Clinical convergence®

A PATIENT-CENTERED APPROACH TO

CHILD & ADOLESCENT BIPOLAR DEPRESSION

AKH Inc. Advancing Knowledge in Healthcare

RMEI MEDICAL EDUCATION FOR BETTER OUTCOMES

Jointly provided by AKH Inc., Advancing Knowledge in Healthcare and RMEI Medical Education, LLC.
Supported by an independent educational grant from Sunovion.

Sara Jones, PhD, APRN, PMHNP-BC, FAANP
Associate Professor, College of Nursing
University of Arkansas for Medical Sciences
Little Rock, AR

Faculty Disclosures

Sara Jones, PhD, APRN, PMHNP-BC, has no conflicts to disclose.

Clinical convergence®

In 2018 and 2019

We discussed

Diagnosing Bipolar Depression in Children and Adolescents

Managing Child and Adolescent Bipolar Depression

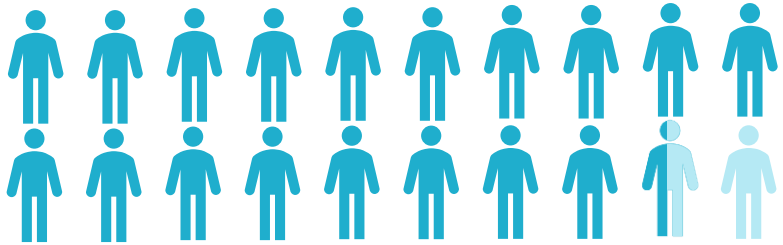
Participants

928 Total Learners

482 Learners in 2018

446 Learners in 2019

92% Psychiatric Nurses



Clinical convergence®

Where Learners Struggled

20%

Correctly identified treatment based on FDA-approved indication

41%

Did well on items related to treatment safety and efficacy

13%

Successfully selected treatment for pediatric bipolar disorder

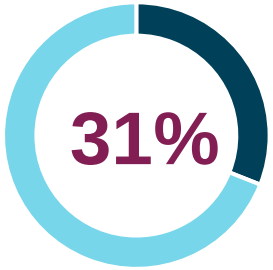
Clinical convergence®

Deeper Dive: Treatment Selection

Learners were presented with a case: Catherine

Catherine is a teenager with bipolar 1 disorder. She was recently discharged from the hospital following a manic episode.

Over the course of the next several months, her treatment was adjusted based on side effects and mood stability.



When asked to select an appropriate antipsychotic for her, only 31% were able to do so.

Clinical convergence®

Factors Related to Proficiency

Practice Setting

Clinicians practicing in a residential facility were more likely to struggle with treatment selection[1]

Role in Diagnosis

Independent diagnosticians were more likely to excel in treatment selection[2]

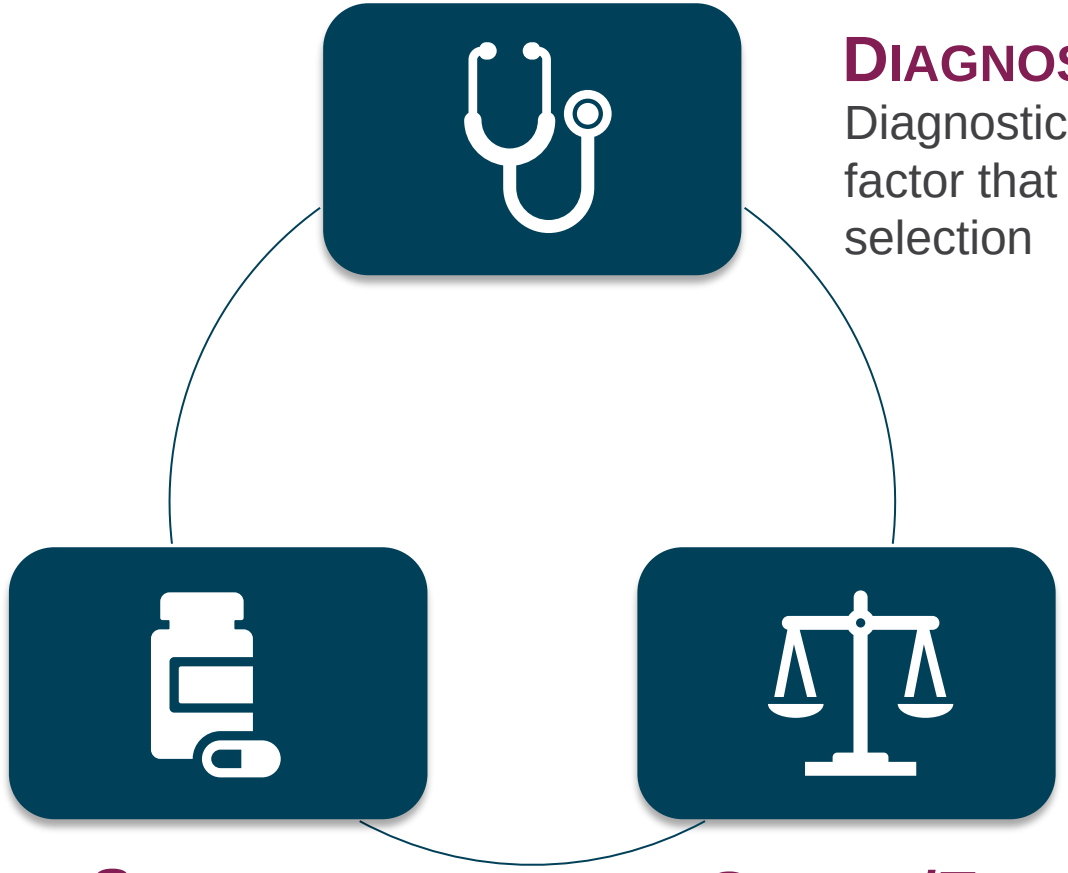
Confidence

Level of confidence was directly related to proficiency

1. As compared to clinicians practicing in other settings (nonprofits, group practice, university teaching hospitals;
2. As compared to clinicians who diagnose in partnership with other clinicians or who do not participate in diagnosis at all.

Clinical convergence®

Continued Educational Needs



Diagnosis

Diagnostic proficiency was identified as a factor that may improve treatment selection

Treatment Selection

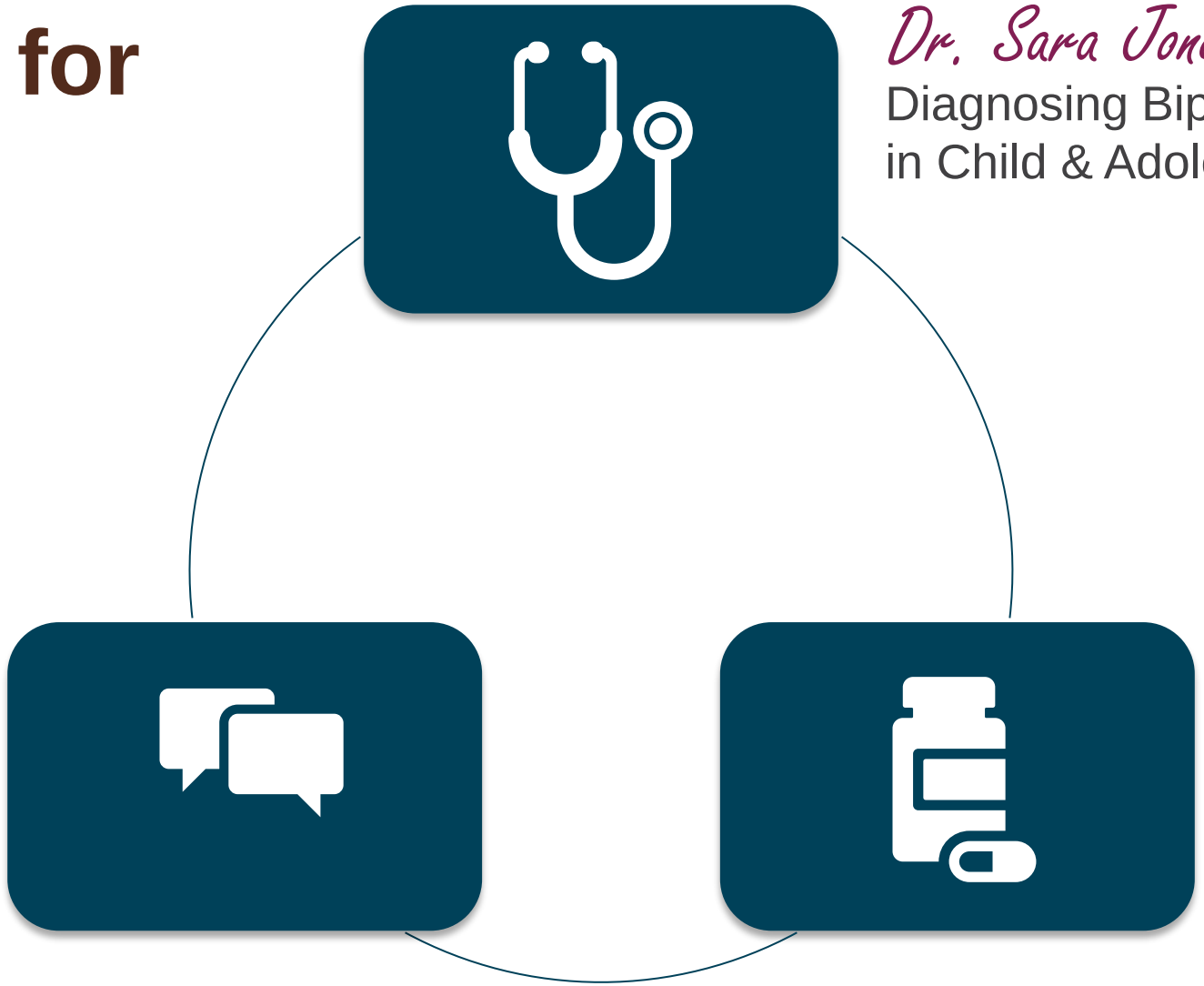
Participants particularly struggled with the role of 2nd generation antipsychotics in the treatment of pediatric bipolar depression

Safety/Efficacy

Additional education is needed on treatment safety, efficacy, and indication

Clinical convergence

Agenda for Today



Dr. Sara Jones
Diagnosing Bipolar Depression in Child & Adolescent Patients

Dr. Robert Kowatch
Managing Child and Adolescent Bipolar Depression

Panel Discussion
…with SURPRISE guests!

