Juvenile Mania: Diagnosis and Treatment 2 parts

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Disclosure and potential conflicts

My spouse and I have the following financial relationship with a commercial interest to disclose:

Research support: PCORI
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Spouse research support: UCB Pharma, NeuroMetrix, Luitpold, NIMH, RLS Foundation

Juvenile Mania: Diagnosis part 1

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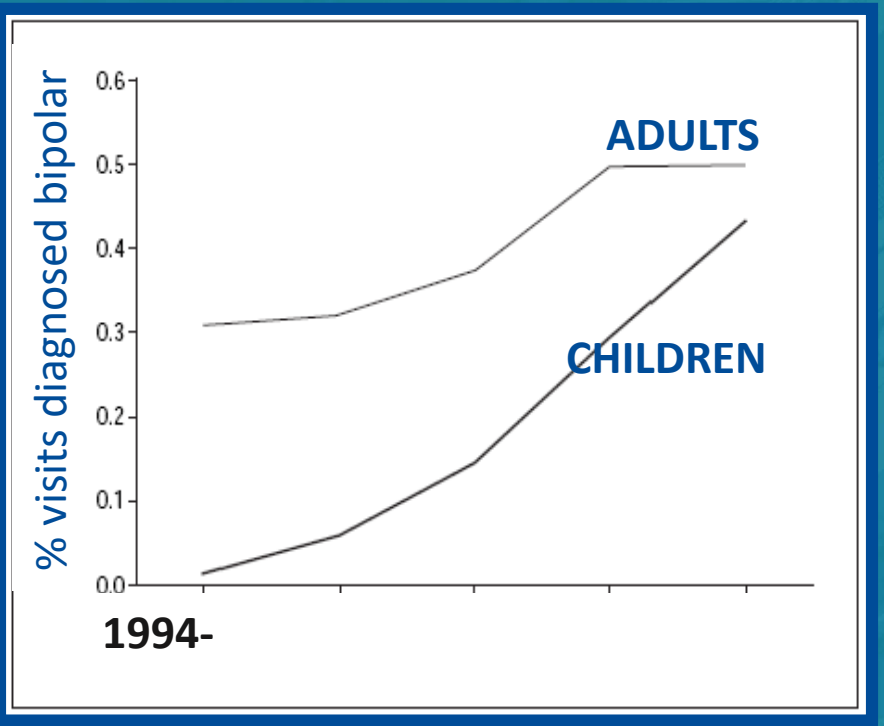
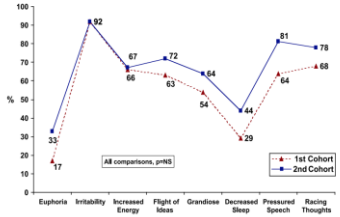


Overview: Switch from pediatric depression to bipolar disorder is common. Pediatric-onset bipolar disorder is a severely impairing disorder which persists into late adolescence.

Antipsychotic medications are most effective for pediatric mania, and comorbid conditions must be addressed. Natural treatments hold promise

Children with MDD often switch: Early depression is a predictor of bipolar disorder



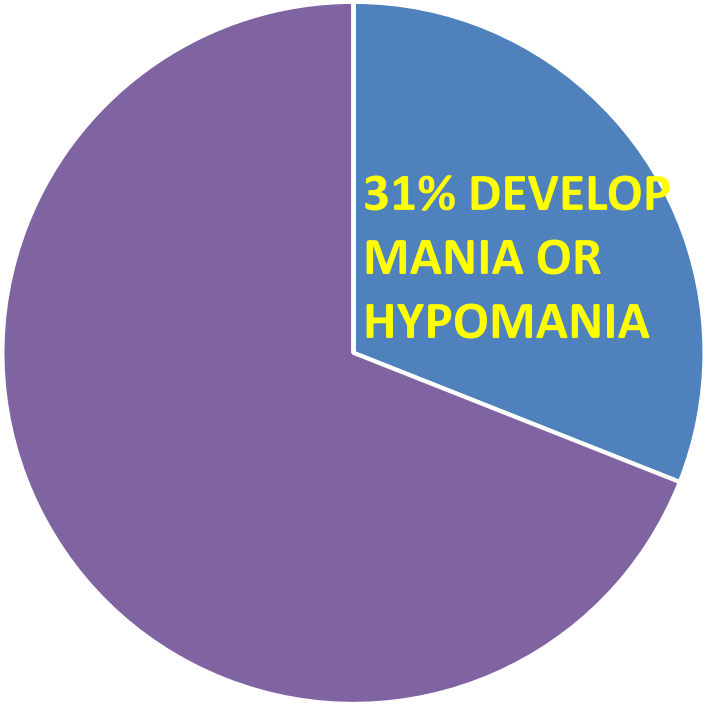
Pediatric Bipolar disorder is a highly morbid condition that affects a significant minority of young children, is familial and persists over time

