chronic, severe irritability and 2) frequent episodes of extreme verbal rages and/or behavioral dyscontrol that are inconsistent with the child’s developmental level.

• These episodes typically occur three or more times a week in at least two settings (eg. Home, school community) and are grossly out of proportion to the provocation.

• These symptoms need to be present for more than 12 months and not absent for more than three months in that time frame. (APA, 2013)
DMDD (cont’d)

• The diagnosis shouldn’t be made before age 6 or after age 18, and symptoms must be present by age 10 years.

• The diagnosis cannot coexist with oppositional defiant disorder, intermittent explosive disorder and bipolar disorder. It can coexist with other disorders, including major depression, ADHD, and conduct disorder. If manic or hypomanic symptoms have ever been present, an individual cannot be diagnosed with DMDD. (APA, 2013)
DMDD (cont’d)

• The new diagnosis was created in part to address concerns related to the over-diagnosis of bipolar disorder (APA, 2013) and rapid increase in the use of atypical antipsychotic medication in children (Olfson).

• Before the existence of the DMDD diagnosis, NIMH studied a disorder they labeled “severe mood dysregulation” (SMD), which is where some of the best data on DMDD comes from. Research on SMD helped establish DMDD as a separate disorder from bipolar disorder (Baweja, 2016).
SMD is different that DMDD in some important ways

• SMD required recurrent temper outbursts, a persistent negative mood (which, unlike DMDD, includes depressed mood), and the presence of at least three “hyperarousal” symptoms (pressured speech, racing thoughts or flight of ideas, intrusiveness, distractibility, insomnia, and agitation).

• These hyperarousal criteria were included because it was these symptoms in persistently irritable children that often led to a concern about mania. Also, age of onset for SMD was before age 12 years and the maximum symptom-free period was 2 months. (Baweja, 2016).
How does one differentiate DMDD from a pediatric bipolar disorder?

- In DSM-5, the diagnosis of bipolar disorder is only used in cases of episodic presentations of bipolar symptoms – **there must be discrete episodes of mood deviation**.

- Elevated or expansive mood and grandiosity are characteristic of bipolar disorder, not DMDD. Severe and *chronic* irritability were being labeled as bipolar disorder in children before the establishment of this new diagnosis (APA, 2013).
How does one differentiate DMDD from oppositional defiant disorder (ODD)?

• ODD symptoms are common in DMDD, but **mood symptoms** (severe and chronic irritability in between outbursts) characteristic of DMDD are **not common** in ODD.

• **DMDD symptoms must occur in at least two settings**, whereas ODD can be diagnosed if symptoms are present in just one setting.

• Most children who meet criteria for DMDD, will also meet criteria for ODD. Only a DMDD diagnosis is given in these cases.

• Only 15% of children with ODD would meet criteria for DMDD – in these cases a DMDD diagnosis only is given. (APA, 2013)
Clinical Presentation of DMDD

• DMDD diagnosis isn’t made before 6 years old

• **Not just severe temper tantrums** – 80% of preschoolers were found to have had severe temper tantrums in last 3 months.

• 46-49% of school-age children were found to have had severe temper tantrums in last 3 months. (Copeland, et al., 2013)
Functional Consequences of DMDD

• Family, peer relationship and school consequences can be severe - “The school-age youth with DMDD experienced significant social impairment (relationship with parents, siblings, and teachers), school suspension, and service use (mental health and general medical)” (Copeland et al., 2013).

• Dangerous behavior, including aggressive behavior and suicidal ideation/suicide attempts “are common” (no actual statistics given - APA, 2013).
Prevalence of DMDD

• Cultural/ethnographic variables – data isn’t available
• Because it’s a new diagnosis, prevalence is unclear. There is data on rates of chronic and severe persistent irritability, the central feature of DMDD, which suggest that the 6-12 month period-prevalence for DMDD is 2%-5% (APA, 2013).
• It’s likely that rates are higher in males than females and higher in school-age children than adolescents (APA, 2013).
• Analysis of three large studies showed DMDD prevalence rate at around 1% for school-age children and around 3.3% for preschoolers. (Copeland et al., 2013)
Etiology and course of DMDD

– Very few children with severe, chronic (non-episodic) irritability develop bipolar disorder. Instead, these children are at risk to develop unipolar depression or anxiety disorders in adulthood (APA, 2013).