Clinical convergence®

Diagnosing Bipolar Depression in Child & Adolescent Patients

Sara Jones, PhD, APRN, PMHNP-BC, FAANP
Associate Professor, College of Nursing
University of Arkansas for Medical Sciences
Little Rock, AR

Episodes of Depression: Bipolar I & II

≥5 OF FOLLOWING SYMPTOMS DURING SAME 2-WEEK PERIOD

- Depressed mood most of day, nearly every day (subj/obj)
- Anhedonia
- Weight loss or gain ≥5%/month; appetite changes
- Sleep changes
- Psychomotor agitation or retardation
- Fatigue, loss of energy
- Worthlessness, excessive/inappropriate guilt
- Decreased concentration
- Recurrent thoughts of death, SI

AT LEAST 1 symptom must be depressed mood OR anhedonia

Symptoms must result in clinically significant distress and impaired functioning and cannot be caused by medical or substance use conditions

American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (5th Ed). Arlington, VA: American Psychiatric Assoc.

Episodes of Mania (Bipolar I) or Hypomania (Bipolar II)

Distinct period of abnormal, persistently elevated, expansive, or irritable mood, increased goal-directed activity and energy: **Mania** ≥1 week, **Hypomania** = 4 days. Cannot be caused by medical or substance use conditions.

≥3 OF FOLLOWING SYMPTOMS*

- Inflated self-esteem or grandiosity
- Decreased NEED for sleep
- More talkative than usual
- Flight of ideas, racing thoughts
- Distractibility
- Increased goal-directed activity or psychomotor agitation
- Excessive involvement in pleasurable activities, high potential for negative consequences

* During mood disturbance; 4 if only irritable

Mania: Severe symptoms that causes marked impairment in functioning
Hypomania: Change in functioning uncharacteristic for individual, but not severe enough to cause marked impairment in functioning; noticed by others*

American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (5th Ed). Arlington, VA: American Psychiatric Assoc.

Diagnosing Pediatric Bipolar Disorder

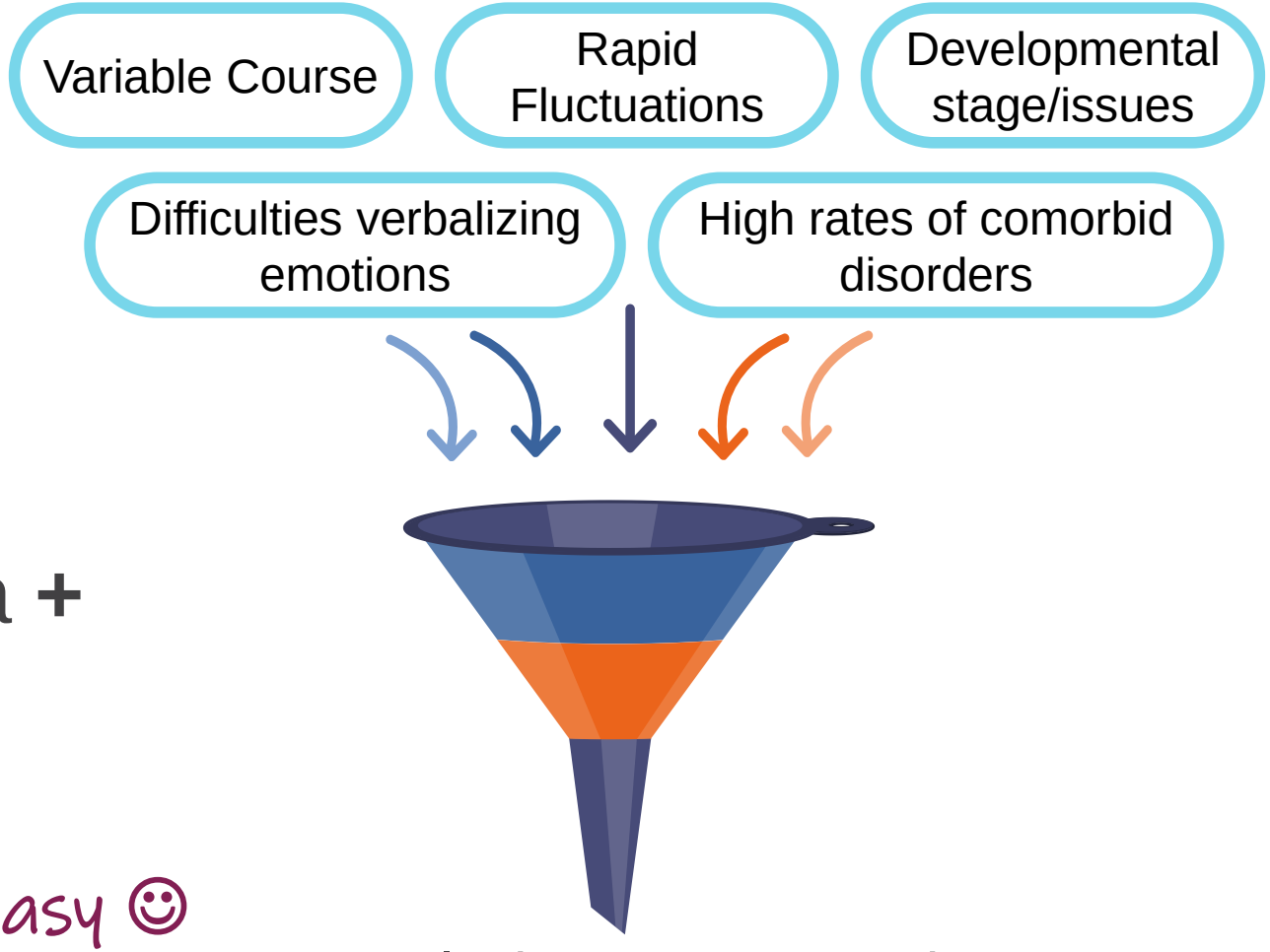
Prevalence

~1 to 2% among children and adolescents

Diagnosis

Mania or Hypomania + Major Depression = Bipolar Disorder

.....If only it were that easy ☺



Complexity & Controversies in Diagnosing!

Birmaher, B. (2017). Bipolar disorder in children and adolescents: Assessment and diagnosis. In D. Brent & D. Solomon (Eds), *Up to Date*. Retrieved on April 25, 2019, from https://www.uptodate.com/contents/bipolar-disorder-in-children-and-adolescents-assessment-and-diagnosis?topicRef=15925&source=see_link.

Clinical convergence®

Clinical Case

Maren
16-year-old
Female

MEDICAL

- 22q11 deletion syndrome > increases risk of mental health d/o
- Issues with platelets, canal dysplasia, impaired hearing, developmental delays

SOCIAL

- Lives with biological parents, middle-to-upper SES, younger brother, 2 dogs
- Home-schooled, minimal social relationships

PSYCHIATRIC HISTORY

Nationwide (Columbus, OH): 22q11 deletion specialist
Seeing me since November 2017: Referred after hospitalization

- Borderline intellectual functioning, ADHD, GAD; recent dx: ASD
- RX: risperidone 1 mg qhs, clonazepam 0.5 mg BID, escitalopram 20 mg

Clinical convergence®

Clinical Case

Maren
16-year-old
Female

Initial Evaluation

- Angry “a lot”, physically aggressive with brother, daily anxiety, impulsivity, poor sleep (decreased need), binge-eating, elevated energy
- PHQ-9: 8, GAD-7: 12, CMRS-Parent: 18
- Modified escitalopram & risperidone

Follow-ups: 2018 to 2019

- Continued aggression, sleep difficulties, still binge eating
- Lisdexamfetamine: Increased agitation/aggression
- Trial lamotrigine: Improvement in 2 weeks….but rash ☹
- Oxcarbazapine: Some “really good days, cautiously optimistic,” less irritable, improved sleep, no binge eating
  - After 3 months: Increased mood lability, sleep problems, increased isolation
  - Symptoms continue to escalate, considering partial day tx; labs WNL, weekly therapy: Taper off oxcarbazepine, start lithium carbonate

Clinical convergence®

Audience Response Question

Which of the following factors is needed to better differentiate Maren's diagnosis?

A. History of trauma
B. Family psychiatric history
C. Laboratory tests
D. All of the above

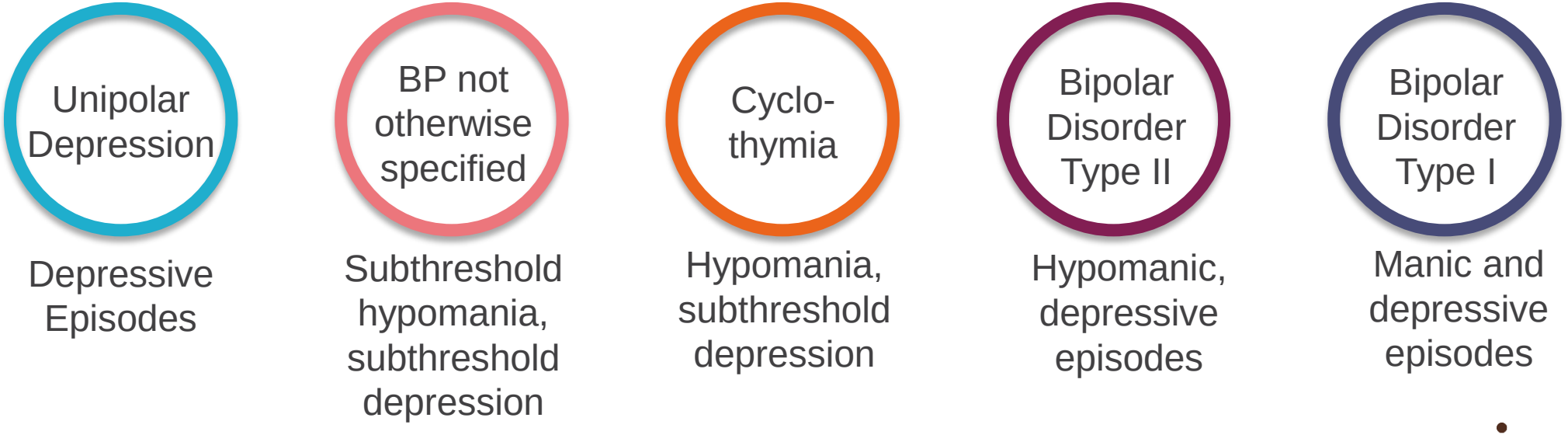
Clinical convergence®

Differential Diagnoses

Unipolar Major Depression (MD)

- **Symptoms of unipolar and bipolar MD are identical**
- Most depressed youth referred to care are experiencing 1st episode of depression; difficulty to differentiate
- Follow longitudinally with ongoing assessment!