Treatment: Pharmacologic treatment with SGAs is generally required for pediatric bipolar disorder and comorbidities need separate treatment: use antidepressants with caution

Natural Treatments hold promise in the treatment of pediatric bipolar disorder

Children with MDD often switch

CHILDREN WITH MDD

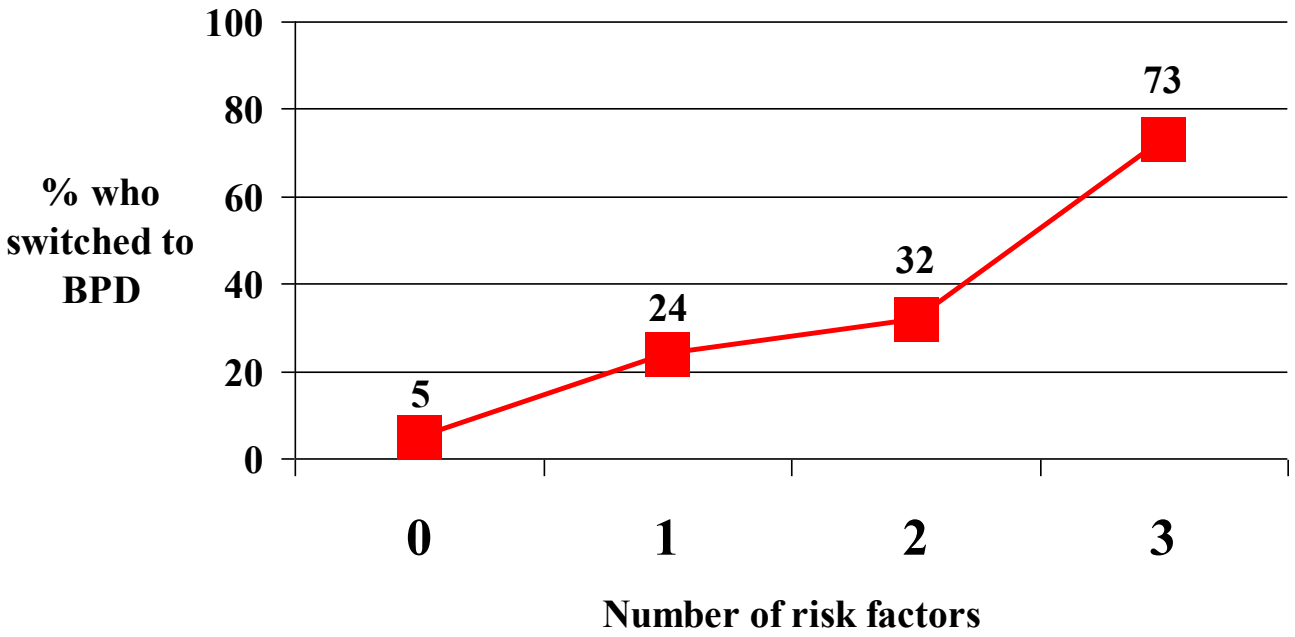


Adult literature has consistently reported that "early onset" (< 25 years) depression poses a risk of switching

