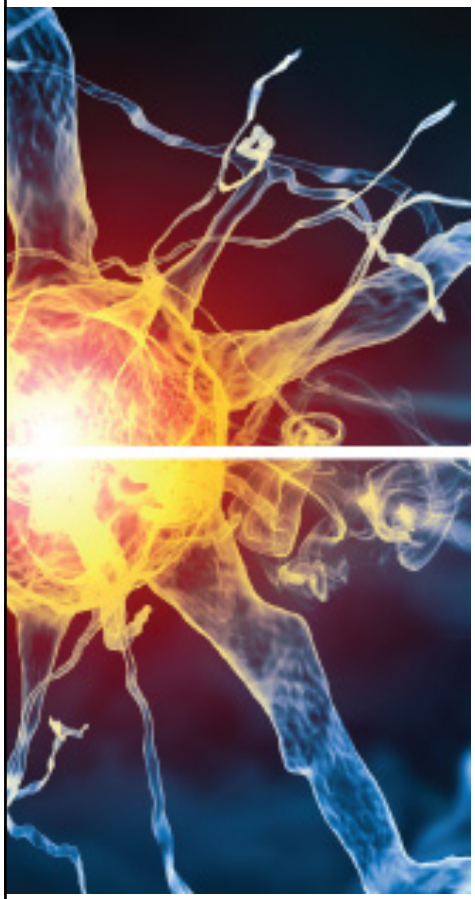
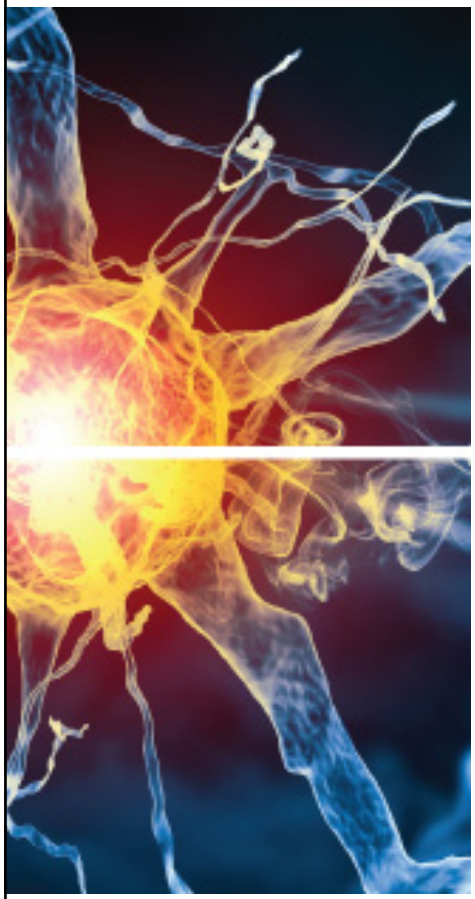


Mood Disorders in Children and Adolescents



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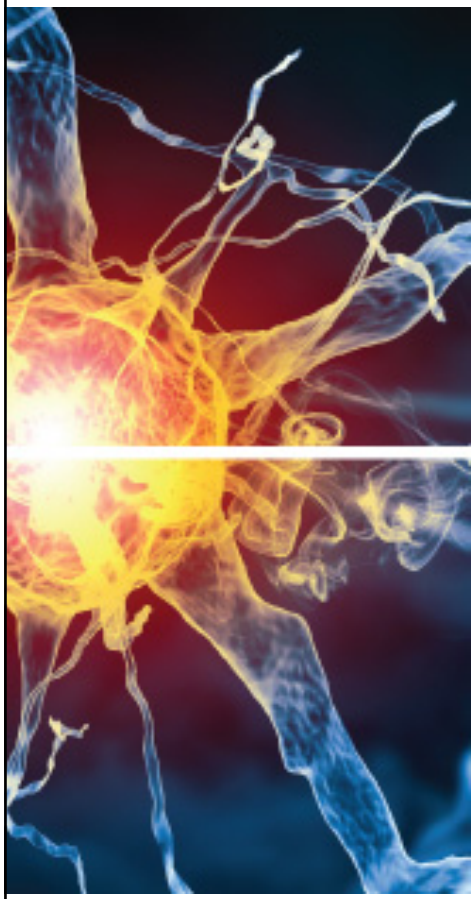
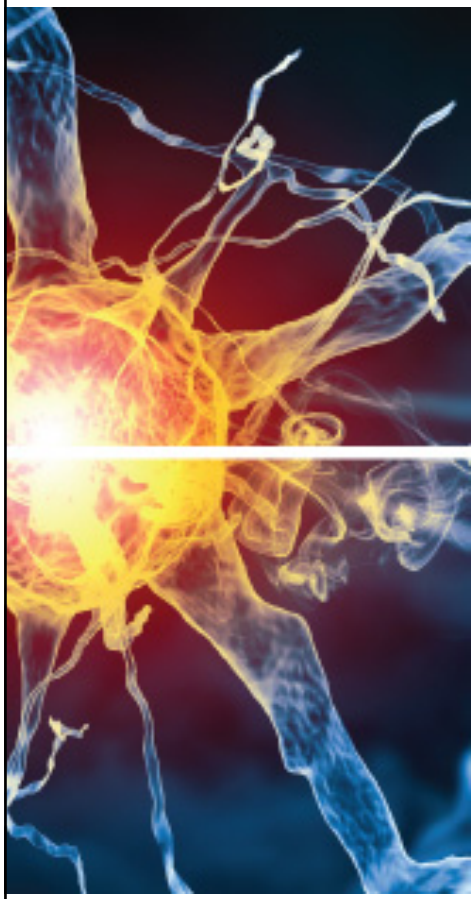
- ***Advisory Board***: Sunovion Pharmaceuticals



1 Learning Objective

Integrate evidence-based, best-practice options in children and adolescents for the management of major depressive disorder (MDD) and bipolar disorder (BD).



2 Learning Objective

Review the safety of early intervention strategies for treating youth with and at high risk for developing mood disorders.

Mechanisms of Mood Disorders

Children vs. Adults

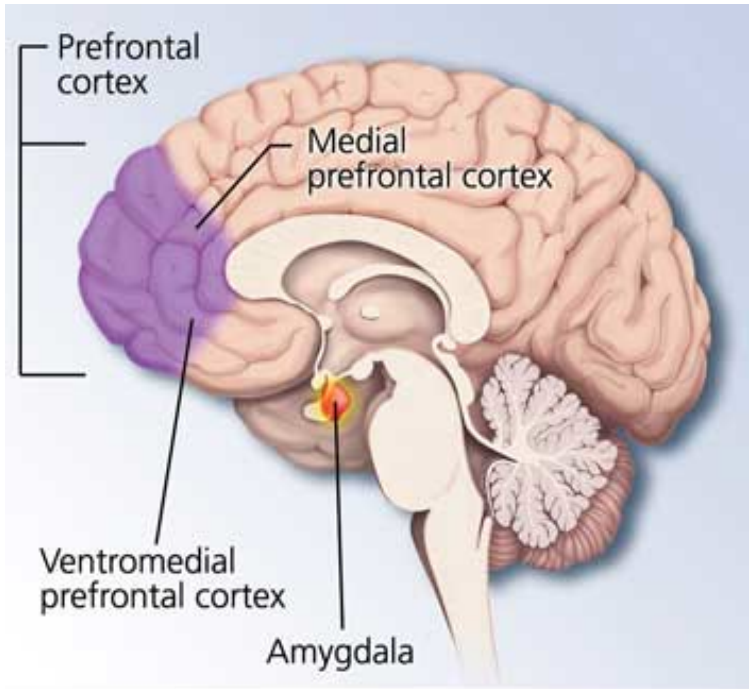
- Overall, the clinical picture of mood disorders in youths is similar to the clinical picture in adults
- Differences may be attributed to a child's physical, emotional, cognitive, and social developmental stages
  - Mood lability, irritability, low frustration tolerance, temper tantrums, somatic complaints, and/or social withdrawal instead of verbalizing feelings of depression
  - Fewer melancholic symptoms and delusions
  - More suicide attempts in adolescents than depressed adults

Birmaher B, et al. *J Am Acad Child Adolesc Psychiatry*. 1996;35:1575-1583; Fergusson DM, et al. *Psychol Med*. 2005;35:983-993; Kaufman J, et al. *Biol Psychiatry*. 2001;49:980-1001; Nock MK, et al. *JAMA* Psychiatry, 2013;70(3):300-310.

Major Brain Mood Centers

Prefrontal cortex:
- Develops more in adolescence
- Executive function
- Regulates emotion

MANIA
Euphoria (3)/irritability (4)
x 1 week plus:
Distractibility
Increased goal directed activity
Grandiosity
Flight of ideas
Accelerated speech
Sleep, decreased need
Trouble



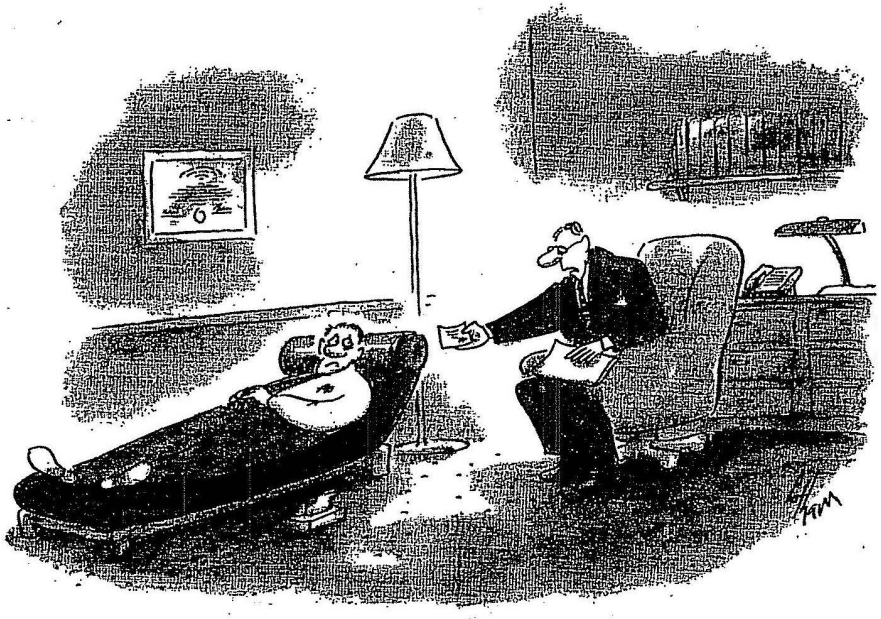
Brain Structures Involved in Dealing with Fear and Stress

DEPRESSION
Sad or Irritable
x 2 weeks plus:
Sleep
Interest
Guilt
Energy
Concentration
Appetite
Psychomotor changes
Suicide

Limbic system:
- Primitive
- Amygdala
- Controls moods
- Fight or flight

American Psychiatric Association. Diagnostic and Statistical Manual (5th ed.). 2013.
Drevets WC, et al. *Brain Struct Funct*. 2008;213(1-2):93-118.