Conventional Diagnostic Classification



Birmaher, B. (2017). Bipolar disorder in children and adolescents: Assessment and diagnosis. In D. Brent & D. Solomon (Eds), *Up to Date*. Retrieved on April 25, 2019, from https://www.uptodate.com/contents/bipolar-disorder-in-children-and-adolescents-assessment-and-diagnosis?topicRef=15925&source=see_link

Clinical convergence®

Possible Indicators of Bipolar Disorder

- Family history
- Presence of psychosis
- History of treatment-resistant depression
- Mixed states, mood reactivity
- Significant agitation/aggression in response to psychostimulant
- Subsyndromal symptoms of mania in response to antidepressant
- History of suicidal ideation/attempt

Birmaher, B. (2017). Bipolar disorder in children and adolescents: Assessment and diagnosis. In D. Brent & D. Solomon (Eds), *Up to Date*. Retrieved on April 25, 2019, from https://www.uptodate.com/contents/bipolar-disorder-in-children-and-adolescents-assessment-and-diagnosis?topicRef=15925&source=see_link

Clinical convergence®

Assessment

Strong history-taking is imperative!

History

- Requires careful probing and longitudinal assessment.
- Family psychiatric history
- History of trauma

FIND

F - Frequency
I - Intensity
N - Number
D - Duration

Impairment

? How is functioning being altered?

Additional Factors

Age, development, intellect, environment, social support (enmeshment versus neglect)

Caregivers

Include caregivers and other adults (eg, teachers) in assessment, but DO NOT EXCLUDE the child

Differentials

Medical
Substance-related

Birmaher, B. (2017). Bipolar disorder in children and adolescents: Assessment and diagnosis. In D. Brent & D. Solomon (Eds), *Up to Date*. Retrieved on April 25, 2019, from https://www.uptodate.com/contents/bipolar-disorder-in-children-and-adolescents-assessment-and-diagnosis?topicRef=15925&source=see_link

Pediatrics

Other Symptoms of Interest

Depression

In pediatrics, this **can be irritable mood**

Psychosis

If valid, particularly with depression, may indicate bipolar

Mania

Increased activity and/or silliness above and beyond what is expected for their developmental stage, not accounted for by the situation

Decreased Need For Sleep

…especially if the child is not tired the next day

"Pleasurable Activities"

Inappropriate sexual behaviors without history of sexual trauma; other indulgences (ie, overeating)

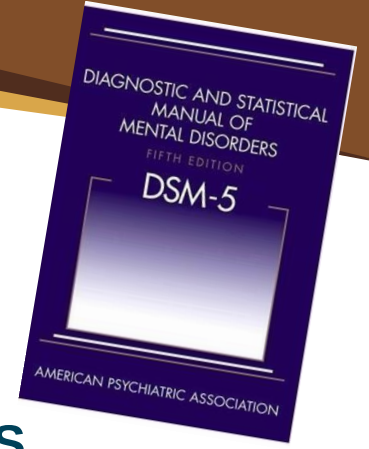
Manic Symptoms

Mild/transient manic symptoms may precede or coexist with depression

American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (5th Ed.) Arlington, VA: American Psychiatric Assoc.
Birmaher, B. (2017). Bipolar disorder in children and adolescents: Assessment and diagnosis. In D. Brent & D. Solomon (Eds), *Up to Date*. Retrieved on April 25, 2019, from https://www.uptodate.com/contents/bipolar-disorder-in-children-and-adolescents-assessment-and-diagnosis?topicRef=15925&source=see_link

Clinical convergence®

Bipolar and Related Disorders



Other Specified Bipolar and Related Disorders

Cyclothymic Disorder

With Anxious Distress

With Seasonal Pattern

With Mixed Features

- MANIA or HYPOMANIA + ≥3 depressive SX
- DEPRESSION + ≥3 manic SX
- IF criteria for both are fully met = Manic episode, with mixed features

With Rapid Cycling

- At least 4 mood episodes/12 months; can occur in any combination
- Remission may partially/fully occur OR instant switch can occur

American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (5th Ed). Arlington, VA: American Psychiatric Assoc.

Clinical convergence®

Screening Tools

Clinician-administered Rating Scales

- **Young Mania Rating Scale (YMRS):** 11 items, ages 5 to 17 years
- **Columbia-Suicide Severity Rating Scale (C-SSRS)**

Parent-administered Rating Scales

- **Young Mania Rate Scale - Parent (P-YMRS):** 11 items, ages 5 to 17 years
- **Child Mania Rating Scale - Parents (CMRS-P):** 21 items
- **The Children Behavior Checklist (CBCL; parent-report):** Used to assess general psychopathology, can also screen for bipolar disorder

**Parental reports: More effective in identifying mania than youth or teacher*

Youth Focused

- **General Behavior Inventory (GBI):** 73 items, broad mood assistant
- **Daily Mood Journal**

For a list of public domain screening tools: www.div12.org/assessment-repository

Clinical convergence®

Maren

2019

Assessment: CMRS-Parent = 31
CC: “Things aren’t good”
Presentation: Erratic sleep, irritability, isolation, poor hygiene, poor self-esteem, decline in school performance
Patient Report: Depression, thoughts of self-harm, “always unhappy”
Treatment Plan: Increased lithium carbonate, altered risperidone doses

Follow-Up 1

Presentation: Symptoms persisted, but “no worse;” risk for hurting brother, self, and elopement
Treatment Plan: Taper off lithium, start lurasidone; modified risperidone & escitalopram

Follow-Up 2

Presentation: Happier, denies SI, brighter, better sleep, no eating issues
Treatment Plan: No change

5 Months

Presentation: Increased irritability, defiance, fighting with brother, poor sleep. Started new school, much improvement in mood and behavior, follows rules.
Treatment Plan: Tried to decrease risperidone d/t irregular menstruation, very volatile; Gradually increased mood lability>>depression>>daily SI

Mid-2019

Hospitalized.
F/U: Consult with specialist and genetic testing

Clinical convergence®

Risks Associated with Misdiagnosis

Difficulty with Diagnosis

- Variability in clinical presentation can make diagnosis difficult!
- Obscured by comorbidities and overlapping symptoms of other psychiatric disorders
- Can take up to 10 years to properly diagnose
- Presentation of early onset is typically more severe, but takes longer to diagnose

Risks of Misdiagnosis

- Label children = lifelong implications: 4th leading cause of disability worldwide
- Expose them to medications with risk of serious side effects and little benefit
- Highest risk for suicide: 32% lifetime risk

Failing to Diagnose…

- Leaves them with untreated illness that may affect normal development
- May expose them to the adverse effects of medications for inaccurately diagnosed conditions

Birmaher, B. (2017). Bipolar disorder in children and adolescents: Assessment and diagnosis. In D. Brent & D. Solomon (Eds), *Up to Date*. Retrieved on April 25, 2019, from https://www.uptodate.com/contents/bipolar-disorder-in-children-and-adolescents-assessment-and-diagnosis?topicRef=15925&source=see_link

Clinical convergence®

Differential Diagnoses

Most Confused

- Attention deficit hyperactivity disorder (ADHD)
- Conduct disorder
- Disruptive mood dysregulation disorder (DMDD)
- Oppositional defiant disorder
- Intermittent explosive disorder

Symptoms Occurring Mainly in Bipolar and Rarely in Above

- Euphoria
- Grandiosity
- Decreased **NEED** for sleep
- Hypersexuality
- Hallucinations and/or delusions

Birmaher, B. (2017). Bipolar disorder in children and adolescents: Assessment and diagnosis. In D. Brent & D. Solomon (Eds), *Up to Date*. Retrieved on April 25, 2019, from https://www.uptodate.com/contents/bipolar-disorder-in-children-and-adolescents-assessment-and-diagnosis?topicRef=15925&source=see_link

Clinical convergence®

Bipolar Disorder versus ADHD

If the ADHD symptoms…	If the child with ADHD…
Appeared later in life (≥12 years old)	Has hallucinations and/or delusions
Appeared abruptly in an otherwise healthy child	Has recurrent severe mood swings, temper outbursts, or rages
Were responding to psychostimulant medications and now are not	Begins to have periods of exaggerated elation, grandiosity, depression, less need for sleep, or inappropriate sexual behaviors
Fluctuate and tend to occur with mood changes	Has a strong family history of bipolar disorder, particularly if not responding to ADHD treatment

SUSPECT BIPOLAR DISORDER

Birmaher, B. (2017). Bipolar disorder in children and adolescents: Assessment and diagnosis. In D. Brent & D. Solomon (Eds), *Up to Date*. Retrieved on April 25, 2019, from https://www.uptodate.com/contents/bipolar-disorder-in-children-and-adolescents-assessment-and-diagnosis?topicRef=15925&source=see_link