– Bipolar disorder is quite rare prior to adolescence (<1%) and increases into early adulthood (1-2%). DMDD is more common in younger children and becomes less common as children age (APA, 2013).
Etiology and course of DMDD (cont’d)

• The presence of co-morbid conditions is more common with DMDD than many other pediatric mental health disorders and the breadth of co-morbid disorders is also greater than with other pediatric mental health disorders (APA, 2013).

  – In a large nationally representative sample, 92.8% of DMDD-positive youth met the criteria for another DSM-IV disorder including mood disorders, conduct/ODD, ADHD, and substance abuse (Baweja, 2016).
Etiology and course of DMDD (cont’d)

- In NIMH studies, youth with SMD had extremely high rates (≥75%) of attention-deficit hyperactivity disorder (ADHD) and oppositional-defiant disorder (ODD), as well as anxiety disorders (58%) (Baweja, 2016).
- The most common co-morbidity is ODD (though if ODD is present, only DMDD diagnosis is given) (APA, 2013).
- Other common co-morbid conditions include major depression, ADHD, anxiety and autism spectrum disorders (APA, 2013).
Risk factors for DMDD

Temperamental: chronic irritability

Genetic: family histories of anxiety disorders, depressive disorders and substance use disorders (APA, 2013)
Assessment of DMDD

• Assessment is entirely through clinical interview, engagement, observation and collateral communication.

• There are no well-validated rating scales to assist in diagnosis of DMDD.
Choosing your treatment approach for DMDD

• First-line options – Because it’s a relatively new diagnosis, there is limited information on diagnosis specific treatment.

• Treatment is informed by evidenced-based interventions for disorders that share core features, including depression, ADHD, ODD and anxiety disorders (NIMH, 2016).
Psychotherapy for DMDD

• CBT is effective in treating depression and anxiety and can be adapted to working with children who have mood dysregulation.

• Cognitive-behavioral-like therapy can be used to help children identify negative thoughts and build frustration tolerance.

• CBT also teaches coping skills and helps children re-interpret agitating stimuli (NIMH, 2016).
Parent training for DMDD

• In parent-training a clinician works directly with the parents to develop more effective ways to respond to their children’s moods and behaviors.

• Parents learn to anticipate triggering events, create predictable routines and consistent responses to behaviors, and reward positive behaviors (NIMH, 2016).
Computer-based training

- There is early evidence to show that children with DMDD misinterpret ambiguous facial expressions as angry (NIHM, 2016) and experience greater fear when viewing neutral faces (Baweja, 2016). Computer-based training can help correct this problem.
Medication Treatment for DMDD

• Stimulants
  – Stimulants may help irritability in children with co-morbid ADHD (NIMH, 2016)

• Antidepressants
  – Research is ongoing as to whether antidepressants may be helpful for DMDD (NIMH, 2016)
Second generation antipsychotics (SGAs) for DMDD

- Reserved for only the most severe cases associated with physical aggression, property damage or self-harm (NIMH, 2016)
  - Aripiprazole and risperidone are FDA-approved to treat irritability in children diagnosed with autism and are sometimes used to treat children with DMDD.
  - There are significant risks associated with SGAs, including potential weight gain, metabolic abnormalities, sedation, movement disorders, hormone changes, and suicidal ideation (NIMH, 2016).
  - SGAs require blood work, which can be challenging to obtain from some children.
Other considerations

• Ensuring these evidence based interventions are available in the service array and accessible

• Workforce development (training, coaching, supervision, certificate programs)

• Fiscal issues (e.g. incentives for implementing EBPs, $ for training and ongoing professional development) need attention in the system to ensure providers to whom youth may be referred are capable of implementing the most effective programs for depressive disorders... esp in light of the 10-15% prevalence rate in adolescents
Other considerations (cont’d)

• Ensuring that care coordinators / wrap facilitators are aware of the need to access relevant EBPs for depression (and other diagnostic categories) when planning with a youth/family/team, and know who provide such treatments

• Building capacity for peer to peer support in a system and service array so that there are other relevant supports readily available, esp. to adolescents who may be struggling with depression and other challenges