Treatment Strategies



"I medicate first and ask questions later."

Balance between behavioral/cognitive/ psychosocial and psychopharmacological interventions

Treatment of Pediatric Depression (Case)

- Jane and Rob took their 9-year-old son Blue to see a psychiatrist when they became concerned about his behavior during their divorce. When his parents separated, Blue was irritable and began defying teachers and having confrontations with other children. Blue's work began to suffer due to poor concentration and unsubmitted homework, and he started having trouble sleeping, often waking up as much as four times in the night. He also complained frequently of no appetite and tummy aches, stopped playing football with his club due to lack of energy, and lost interest in all of his after school activities.

FDA-Approved Agents for Pediatric Depression

Acute Depression

- 1987 Fluoxetine (8-18 years)
- 2002 Escitalopram (12-17 years)
- SSRIs most frequently prescribed (63.7%)
- Only 9.2% of the visits with FDA-approved indications
- Visits made to pediatricians (adjusted OR = 2.4; 95%CI: 1.1-5.1), family physicians, and other offices (adjusted OR = 1.9; 95%CI: 1.2-3.1) were more likely to be associated with off-label prescribing as compared with visits to a psychiatrist's office

SSRI = Selective serotonin reuptake inhibitor

Lee E, et al. *Pharmacoepidemiol Drug Saf.* 2012;21(2):137-144.

Phases of Treatment and Tools

Phases

- Acute (6-12 weeks)
- Continuation (to prevent relapses) (6-12 months)
- Maintenance (to prevent recurrences) (≥ 1 year)

Tools

- Psychoeducation
- Psychotherapy
  - Psychodynamic Psychotherapies
  - Cognitive Behavioral Therapy (CBT)
  - Interpersonal Psychotherapy (IPT)
  - Supportive Psychotherapy
  - Family Therapy
  - Group Psychotherapy
  - Most studies utilize CBT and to a lesser extend interpersonal psychotherapy (IPT)
  - Most studies have been done with adolescents
  - Overall results: **60%-70% vs. Controls: 30%-50%**
- Pharmacotherapy

Wenzel, A. (Ed.). *The sage encyclopedia of abnormal and clinical psychology* (Vols. 1-7). Thousand Oaks, CA: SAGE Publications Ltd. 2017.

Controlled Pediatric MDD Studies[1]

	Medication	Reference	Ages	Number of studies
Positive studies*	Fluoxetine	Emslie et al. [16], Emslie et al. [17], TADS [19], Almeida-Montes & Friederichsen [15]	6–17	4
	Escitalopram	Emslie et al. [20]	12–17	1
	Sertraline	Wagner et al. [22] **	6–17	1 (a priori pooled analysis, individual trials negative)
Negative studies	Escitalopram	Wagner et al. [21]	6–17	1
	Citalopram	von Knorring et al. [23]	13–18	1
	Paroxetine	Keller et al. [25], Emslie et al. [27], Berard et al. [26], Paroxetine Trial 1 [28]	7–17	4
	Venlafaxine	Emslie et al. [29]**	7–17	2
	Mirtazapine	Mirtazapine Trials 1 & 2 [30]**	7–17	2

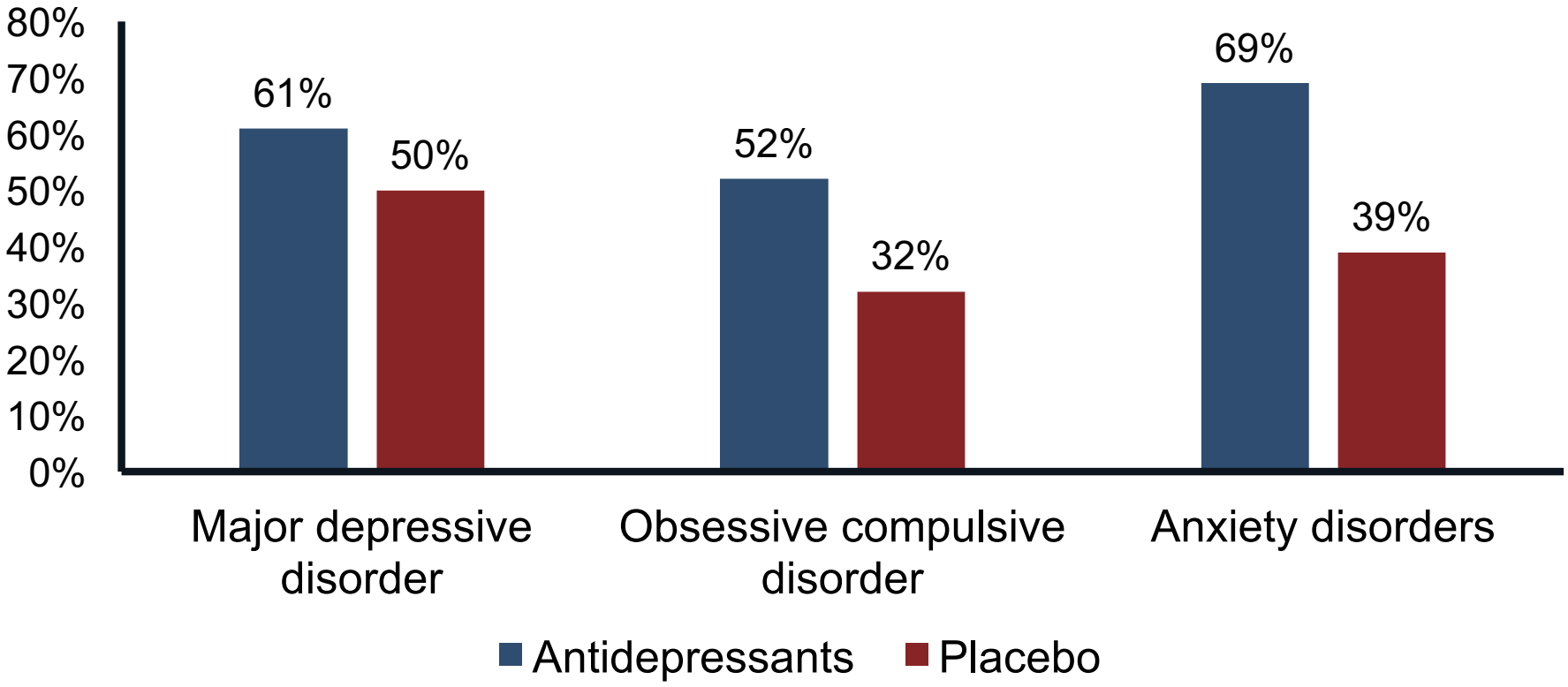
*On primary outcome measure

**References 22, 29 and 30 include two trials in one paper

Additional Negative study: Duloxetine, ages 7-17, 2 studies[2,3]

1Soutullo C, et al. Curr Psychiatry Rep. 2013;15(7):366; 2Emslie GJ, et al. *J Child Adolesc Psychopharmacol*. 2014; 24(4):170–179; 3Atkinson SD, et al. *J Child Adolesc Psychopharmacol*. 2014;24(4):180-189.

Acute Effects of SSRIs for MDD, Anxiety and OCD



Bridge JA, et al. *JAMA*. 2007;297(15):1683-1696.

Antidepressants Dosages Commonly Used MDD Treatment in Youth

Medication group	Medication	Starting dosage (mg/day)*	Dosage range (mg/day)*
SSRIs	Citalopram**	20	20–40[a]
	Escitalopram	10	10–20
	Fluoxetine	10	10–20
	Fluvoxamine**	25	50–150
	Paroxetine**	20	20–50
	Sertraline**	50	50–200

[a]Dose adjusted by U.S. Food and Drug Administration recently because of concerns about QT prolongation.

***With the exception of escitalopram and fluoxetine, indicated dosages are for adults. In children consider using lower dosages.**

**Citalopram, fluvoxamine, paroxetine, and sertraline not FDA-approved for the treatment of MDD in youths [Package Inserts]. Drugs@FDA Website

Antidepressants Dosages Commonly Used MDD Treatment in Youth (cont.)

Medication group	Medication	Starting dosage (mg/day)*	Dosage range (mg/day)*
SNRIs	Venlafaxine XR**	37.5-75	37.5–225
	Duloxetine**	40-60	60- 120
Others	Bupropion SR**	150	150–400
	Bupropion XL**	150	150–450

SNRI = serotonin-norepinephrine reuptake inhibitor; SR = sustained release; XL = extended release; XR = extended release

*I**ndicated dosages are for adults. In children consider using lower dosages.**

**Not FDA-approved for the treatment of MDD in youths

[Package Inserts]. Drugs@FDA Website.