Bipolar Disorder versus ODD or CD

If the behavior problems…	If the child has/had…
Only occur when the child is in the midst of an episode of mania or depression	Severe behavior problems that are not responding to treatment
Disappear when mood symptoms improve	“Off and on" oppositional or conduct symptoms
	Family history of bipolar disorder

OTHER DIFFERENTIALS:

- **Anxiety disorders**
  - Comorbidity ranges from 40% to 66%
  - Typical onset: Prior to 1st manic episode
- **Schizophrenia**
  - Very rare; must R/O mood disorder
- **Autism spectrum disorder**
  - Can present with mood lability, aggression, and agitation
- **Disruptive mood dysregulation disorder**
  - Constant irritability; not episodic
- **Substance use disorder**
  - May self-medicate if underlying mood d/o

American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (5th Ed.) Arlington, VA: American Psychiatric Assoc.
Birmaher, B. (2017). Bipolar disorder in children and adolescents: Assessment and diagnosis. In D. Brent & D. Solomon (Eds), *Up to Date*. Retrieved on April 25, 2019, from https://www.uptodate.com/contents/bipolar-disorder-in-children-and-adolescents-assessment-and-diagnosis?topicRef=15925&source=see_link

Clinical convergence®

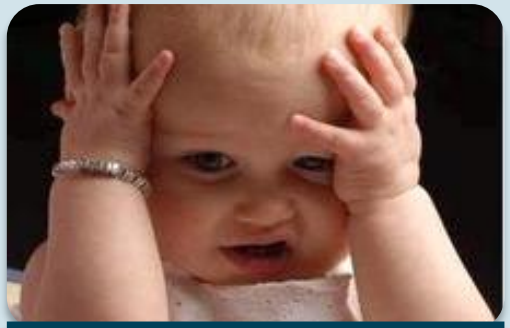
Differential Diagnosis: Other Considerations

Chronic symptoms (hyperactivity, distractibility) should not be considered evidence of mania unless:

Occur episodically

Clearly intensify with onset of mood symptoms

Prolonged presentations of manic-like symptoms that do not change in intensity should raise possibility of a diagnosis other than bipolar disorder



A child CAN have co-occurring disorders:

Estimated to occur in over 50% with bipolar I*

Always consider:

Social stressors, adjustment issues

Medical problems

Trauma history

*American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (5th Ed.) Arlington, VA: American Psychiatric Assoc.
Birmaher, B. (2017). Bipolar disorder in children and adolescents: Assessment and diagnosis. In D. Brent & D. Solomon (Eds), *Up to Date*. Retrieved on April 25, 2019, from https://www.uptodate.com/contents/bipolar-disorder-in-children-and-adolescents-assessment-and-diagnosis?topicRef=15925&source=see_link

Clinical convergence®

Maren Today

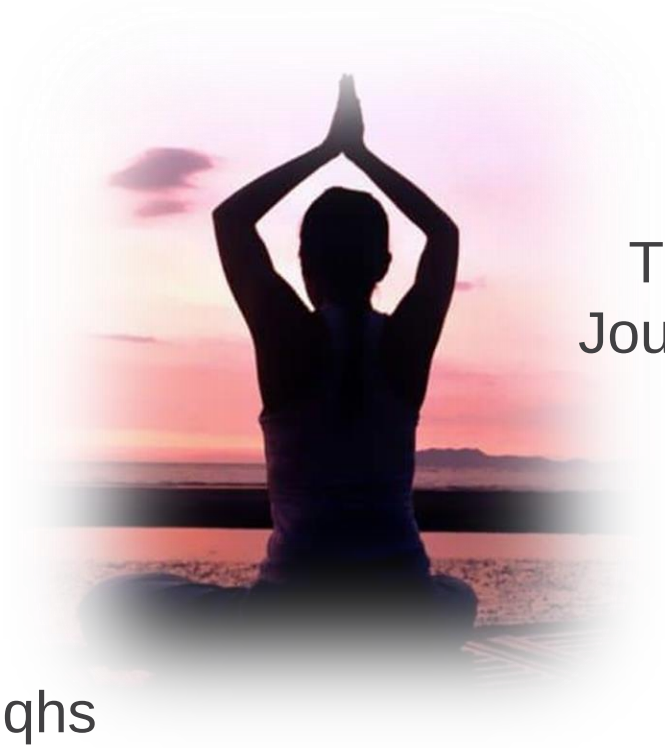
SO. MUCH. GROWTH!

Current Diagnosis

Bipolar I Disorder, in full remission

Medication

Escitalopram, 10 mg
Risperidone, 2 mg
Aripiprazole, 10 mg
Clonazepam, 0.5 mg qam/1 mg qhs



Nonpharmacologic Therapy

Therapy every other week: CBT, MI
Journaling, writing, YouTube Channel
Yoga and Meditation
“Self-care” days

Clinical convergence®

Managing Child and Adolescent Bipolar Depression

Robert A. Kowatch, MD, PhD
Ohio State School of Medicine
Division of Pulmonary Medicine and Behavioral Health
Nationwide Children's Hospital
Columbus, OH

Clinical convergence®

Disclosures

Robert A. Kowatch, MD, PhD, has affiliations with Forest, Pfizer *(Data Monitoring Safety Committee (DMSC)*; PAA/Nationwide Children's Hospital, Ohio State University Medical Center *(Employee/Salary).*

Program Outline

Child and Adolescent Bipolar Disorder (BPD) Depression

Current FDA-approved treatment options

Evidence for emerging and novel treatments

Combination therapy

Psychosocial Interventions

Clinical convergence®

FDA Indicated Agents for Pediatric Bipolar Disorder

Acute Mania		Acute Depression		Longer Term	
Year	**Drug**	**Year**	**Drug**	**Year**	**Drug**
1970	Lithium [a]	2013	Olanzapine/Fluoxetine [b]	1974	Lithium [a]
		2018	Lurasidone [a]		
2007	Risperidone [b]				
2008	Aripiprazole [b]			2008	Aripiprazole [b]
2009	Quetiapine [b]				
2009	Olanzapine [c]				
2015	Asenapine [b]				

IMPORTANT UNMET NEED:

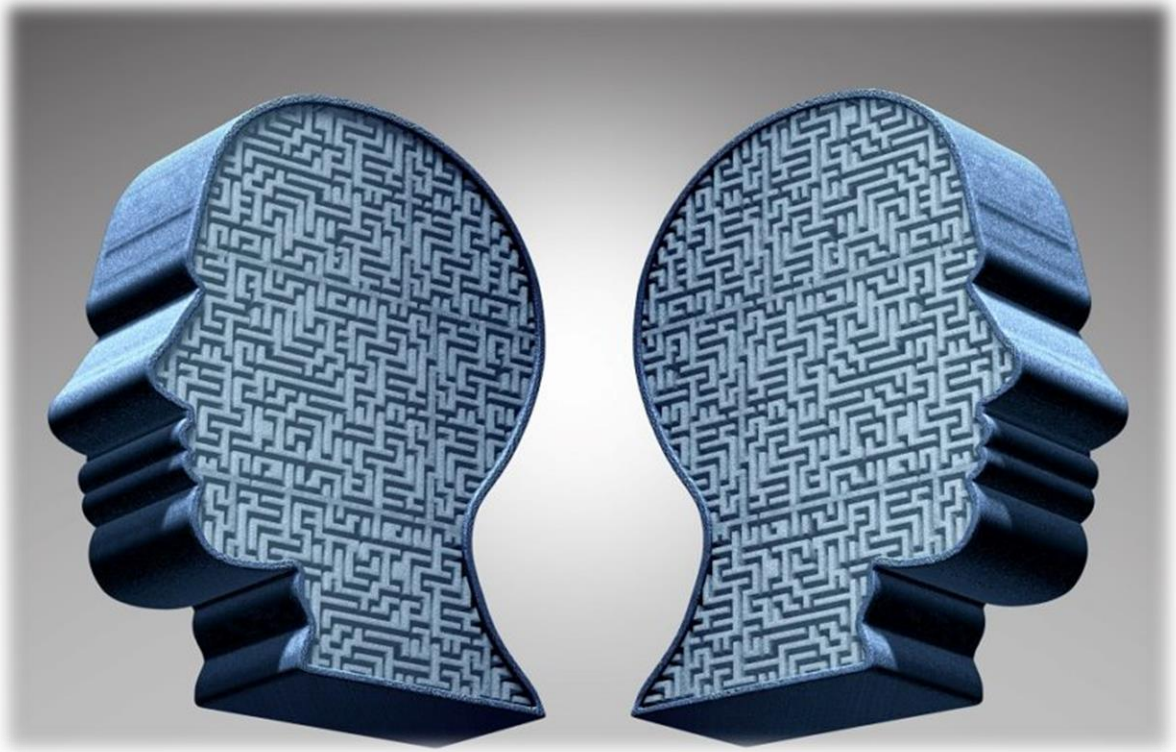
Well-tolerated treatments for acute depression and maintenance treatment

*Adjunctive (as well as monotherapy); [a]Ages 7 to 17; [b]Ages 10 to 17; [c] Ages 13 to 17

Clinical convergence®

Therapeutic Approaches For Bipolar Depression

- Pharmacotherapy
  - Antidepressants
  - Lithium
  - Antipsychotics
    - Quetiapine
    - Olanzapine/Fluoxetine (OFC)
    - Lurasidone
  - Antiepileptics
    - Lamotrigine
- Psychosocial Interventions



Clinical convergence®

Antidepressants

SSRIs

Agents: Fluoxetine, escitalopram, paroxetine, others

Concerns: Potential P450 interactions with atypical antipsychotics, particularly with agents listed above; Large concern about inducing mania or rapid cycling

Advantages: Can also be used to treat anxiety, OCD

Others

Agents: Bupropion

Advantages: Less concern about switching

SSRI Induced Mania

Demography

May be seen in as high as 50% of children with bipolar disorder

Differential

Not to be confused with “behavioral disinhibition”