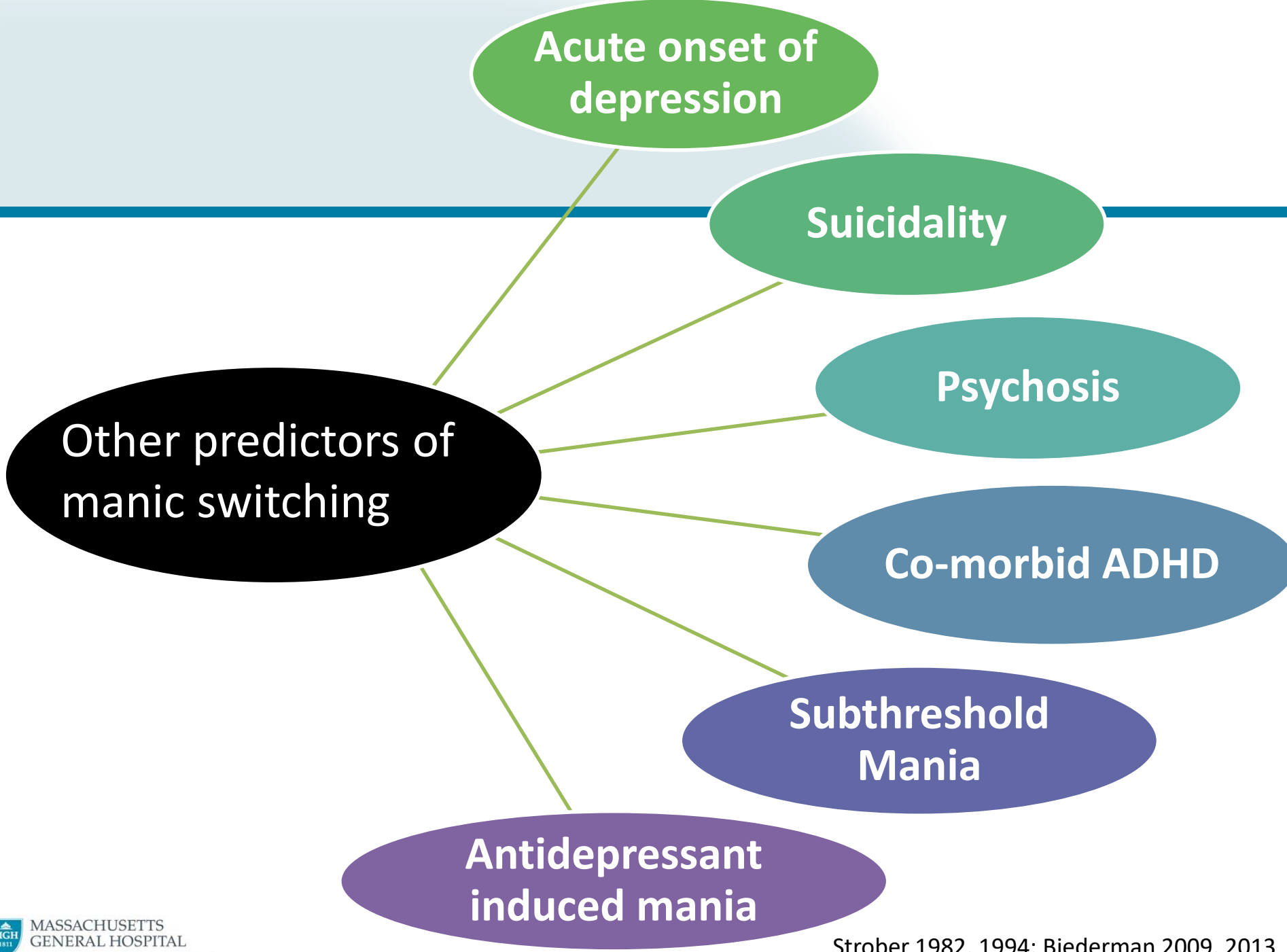
Weissman 1999; Geller 1994

There is a 'dose response' of multiple risk factors contributing to manic switch

- conduct disorder
- school behavior problems
- parental mood disorder



Biederman 2009



Strober 1982, 1994; Biederman 2009, 2013

Antidepressants can lead to switching
Use with caution

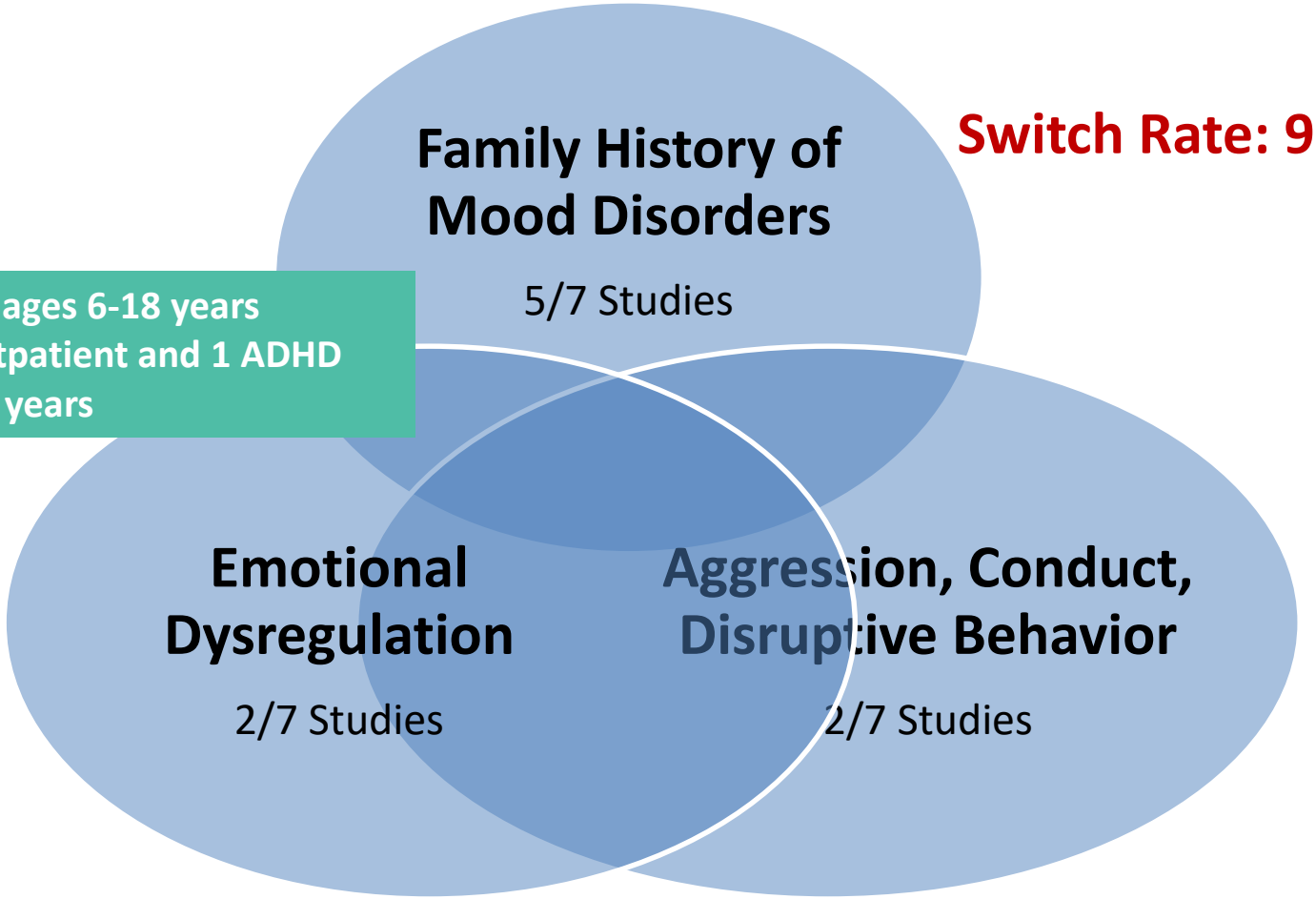
pharmacologically induced hypomania was a predictor of a bipolar course

antidepressant induced mood change was seen more in BP MDD

rate of switching higher in subjects with history of receiving antidepressants especially in children

Strober; Shon; Martin

Top features of pediatric depression found which predict subsequent switch to bipolar disorder from 7 prospective studies (4 samples)