Medication for Youth Depression: SSRI Side Effects

Number Needed to Harm (NNH) = 112

Side Effects of SSRIs: May attenuate over several weeks. In general, any SSRI may cause: nausea, anxiety, agitation, anorexia, tremor, somnolence, sweating, dry mouth, headache, dizziness, diarrhea, constipation, sexual dysfunction

Medication	Anticholinergic Side Effects	Sedating Effects	
Fluoxetine	+, especially nausea, sexual dysfunction	+	FDA-approved for MDD
Escitalopram	+	+	FDA-approved for MDD
Citalopram	+	+	
Sertraline	0, especially diarrhea & male sexual dysfunction	+	FDA-approved for teen OCD

[Package Inserts]. Drugs@FDA Website

Common Side Effects: Other Agents

Name/Class	Side Effects
Bupropion	Hypertension, tachycardia, headache, tremors, dizziness **Serious (rare):** seizures, cardiac dysrhythmia, anaphylaxis
Venlafaxine XR	Tachycardia, hypertension, sweating, weight loss, loss of appetite, nausea, constipation, dizziness, headache, insomnia, somnolence, blurred vision, abnormal ejaculation **Serious (rare):** hyponatremia, hepatitis, seizure, NMS
Duloxetine	Nausea, headache, decreased weight, and abdominal pain.
Trazadone	Sedation, sweating, constipation, diarrhea, nausea, dizziness, headache, insomnia, memory impairment, blurred vision. **Serious (rare):**Priapism in males, cardiac dysrhythmia
Nefazadone	Cough; **Serious (rare):** orthostasis, liver failure, seizure
Mirtazapine	Sedation, weight gain, hypercholesterolemia, constipation, liver dysfunction, dizziness **Serious (rare):** agranulocytosis, neutropenia, seizure
Tricyclic Antidepressants	Weight change, bloating, constipation, appetite loss, nausea, dry mouth, asthenia, dizziness, headache, somnolence, blurred vision, fatigue. **Serious (rare):** cardiac dysrhythmia, myocardial infarction, sudden death, agranulocytosis

[Package Inserts]. Drugs@FDA Website.

Treatment of Resistant Depression in Adolescents (TORDIA)

- Depressed adolescents who failed to respond to an 8 week trial with a SSRI were randomly assigned for another 12 weeks to:
  - Another antidepressant (citalopram/fluoxetine), venlafaxine, or SSRI + CBT, or venlafaxine plus CBT
- Response rates were better for CBT+ antidepressant (55%) than antidepressants alone (41%)
- Predictors of response: less severe depression, less family conflict, no self-injurious behavior

Wagner KD, et al. *J Child Adolesc Psychopharmacol*. 2012;22(1):5-10.

Treatment Recommendations

- Management of negative events, school issues, etc
- Treatment of Parents – Family
- Ultimate goal is REMISSION
- Management of disorder “side effects”
- Management of comorbid disorders

Treatment Challenge: How should we treat depressed youth who are at high-risk for BD?

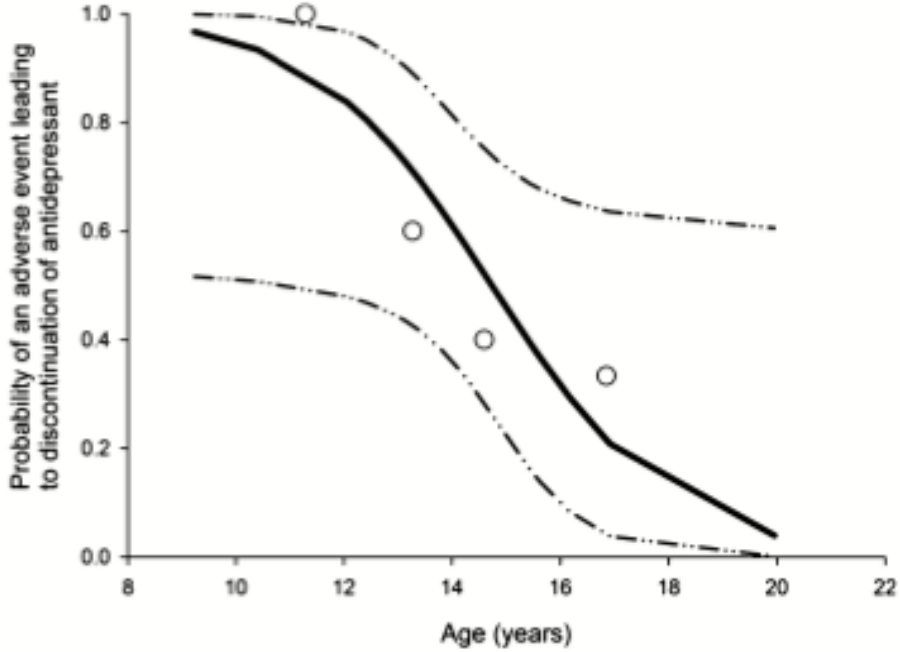
Well…definitely therapy first if possible…then…

- SSRI?
- Buproprion?
- Lamotrigine?
- Lithium?
- Quetiapine?

BD = bipolar disorder

Mania in SSRI Trials in Youth

- At least 29 published case reports describe pediatric patients with treatment emergent mania or hypomania when exposed to SSRIs
- Pooled together these studies report hypomanic or manic symptoms that appear any time between 2 wks to 1 yr after initial SSRI exposure.
- In 21% of such patients represented in these studies, there was a family history of BD.



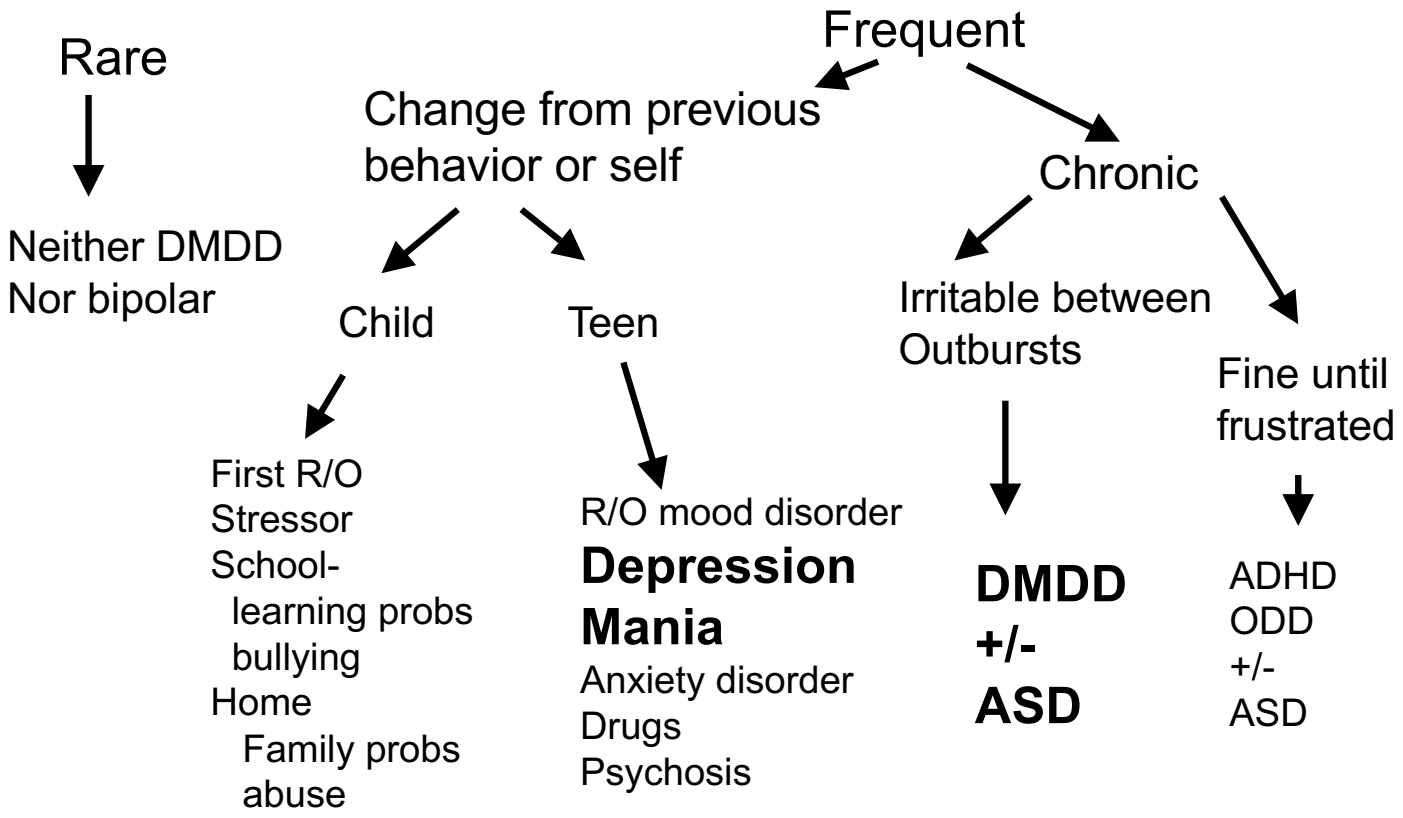
Goldsmith M, et al. *Paediatr Drugs*. 2011;13(4):225-243.
Strawn JR, et al. *Bipolar Disord*. 2014;16(5):523-530.