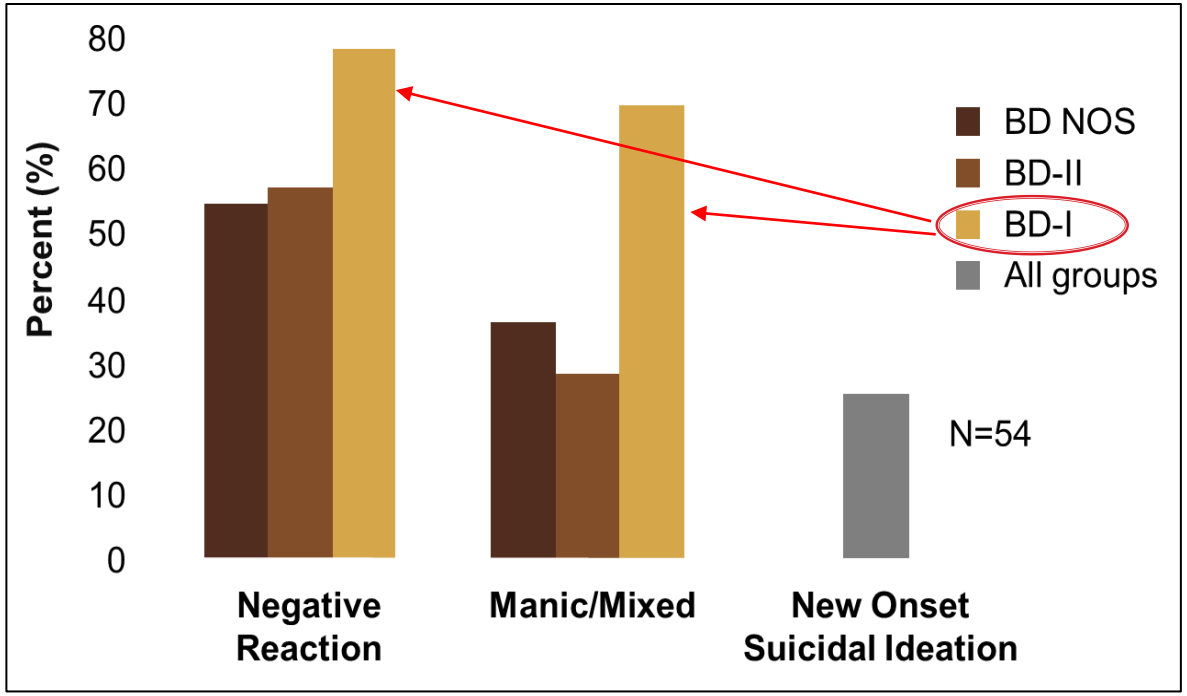
Suicidality

May account for reports of increased suicidality in children treated with SSRIs

Risk factors in patients with Depression

Bipolar family history
Psychomotor retardation
Atypical depression
Acute onset of depression

Negative Reactions to Antidepressants in Pediatric Bipolar Disorder



Baumer FM, et al. *Biol Psychiatry*. 2006;60(9):1005-1012.

Clinical convergence

Catherine

Mood	Months	Notes
Manic Episode	0	16 years old. Diagnosis: bipolar I disorder. Discharged on **lithium**, **risperidone**, and **melatonin** after a 10-day hospital stay for a manic episode. **PMH**: No acute/chronic diseases; mixed episode 1 year ago. **Medication**: Birth control implant. **Labs**: WNL. **FH**: Bipolar Disorder (Dad with Bipolar I) and depression.
Stable	6	**Metformin** and **levothyroxine** were added due to weight gain and elevated TSH, respectively
Stable	9	Developed lactation: Risperidone tapered
Depressed x 2 months	12	Developed **severe acne:** Lithium tapered

Clinical convergence®

Audience Response Question

What would you do next?

A. Start aripiprazole
B. Start quetiapine
C. Start olanzapine/fluoxetine
D. Start lurasidone

Lithium

FDA Indication: For the treatment of manic episodes of manic-depressive illness.
Pediatrics: Ages 7 to 17 years

Study
Lithium for adolescent BP I depression

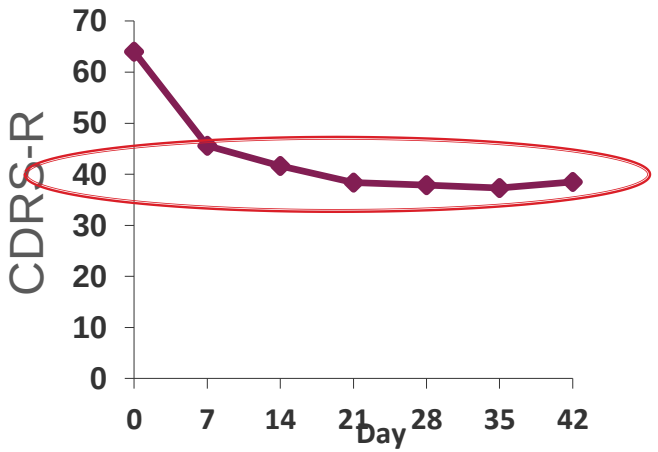
Design
42-day prospective open-label, N=30

Subjects
Lithium titrated to level of 1.0 to 1.2 mEq/L (Mean = 1.1 + 0.2 mEq/L)

Measures
Remitters: CDRS-R <28 and CGI-I <2

Results

Efficacy



Safety

- Headache (74%),
- Nausea/vomiting (67%)
- Polyuria/polydypsia (37%)

Patel NC, et al. *J Am Acad Child Adolesc Psychiatry*. 2006;45(3):289-297.

Clinical convergence

Management of Common Lithium Side Effects

System	Side Effect	Tactic
Central Nervous System	Tremor, sedation, headache	Use a slow-release formulation dose twice daily
Dermatological	Acne	Collaborative with primary care physician for management of acne
Endocrine	Hypothyroidism	Consult with endocrinologist, augment with T3
Gastrointestinal	Nausea, diarrhea	Split into 2 to 3 daily doses; Use a slow release formulation
Metabolic	Weight gain	Encourage diet and exercise; Consider a trial of Metformin[1]
Renal	Polyuria, decreases in renal function	Write note to allow for frequent trips to the bathroom during school; monitor serum creatinine or creatinine clearance, BUN and urine osmolality every 6 months

[1]Klein DJ, et al. *Am J Psychiatry*. 2006;163(12):2072-2079.

Clinical convergence®

Lamotrigine

Study
Adjunctive Maintenance Lamotrigine for Pediatric Bipolar I Depression

Subjects
Patients with BP I receiving conventional treatment
Ages: 10 to 17 years

Design
Placebo-Controlled, Randomized Withdrawal Study

Treatment
Open-Label Phase: Lamotrigine x18 weeks
Double-Blind Phase: Patients maintaining a stable lamotrigine dose for 2 weeks and a CGI-BP[S] score of 3 for 6 consecutive weeks were randomized to double-blinded treatment for up to 36 weeks

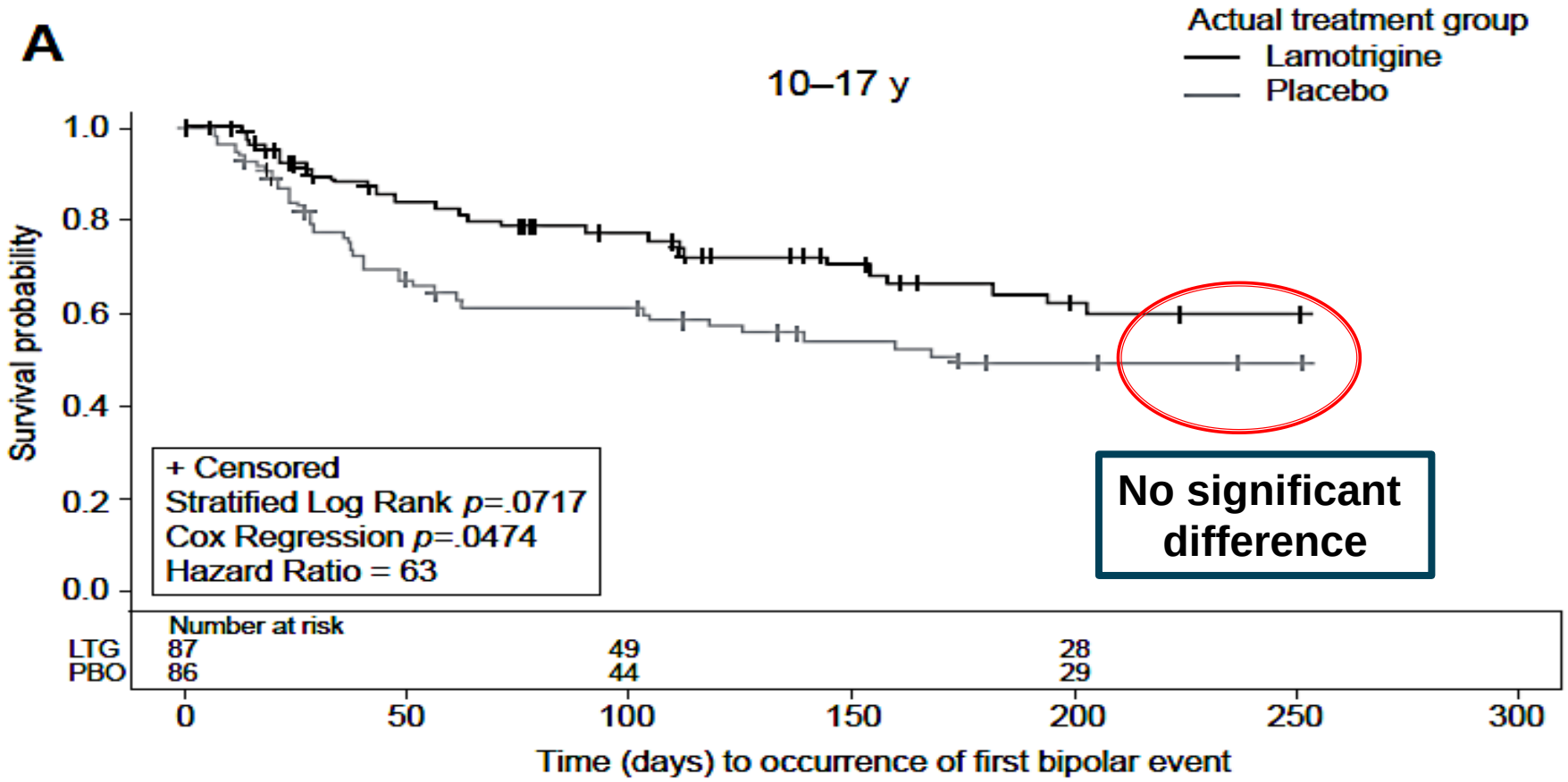
CGI-BP[S], Clinical Global Impression–Bipolar Severity of Illness

Finding RL, et al. *J Am Acad Child Adolesc Psychiatry.* 2015;54(12):1020-1031.