Pharmacological Studies in High-Risk Bipolar Offspring

Authors	Sample size and Population	Drug	Design	Outcome
Geller et al., 1998	30 Prepubertal (mean age 10.7 years) depressed children; 80% had Family History of BP-I or mania (40% of parents had BP-I or mania); and 20% with loaded or multigenerational MDD but no mania.	**Lithium** (N=17) vs Placebo (N=13)	Double-blind placebo controlled	No difference between active and placebo groups.
Chang et al., 2003	24 (6-18 year old) youth with mood and behavioral disorders, at least mild affective symptoms, and at least one parent with BD.	**Divalproex**	12-week Open-label	78% response rate. Well tolerated with no discontinuations due to adverse effects.
Findling et al., 2007	56 symptomatic youth (ages 5-17) with bipolar disorder not otherwise specified (NOS) or cyclothymia who also had at least 1 biological parent with bipolar illness.	**Divalproex (N=29) vs Placebo (N=27)**	Double-blind placebo controlled	No difference in survival time for discontinuation for any reason (p = .93) or due to a mood event (p = .55). Both groups had improved mood sx and psychosocial function.
DelBello et al., 2007	20 symptomatic adolescents (12-18 years old) at high risk for developing BD by virtue of having at least one first-degree relative with BD I.	**Quetiapine**	12-week single blind open label trial	87% responded (CGI-I < or = 2) at week 12. Decreased YMRS and CDRS scores from baseline to endpoint.
Findling et al., 2009	9 children (7-16 years old) with MDD and at least one parent with BD	**Paroxetine vs Paroxetine + Divalproex**	Open-label	Neither treatment was effective. 50% had mania symptoms.

Findling RL, et al. *J Child Adolesc Psychopharmacol.* 2008;18(6):615-621.

Explosive Outbursts and Irritability



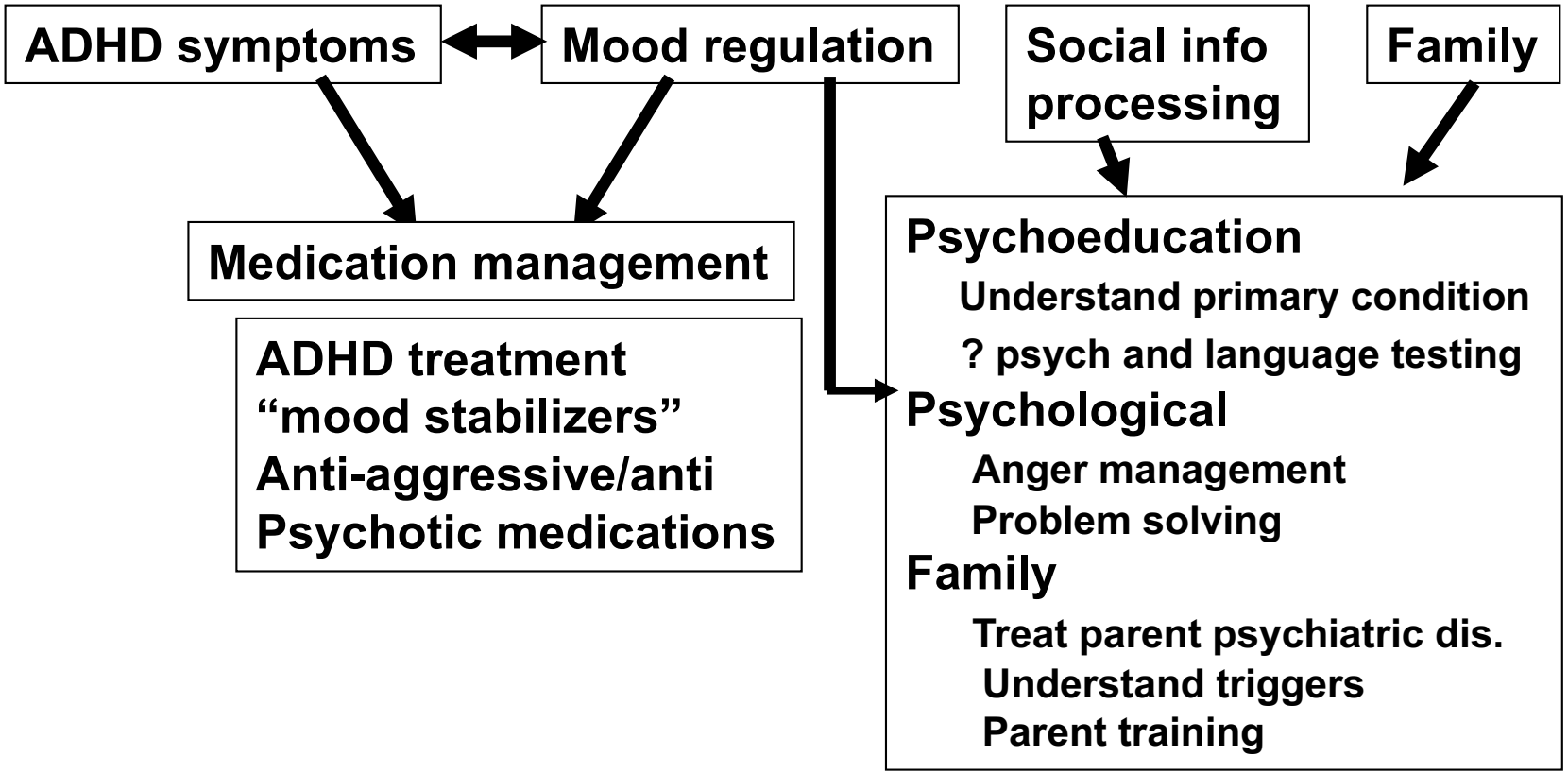
DMDD=disruptive mood dysregulation disorder; ASD=Autism spectrum disorder

Psychiatric Approach for Most Children with "Mood Dysregulation"

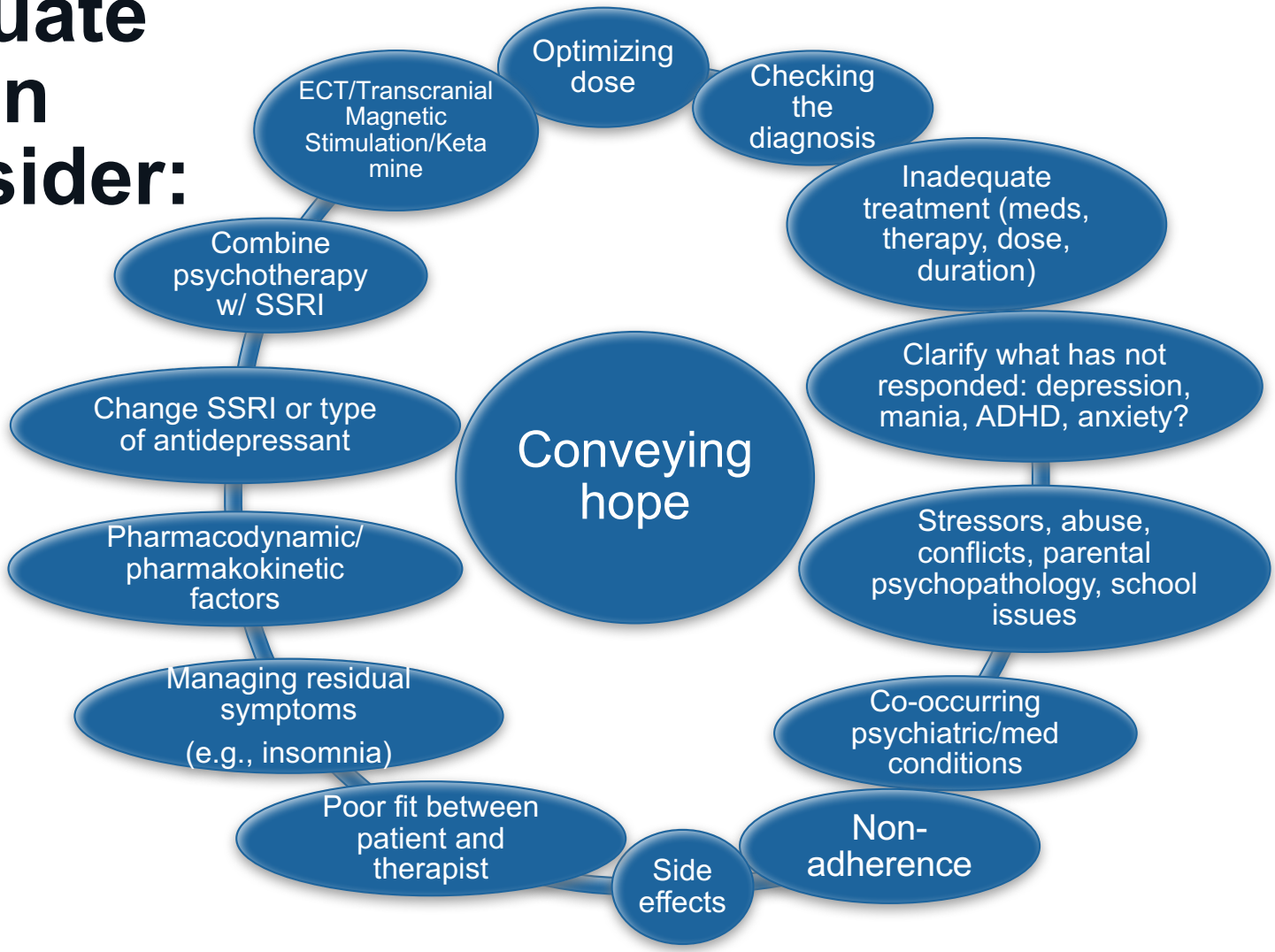
- Good diagnostic assessment
  - Combined ADHD/ODD is most common (~75%);
  - anxiety, depression and autism are other common primary disorders; it is why they are "rule outs" for DMDD.
  - Keep careful records of frequency, intensity, number, and duration of outbursts.
- Maximize the treatment of the base condition.
  - My experience/most data: it is ADHD, combined
  - If symptoms remain, add another medication – atypical antipsychotic (AAP), conventional antipsychotic (CAP), or mood stabilizer or possibly alpha agonist.
  - Pay attention to weight gain immediately
- We desperately need medications for severe outbursts whatever they are called
- >40% of kids remain symptomatic in spite of best treatment
  - the "press" goes on about giving kids "powerful" drugs. For these kids, the power of their disorder is much greater than our treatments.