Clinical convergence®

Lamotrigine

Time to the Occurrence of a Bipolar Event (TOBE)



Finding RL, et al. *J Am Acad Child Adolesc Psychiatry.* 2015;54(12):1020-1031.

Clinical convergence®

Quetiapine

Study
Quetiapine XR versus Placebo for Pediatric Bipolar Depression

Design
Multicenter, DBPC; N=193

Subjects
BP I or II

Current Episode: Depressed

Ages: 10 to 17 years

Treatment
8 weeks of monotherapy, titrated according to schedule up to 150 to 300 mg/day

Day 1	Day 2	Day 3
50 mg	100 mg	150 mg

Measures
CDRS-R score >45, YMRS <16

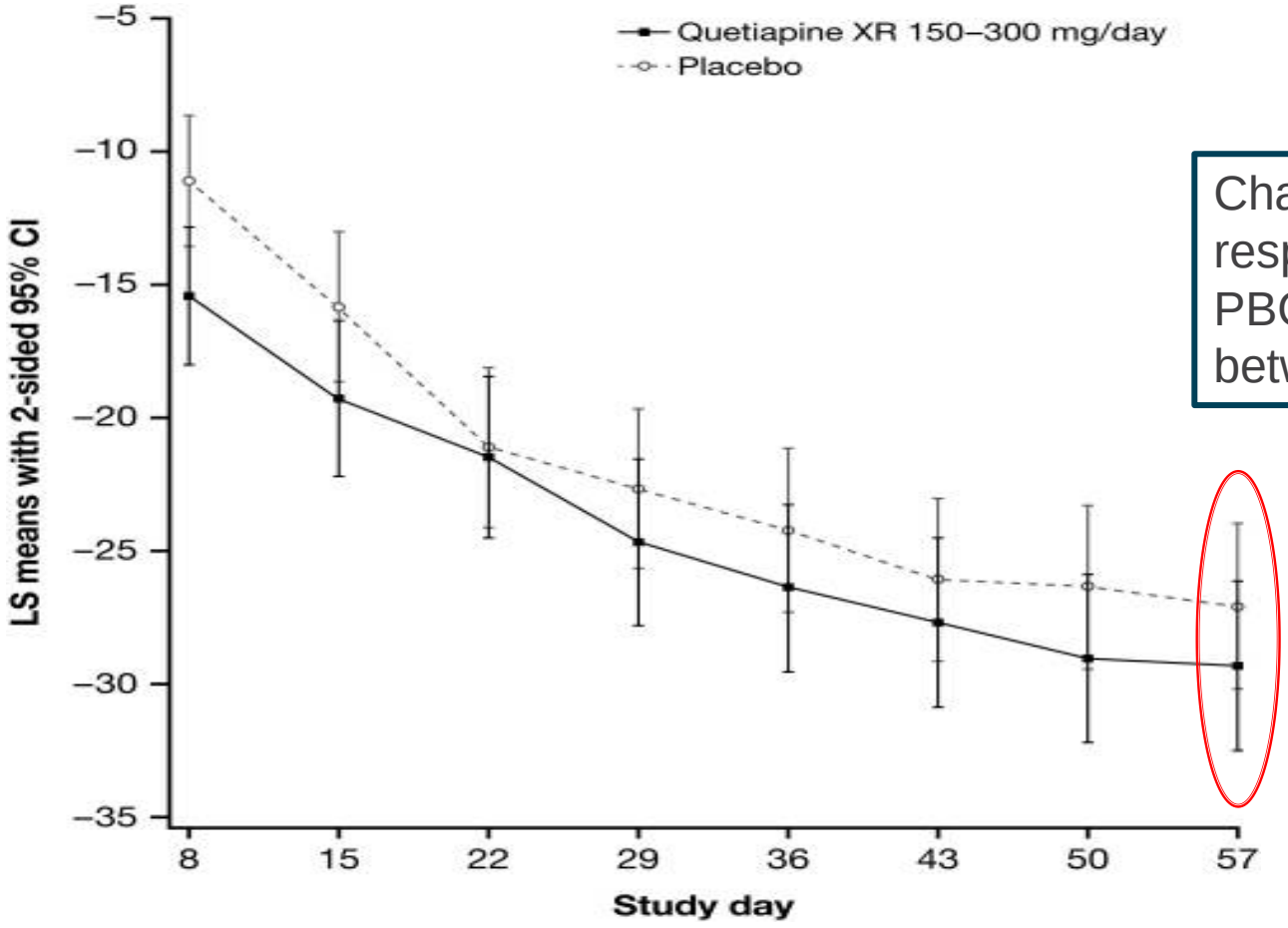
DBPC, Double blind, placebo controlled

DelBello MP, et al. *J Child Adolesc Psychopharmacol*. 2014;24(6):311-317.

Clinical convergence®

Quetiapine

Quetiapine XR versus Placebo in Pediatric Bipolar Depression



Change in CDRS (*P*=.25) and response rates (quetiapine 63%, PBO 55%) not significantly different between groups

DelBello MP, et al. *J Child Adolesc Psychopharmacol*. 2014;24(6):311-317.

Clinical convergence®

Olanzapine/Fluoxetine

FDA Indications:
(1) Acute depressive episodes associated with bipolar I disorder; (2) Treatment resistant depression

Study

Olanzapine/Fluoxetine versus Placebo for Pediatric Bipolar Depression

Design

2:1 Randomized Double-blind Placebo-controlled Trial, N=255

Subjects

BP I Inpatients or Outpatients
Current Episode: Depressed
Ages: 10 to 17 years

Treatment

OFC (6/25 to 12/50 mg/day) or placebo for up to 8 weeks

Measures

Baseline CDRS-R ≥40 and YMRS ≤15
Primary Outcome: CDRS-R total score via MMRM methodology

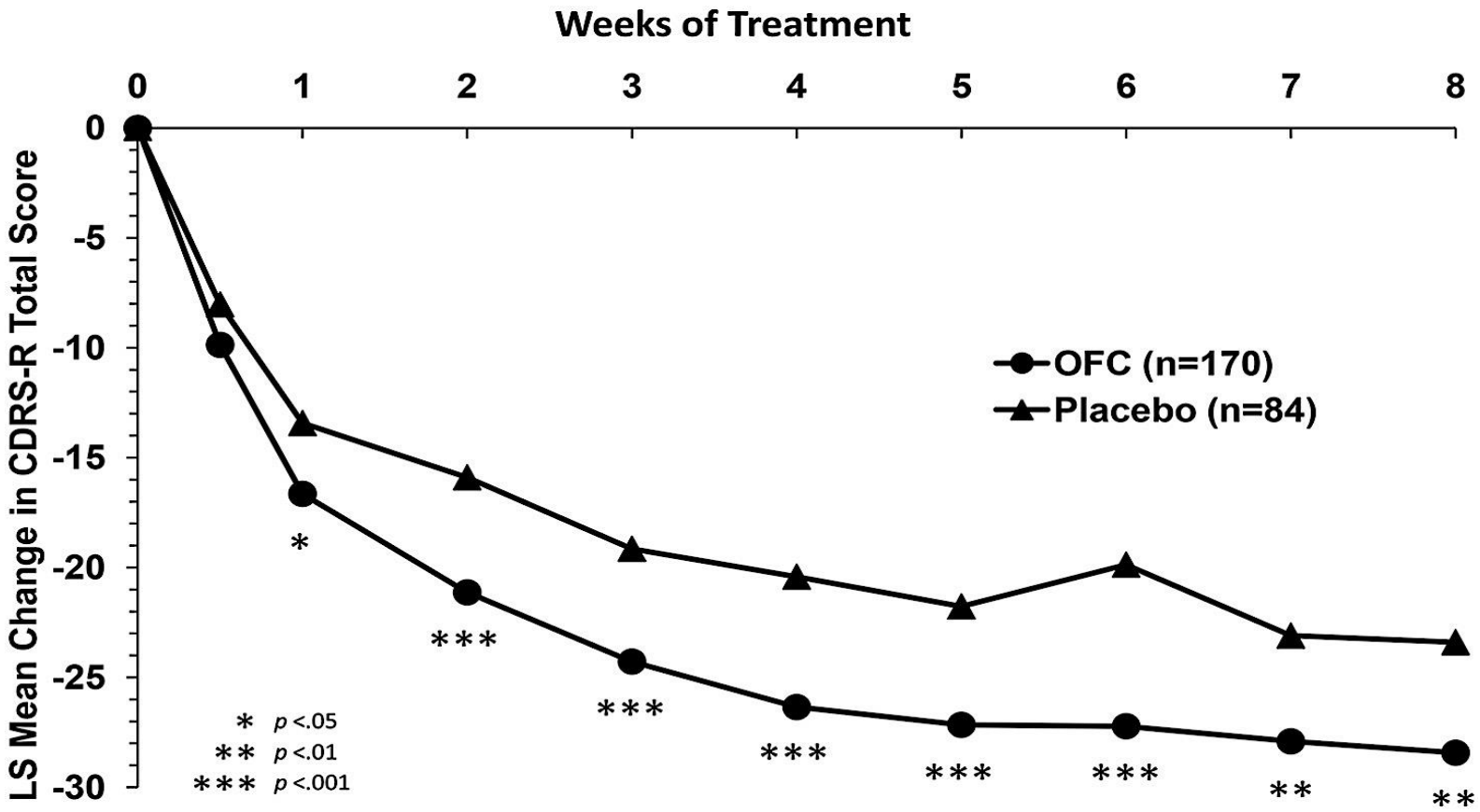
Detke HC, et al. *J Am Acad Child Adolesc Psychiatry.* 2015;54(3):217-224.

MMRM: Mixed Model Repeated Measures.

Clinical convergence®

Olanzapine/Fluoxetine

Change in CDRS-R Total Score

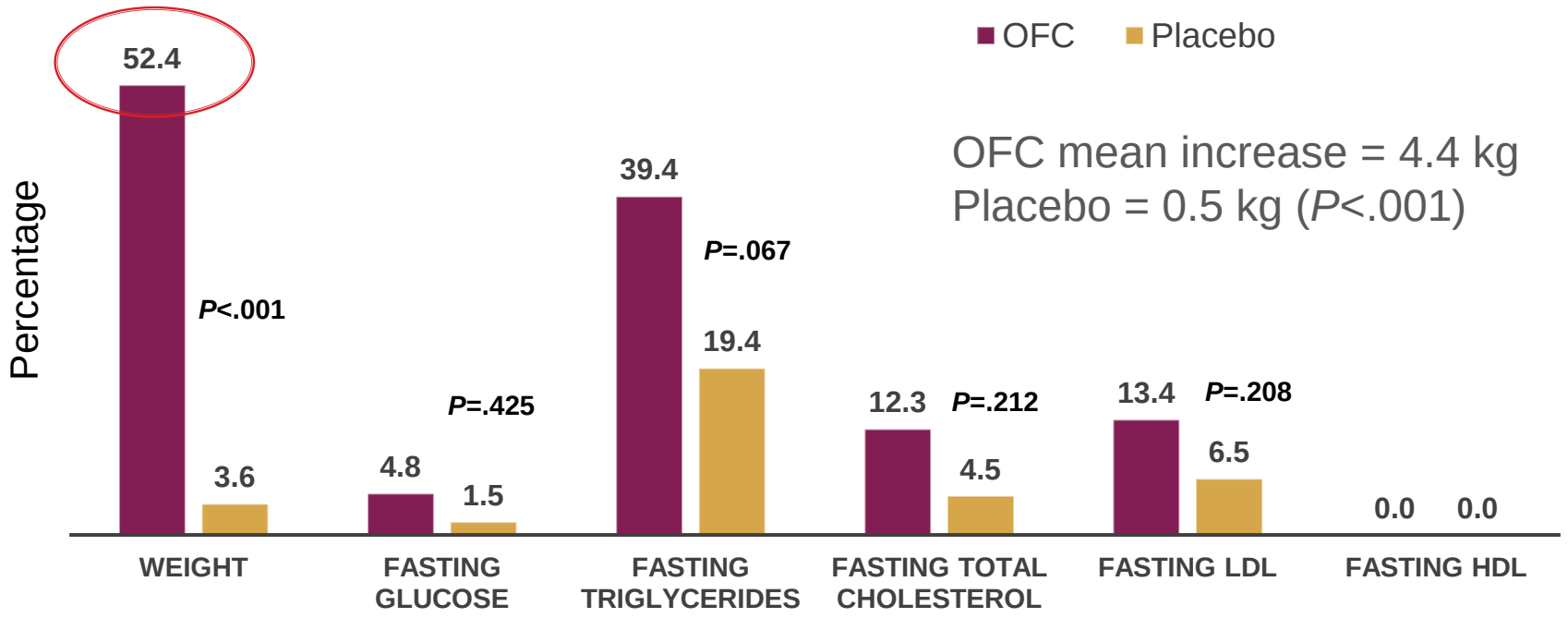


Detke HC, et al. *J Am Acad Child Adolesc Psychiatry.* 2015;54(3):217-224

Clinical convergence®

Olanzapine/Fluoxetine

Changes in Weight, Glucose, and Lipids



OFC mean increase = 4.4 kg
Placebo = 0.5 kg (*P*<.001)

	Baseline (mg/dL)	Fasting (mg/dL)
Glucose	<100	≥126
TG	<90	≥130
TC	<170	≥200
LDL	<110	≥130
HDL	>65	<35
Weight	≥7% change from baseline	

TG: Triglycerides, TC: Total Cholesterol

Detke HC, et al. *J Am Acad Child Adolesc Psychiatry.* 2015;54(3):217-224

Clinical convergence®

2nd Generation Antipsychotic

Lurasidone

FDA Indications: (1) Adult schizophrenia; (2) Bipolar depression in adults taking lithium or valproate; (3) Bipolar depression in adults, children, teens (10 to 17 years) on its own

Study

Efficacy and Safety of Lurasidone in Children/Adolescents with BP I Depression

Treatment

Lurasidone (flexible dosing of 20 to 80 mg/day) or placebo for 6 weeks

Design

DBPC, N=347

Pharmacology

Antagonist: D_2, 5-HT_{2A}, 5-HT_7 receptors
Partial Agonist: 5-HT_{1A} receptors

Subjects

Patients with BP I Depression
Ages: 10 to 17 years

Measures

Baseline CDRS-R ≥40 and YMRS ≤15
Primary Outcome: CDRS-R

CDRS-R, Children's Depression Rating Scale–Revised; DBPC, Double Blind Placebo Controlled

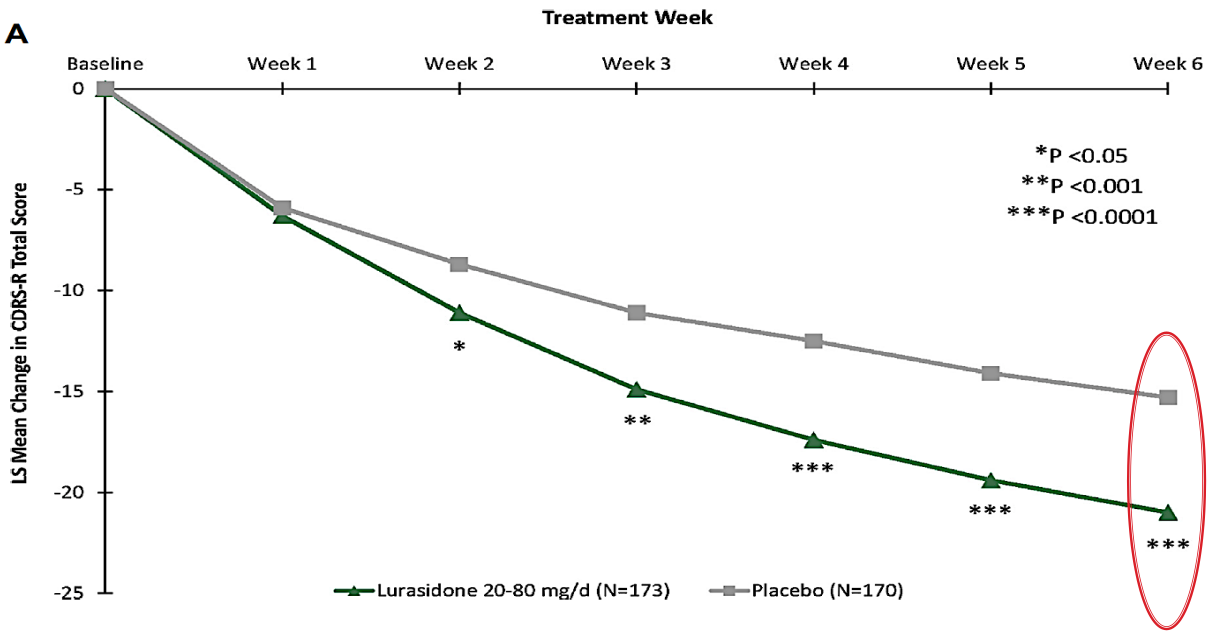
DelBello MP, et al. *J Am Acad Child Adolesc Psychiatry*. 2017;56(12):1015-1025.

Clinical convergence®

Lurasidone

PRIMARY ENDPOINT

CDRS-R Total Score Change From Baseline



ADVERSE EFFECTS

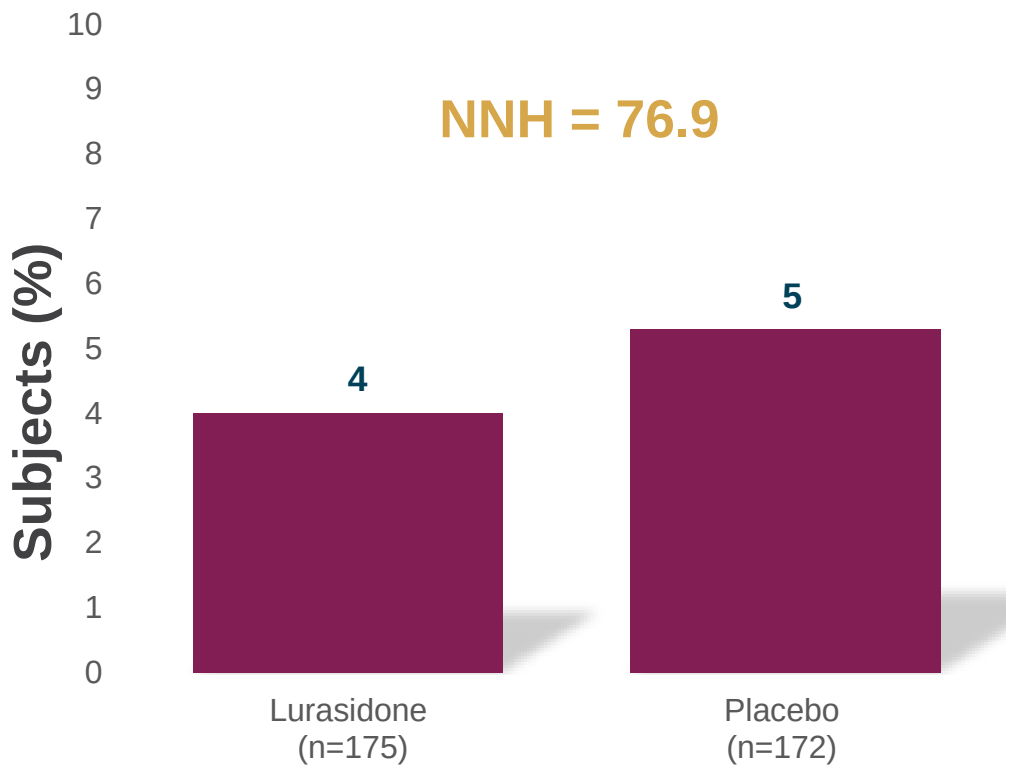
Adverse Event	Lurasidone	Placebo
Nausea	16%	5.8%
Somnolence	11%	5.8%
↑Weight	6.9%	1.7%
Vomiting	6.3%	3.5 %
Dizziness	5.7%	4.7%
Insomnia	5.1%	2.3%

DelBello MP, et al. *J Am Acad Child Adolesc Psychiatry*. 2017;56(12):1015-1025.