Baweja R, et al. *J Child Adolesc Psychopharmacol*. 2016;26(2):154-163.

Proposed Management



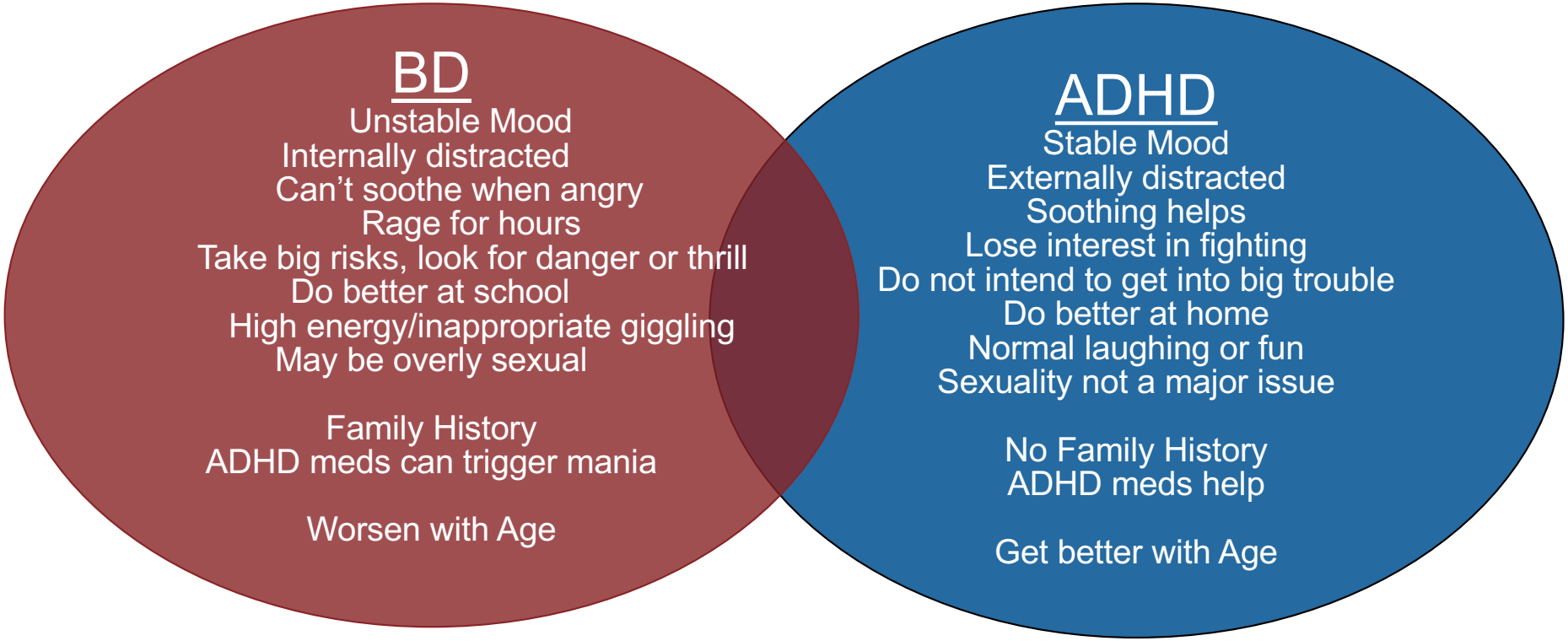
For Inadequate Response in Youth Consider:



Treatment of Pediatric BD (Case)

Joy is a 15-year-old sophomore in high school who reports that for the past week, she has gone without any sleep in a heightened state of activity, with distractibility from racing thoughts, rapid speech, and rapid mood swings. She describes herself as being "out of control." She recently proclaimed to a group of friends that she did not menstruate because she was "of a third sex, a gender above the human sexes." When her friends questioned her on this, she explained that she is a "superwoman" who can avoid human sexuality and still give birth.

Comparing Pediatric BD to ADHD



Comorbidity-ADHD

- Rates depend on whether or not symptoms of mania and ADHD are "double counted"
- Comorbidity rates are much higher when they are
  - 75-98% children
  - 25-60% in teens;
  - 10-20% in adults
- Even accounting for that, rates of ADHD appear to be somewhat higher than expected by chance
- ADHD comorbidity
  - lengthens a manic episode
  - Decreases time to relapse
  - Worsens treatment response

Consoli A, et al. *Can J Psychiatry*. 2007;52(5):323-328.; Strober M, et al. *J Affect Disorder.* 1998;15:255-268.

Treatment Challenge: Limited Evidence Base/Approved Agents for ADHD in BD

Good News

- On average, over time, symptoms become less severe
- A variety of interventions clearly can reduce symptoms, at least in the short run

Bad News

- No RCTs have examined efficacy and safety of ADHD treatment in youth at risk for mood disorders
- No existing treatments seem to change the long-term course of ADHD
- Inadequately treated ADHD makes other developmental goals much harder to attain
- When ADHD occurs with another problem (about 2/3 of the time) outcomes tend to be worse
- All treatments have the potential for side effects

Possible Points of Intervention

Environmental
- Structural
- Programmatic

Psychological
- Cognitive
- Behavioral

Biological
- Medications
- Nutritional changes

- Stimulants
  - Methylphenidate
  - Amphetamine
  - Lisdexamfetamine
- Non-Stimulants
  - Atomoxetine
    Guanfacine
  - Clonidine*
  - Other less well established or less used:
    - Bupropion*
    - Imipramine*
    - Nortriptyline*
    - Venlafaxine*
    - Modafinil*

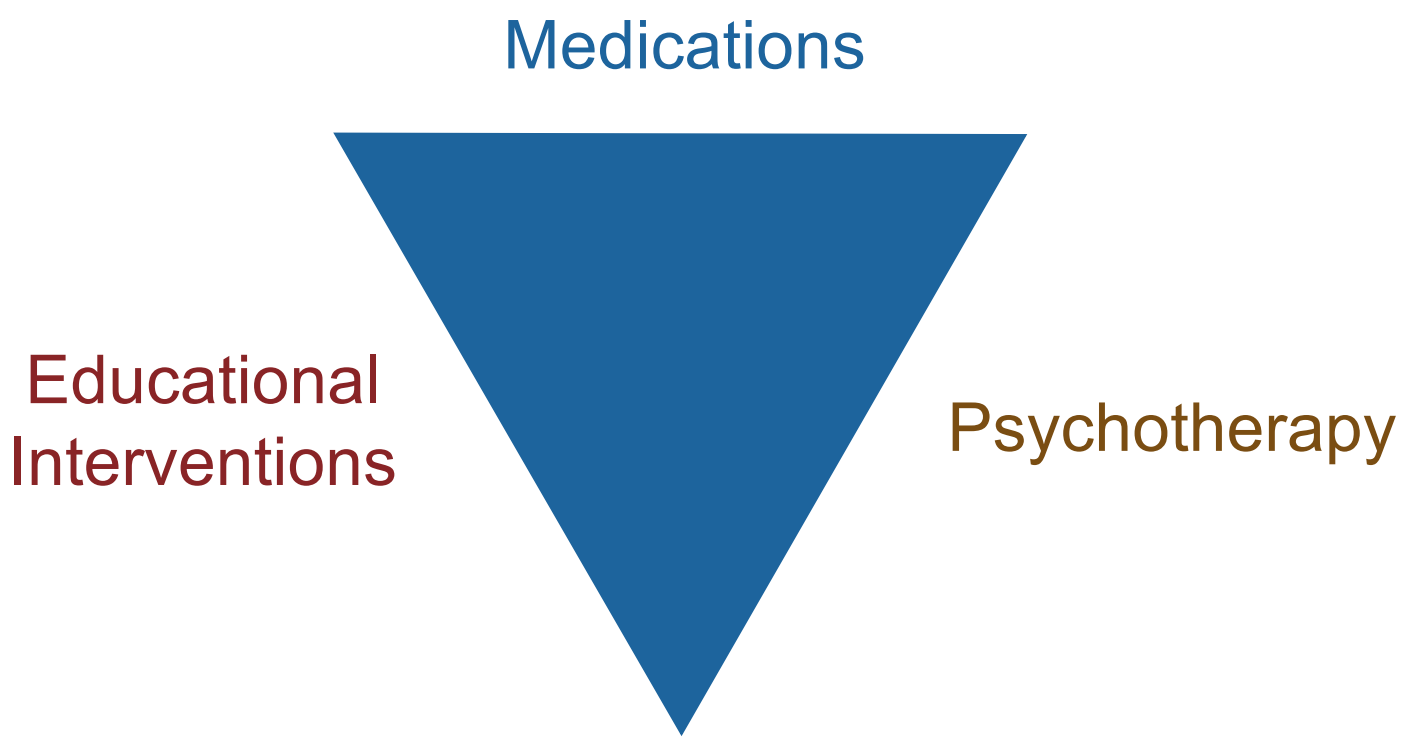
*Clonidine, bupropion, imipramine, nortriptyline, venlafaxine, and modafinil are not FDA-approved for ADHD

Use of Stimulants in the Context of Mania

- Studies suggest that:
  - Children with bipolar disorder/severe mood dysregulation/disruptive mood dysregulation disorder (DMDD) are not harmed by stimulants and could help[1]
  - Children with bipolar disorder find stimulants in addition to mood stabilizers add further to treatment response[2]
  - Children with ADHD and irritability/aggression respond better to mood stabilizers or atypicals versus placebo if the ADHD is maximally treated first[3]
  - Conversion from ADHD to BD/severe mood dysregulation happens less often in children given stimulants[4]

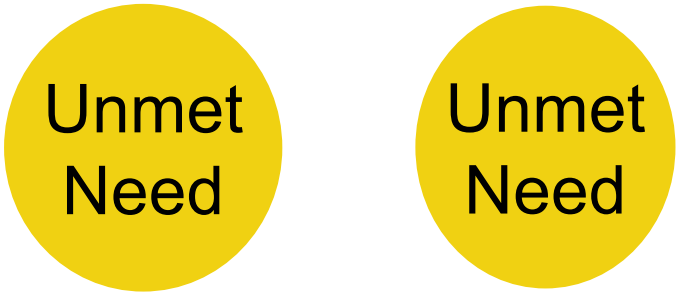
[1]Galanter CA, et al. *J Child Adolesc Psychopharmacol*. 2003;13(2):123-136; [2]Findling RL, et al. *J Clin Psychopharmacol*. 2008;28(4):441-446; [3]Aman MG, et al. *J Am Acad Child Adolesc Psychiatry*. 2014;53(1):47-60; [4]Tillman R, et al. *Dev Psychopathol*. 2006;18(4):1037-1053.