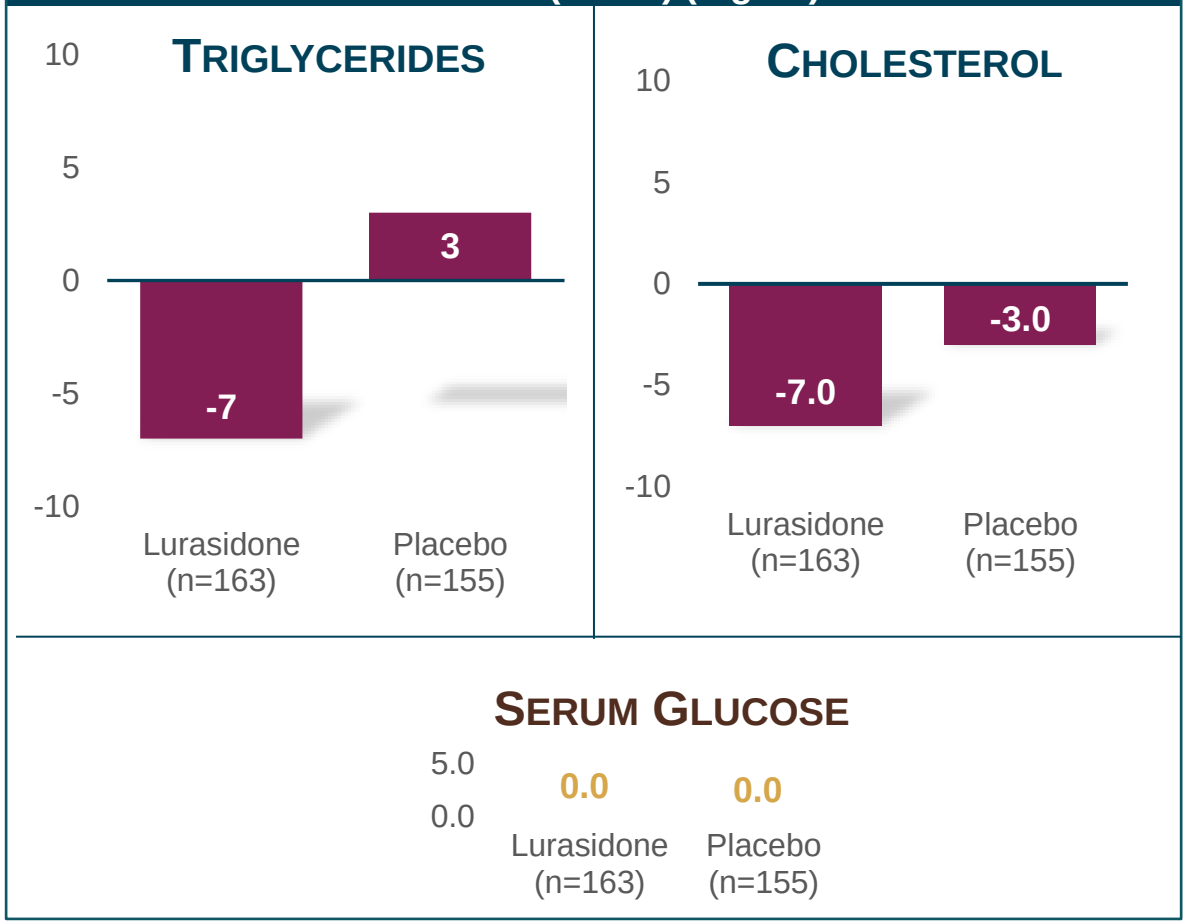
Clinical convergence®

Lurasidone

≥7% Increase in Body Weight



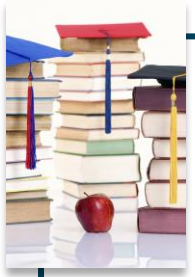
Median Change From Baseline at Week 6 (LOCF) (mg/dL)



Lurasidone dose: 20 to 80 mg/day

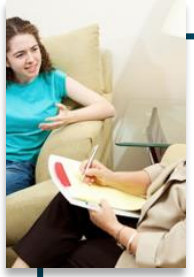
DelBello MP, et al. *J Am Acad Child Adolesc Psychiatry*. 2017;56(12):1015-1025.

Psychosocial Interventions for Bipolar Disorder



Psychoeducation

- Multi-Family Psychoeducational Psychotherapy (MF-PEP)



Cognitive Behavioral Therapy

- Depression and anxiety

Dialectical Behavioral Therapy

- Suicidality

Circadian Rhythm Hygiene

Intensive Behavioral/ Environmental Interventions

- Wraparound services; emotional support classes; approved private schools; partial hospitalization

Clinical convergence®

Case: Catherine Now

Moods

Lurasidone was added and she is stable on her current regimen

No longer depressed

Euthymic

Psychosocial Intervention

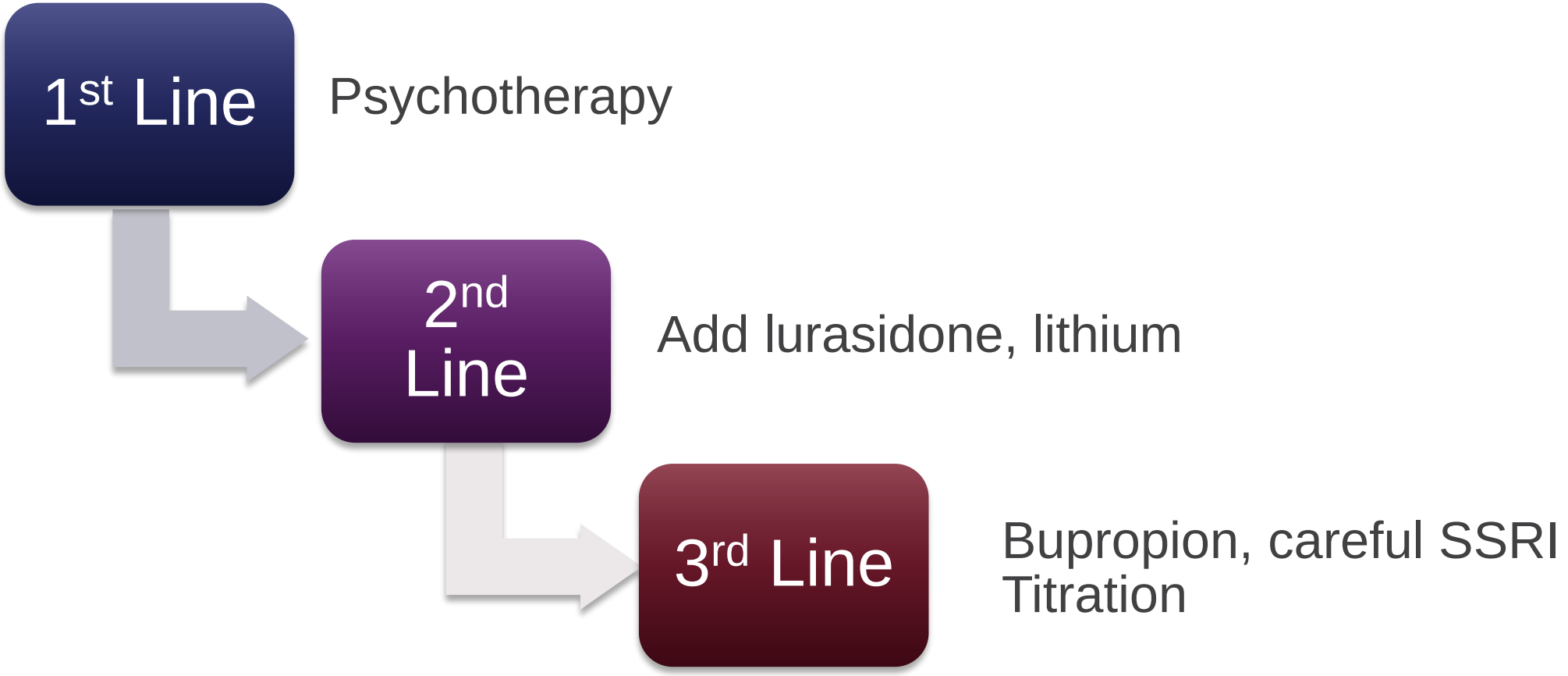
Started Cognitive Behavioral Therapy

Medications

Levothyroxine 100 mcg QD
Lurasidone 20 mg QD
Metformin 500 mg BID
Valproate 1500 mg QD
(for hypomanic symptoms)

Clinical convergence®

Summary of Treatment for Pediatric Bipolar Depression



Clinical convergence

Panel Discussion

Thank you!

Please remember to take the post-test and complete the evaluation form in order to receive credit. A certificate will immediately be available to print after successfully passing the post-test and submitting your completed evaluation form.