Comprehensive Treatment for Pediatric Bipolar Disorder



FDA-Approved Agents for Pediatric BD

Acute Mania		Acute Depression		Longer-Term	
Year	Drug	Year	Drug	Year	Drug
1970	Lithium[a]	2014	Olanzapine+fluoxetine combination[b]	1974	Lithium[a]
2007	Risperidone[b]			2008	Aripiprazole (b->e)
2008	Aripiprazole[b, (*->e)]				
2009	Quetiapine[b]				
2009	Olanzapine[c]				
2015	Asenapine[b]				



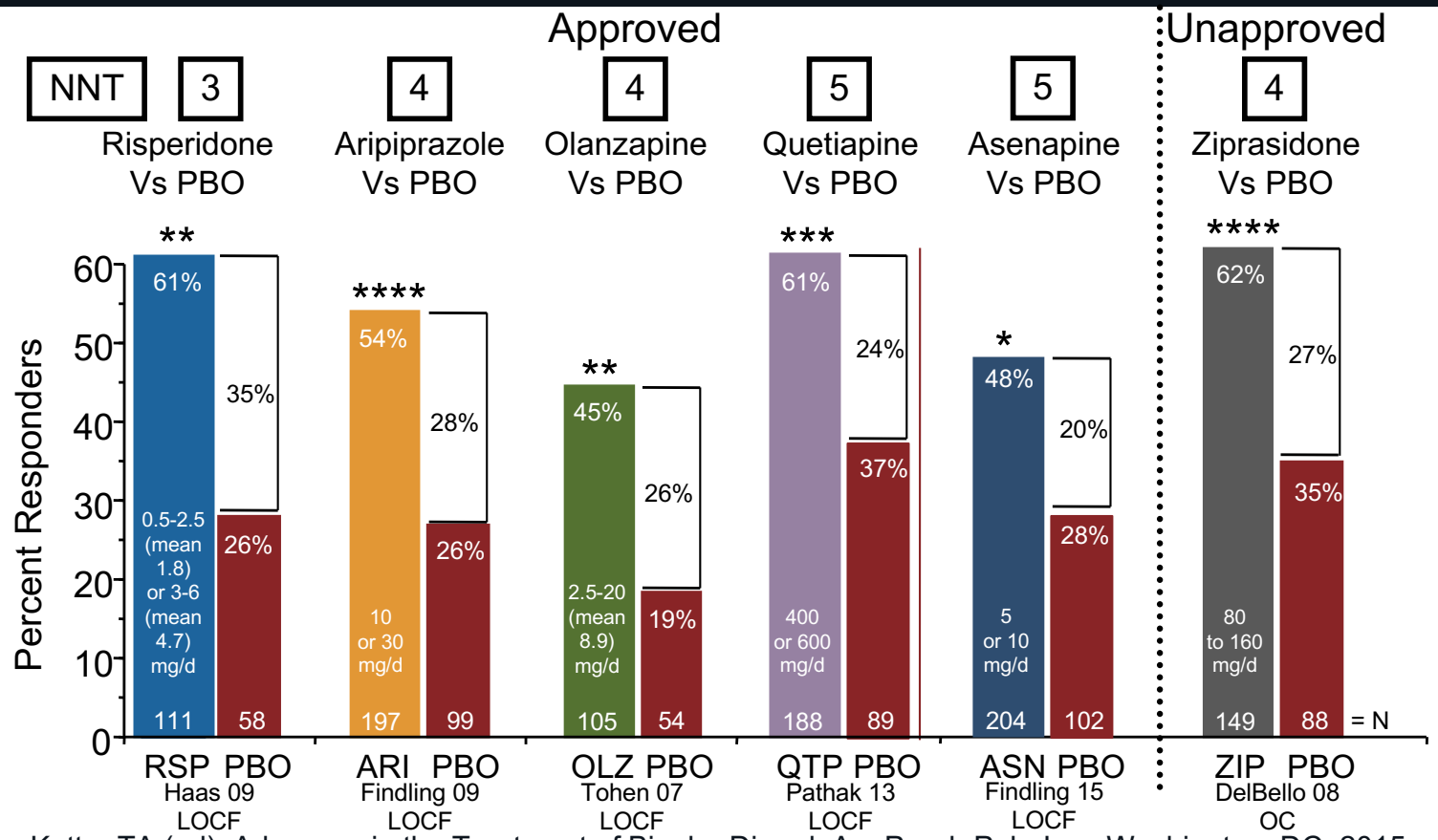
Important unmet needs - well-tolerated treatments for acute depression and maintenance.

*Adjunctive (as well as monotherapy); [a]Age ≥ 12-17; [b]Age 10-17; [c]Age 13-17;(->e)Extrapolated indication

Adapted from: Ketter TA (ed). Advances in the Treatment of Bipolar Disorder, Am Psych Pub, Inc., Washington, DC, 2015.

Overview of Pediatric Acute Mania Studies

Number Needed to Treat for Response, Rates



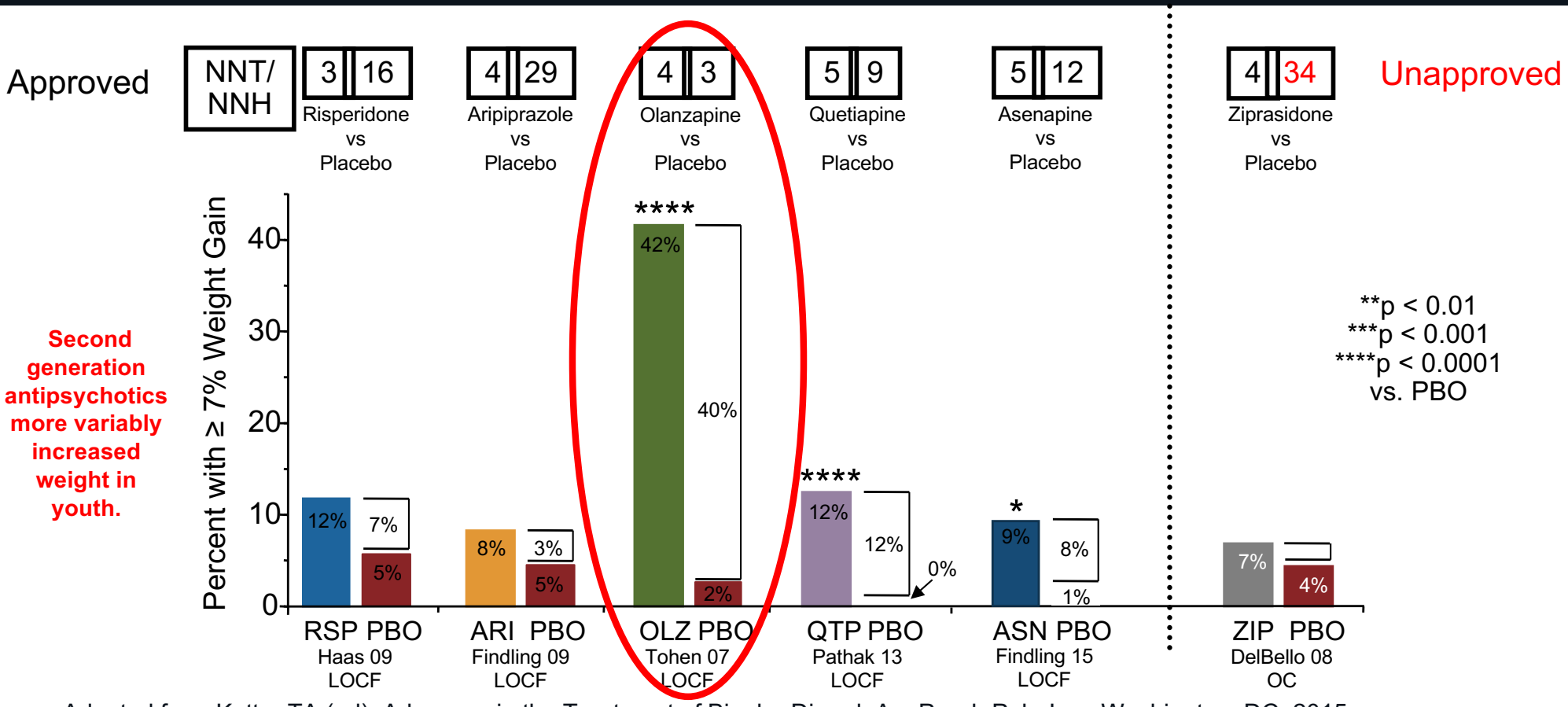
Second generation antipsychotics consistently increased pediatric antimanic response rates.

**p < 0.01
***p < 0.001,
****p < 0.0001
vs. PBO.

Adapted from Ketter TA (ed). Advances in the Treatment of Bipolar Disord, Am Psych Pub, Inc., Washington, DC, 2015.

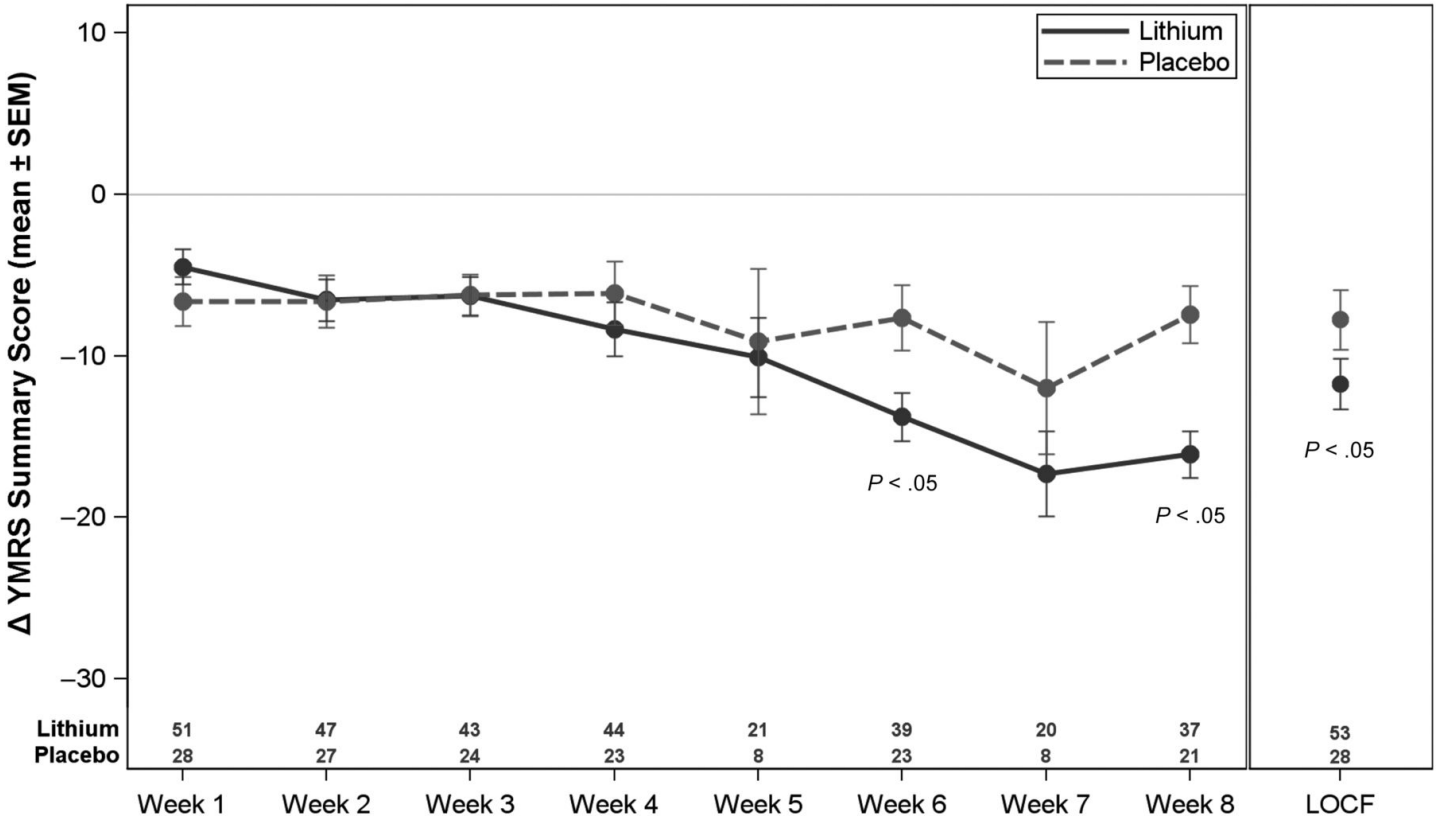
Overview of Pediatric Acute Mania Studies

Numbers Needed to Treat and Harm, ≥ 7% Weight Gain Rates



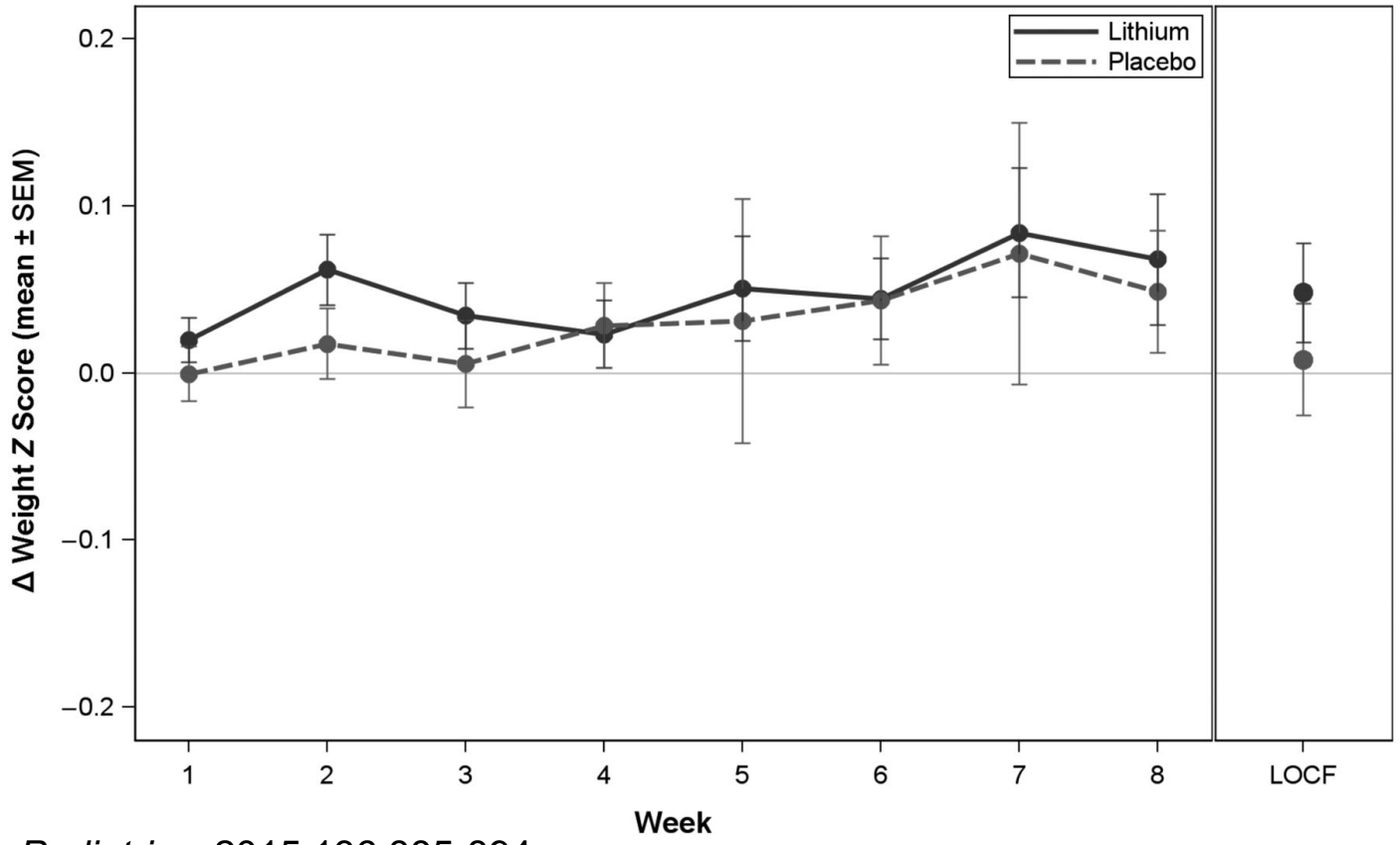
Adapted from Ketter TA (ed). Advances in the Treatment of Bipolar Disord, Am Psych Pub, Inc., Washington, DC, 2015.

Lithium vs. Placebo in 81 Youth with Acute Mania



Findling et al. *Pediatrics.* 2015;136:885-894.

Lithium vs. Placebo: Weight Gain Over 8 Weeks



Findling et al. *Pediatrics.* 2015;136:885-894.

"Mood Stabilizers" in Pediatric BD: 2017

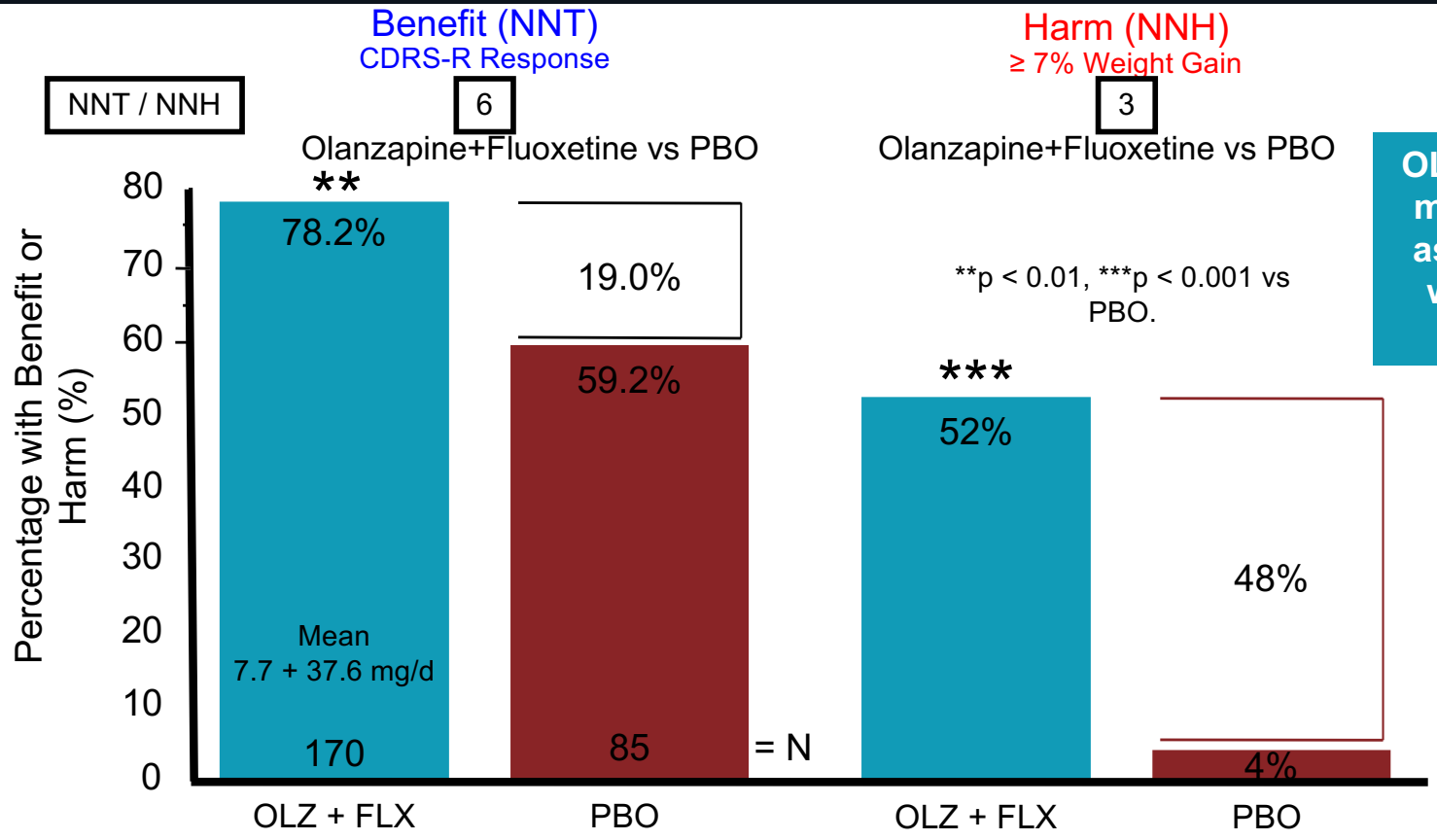
- Lithium:* FDA approved down to age 12 y/o. Lithium superior to PBO in children with BD, little weight gain[1]
- Divalproex:* Extended Release (ER) form with negative pediatric data (24% response) for acute mania. Unpublished data suggests Immediate Release (IR) more effective than PBO[2]
- Carbamazepine:* ER form with open label data showing mild to moderate improvement in pediatric mania.[3]
- Lamotrigine:* Open studies find efficacy in pediatric acute mania, mixed mania, depression. Maintenance study completed, mild-moderate effects.[4]
- Oxcarbazepine:* Negative for acute mania in children and adolescents[5]

*Not FDA-approved for pediatric bipolar disorder

[1]Findling RL, et al. *Pediatrics*. 2015;136(5):885-894; [2]Wagner KD, et al. *J Am Acad Child Adolesc Psychiatry*. 2009;48(5):519-532; [3]Joshi G, et al. *J Child Adolesc Psychopharmacol*. 2010;20(1):7-14; [4]Chang K, et al. *J Am Acad Child Adolesc Psychiatry*. 2006;45(3):298-304; [5]Biederman J, et al. *CNS Neurosci Ther.* 2010;16(2):91-102.

8-Week Olanzapine + Fluoxetine in Pediatric Bipolar I Depression

Numbers Needed to Treat and Harm, Response and ≥ 7% Weight Gain Rates



OLZ-FLX vs. PBO more than twice as likely to yield weight gain as response.

Detke HC, et al. *JAACAP*. 2015; 54(3):217-224.

Selected Agents Lacking FDA-Approval for Pediatric Bipolar Disorder*

- Antidepressants (other than fluoxetine + olanzapine) – any
- Divalproex, carbamazepine, lamotrigine – any
- Lithium – BD depression
- Olanzapine, quetiapine, risperidone – BD depression; maintenance
- Aripiprazole – BD depression; maintenance (LAI)
- Asenapine – adjunctive mania; BD depression; maintenance
- Ziprasidone, lurasidone, caripazine, brexpiprazole – any
- Chlorpromazine – any
- Armodafinil – any
- Negative studies in pediatric BD: oxcarbazepine, topiramate

*As of early 2017; BD = bipolar disorder; LAI = long-acting injectable formulation.
Adapted from Ketter TA (ed). Advances in the Treatment of Bipolar Disord, Am Psych Pub, Inc., Washington, DC, 2015.

Pediatric Bipolar Depression

First Line: Psychotherapy

Second Line: **L**ithium,* **L**amotrigine,* **L**urasidone*
(Olanzapine-Fluoxetine is FDA approved)

Third Line: Quetiapine, Bupropion,*
careful SSRI titration

*Not FDA-approved for pediatric bipolar depression.

Mood Stabilizers: Safety and Tolerability Concerns

Lithium	Valproate	Carbamazepine	Lamotrigine
Gastrointestinal	Gastrointestinal	Gastrointestinal	Gastrointestinal
Weight gain	Weight gain	Rash	Rash
Neurotoxicity	Tremor	Neurotoxicity	Headache
Renal toxicity	Hepatotoxicity	Hepatotoxicity	Dizziness
Thyroid toxicity	Thrombocytopenia	Thyroid changes	Pruritis
Hair Loss	Hair Loss	Blood dyscrasias	Dream abnormality
Cardiac toxicity	Pancreatitis	Cardiac toxicity	
Acne, Psoriasis	PCOS	Hyponatremia	
Teratogen	Teratogen	Teratogen	Teratogen
	Suicidality	Suicidality	Suicidality

All mood stabilizers have at least one boxed warning.

= boxed warning in prescribing information.

[Package Insert]. Drugs@FDA Website.; Ketter TA (ed). *Clinical Manual of Bipolar Disorder*, Am Psychiat Pub, Inc., Washington, DC (In Press).

Antipsychotic Safety and Tolerability Concerns: All Antipsychotics Have at Least One Boxed Warning

First-Generation	Second-Generation
Depression	Weight gain, Sedation
Akathisia	Hyperglycemia, Diabetes[b]
Acute dystonia	Suicidality in age ≤ 24[c]
Tardive dyskinesia[a]	Akathisia
Weight gain, Sedation	Hyperprolactinemia
Anticholinergic	Cerebrovascular in elderly[d]
Cardiac, Orthostasis	Cardiac, Orthostasis
Hyperprolactinemia	Tardive dyskinesia[a]
Neuroleptic malignant[a]	Neuroleptic malignant[a]
Leukopenia, Neutropenia,	Leukopenia, Neutropenia,
Agranulocytosis[a]	Agranulocytosis[a]
Cardiac/pneumonia in older adults[a]	Cardiac/pneumonia in older adults[a]

Warnings - ▭ boxed; [a] Antipsychotic class warning/precaution; [b] Second generation antipsychotic class warning; [c]Aripiprazole, quetiapine, olanzapine + fluoxetine combination (antidepressant class warning);[d] risperidone, olanzapine, aripiprazole.

Ketter TA (ed). Handbook of Diagnosis and Treatment of Bipolar Disorder, APPI., Washington, DC, [Package Insert]. Drugs@FDA Website.

ADA Consensus on Antipsychotic Drugs: Monitoring Protocol for Patients on Second Generation Antipsychotics*

		Short Term			Long Term		
	Baseline	4 wk	8 wk	12 wk	Quarterly	Annually	Every 5 y
Personal/family history	X						
Weight (BMI)	X	X	X	X	X		
Waist circumference	X					X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X			X			X

*More frequent assessments may be warranted based on clinical status

American Diabetes Association et al. Diabetes Care. 2004;27:596-601.

SMART Goals

- For every child who presents with mood symptoms, assess for both depression and mania
- Ensure adequate dosing and trial before trying different antidepressant and watch for treatment-emergent mania
- Treat comorbid conditions (e.g. ADHD) after addressing primary mood disorder
- Evidence supports atypical antipsychotic and lithium use for acute mania
- Psychotherapy, and 3 L's: lurasidone,* lithium,* and lamotrigine* may be effective for bipolar depression; potential for maintenance
- Weight gain and sedation are the most common and problematic adverse effects

*Not FDA-approved for pediatric bipolar depression

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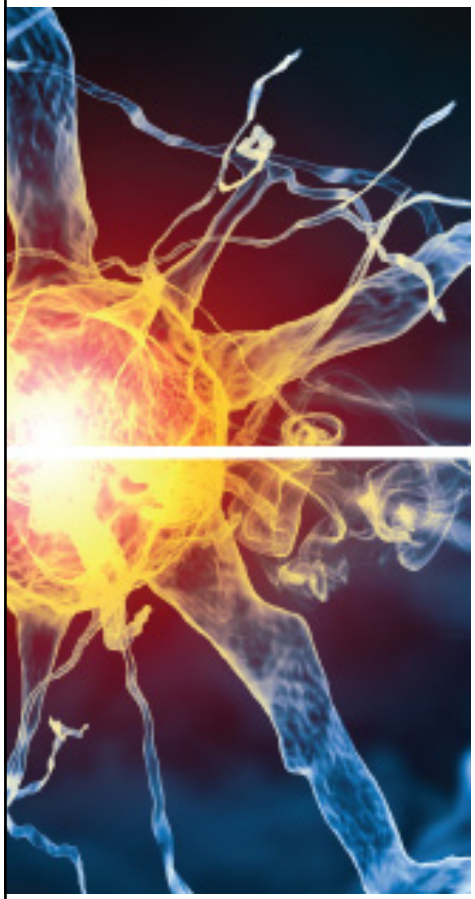

Questions & Answers