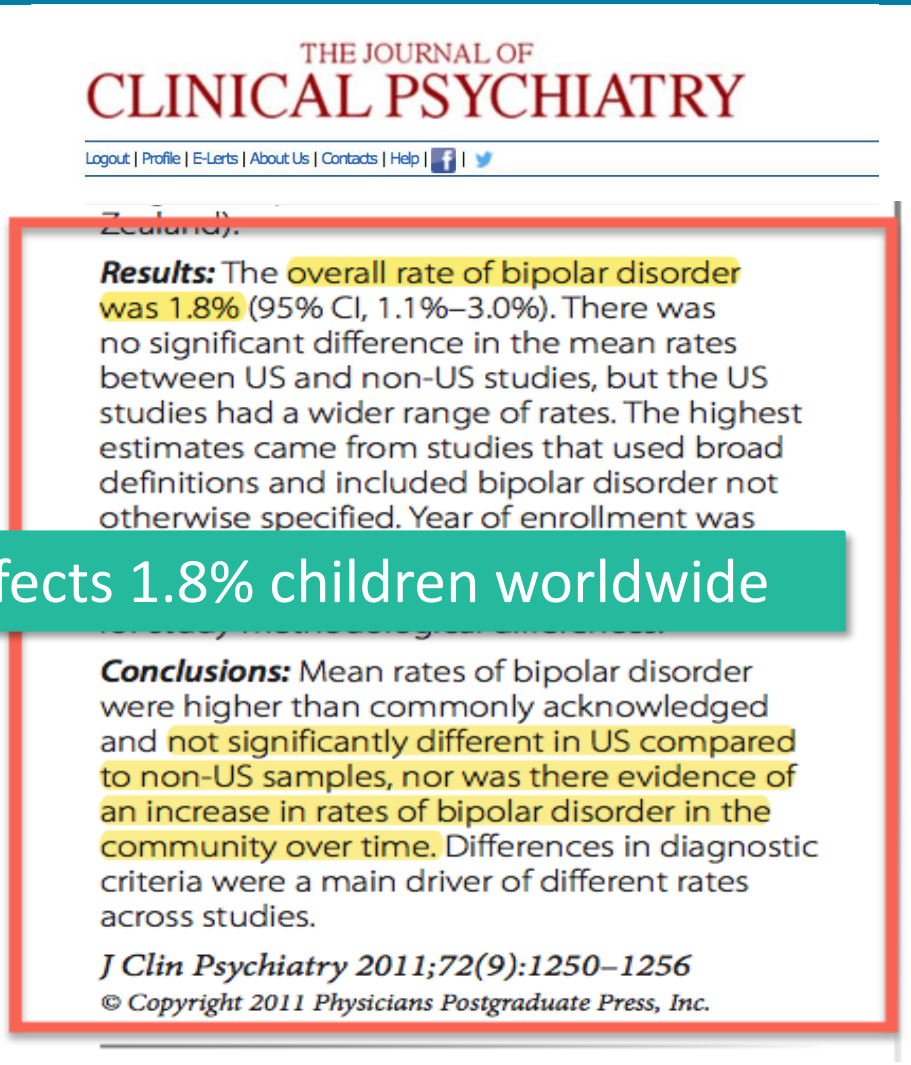


Switch Rate: 9% - 43%

N= 985 subjects, ages 6-18 years
2 inpatient, 1 outpatient and 1 ADHD
Follow up: 1 - 11 years

Strober 1982,1993; Geller 1994,2001; Kochman 2005; Biederman 2009, 2013

In a meta-analysis of international studies, the rate of pediatric bipolar disorder was 1.8%



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Results: The overall rate of bipolar disorder was 1.8% (95% CI, 1.1%–3.0%). There was no significant difference in the mean rates between US and non-US studies, but the US studies had a wider range of rates. The highest estimates came from studies that used broad definitions and included bipolar disorder not otherwise specified. Year of enrollment was

Bipolar Disorder affects 1.8% children worldwide

Conclusions: Mean rates of bipolar disorder were higher than commonly acknowledged and not significantly different in US compared to non-US samples, nor was there evidence of an increase in rates of bipolar disorder in the community over time. Differences in diagnostic criteria were a main driver of different rates across studies.

J Clin Psychiatry 2011;72(9):1250–1256

Van Meter J Clin Psych 2011

The symptoms of mania are the same in children and adults

Mania:

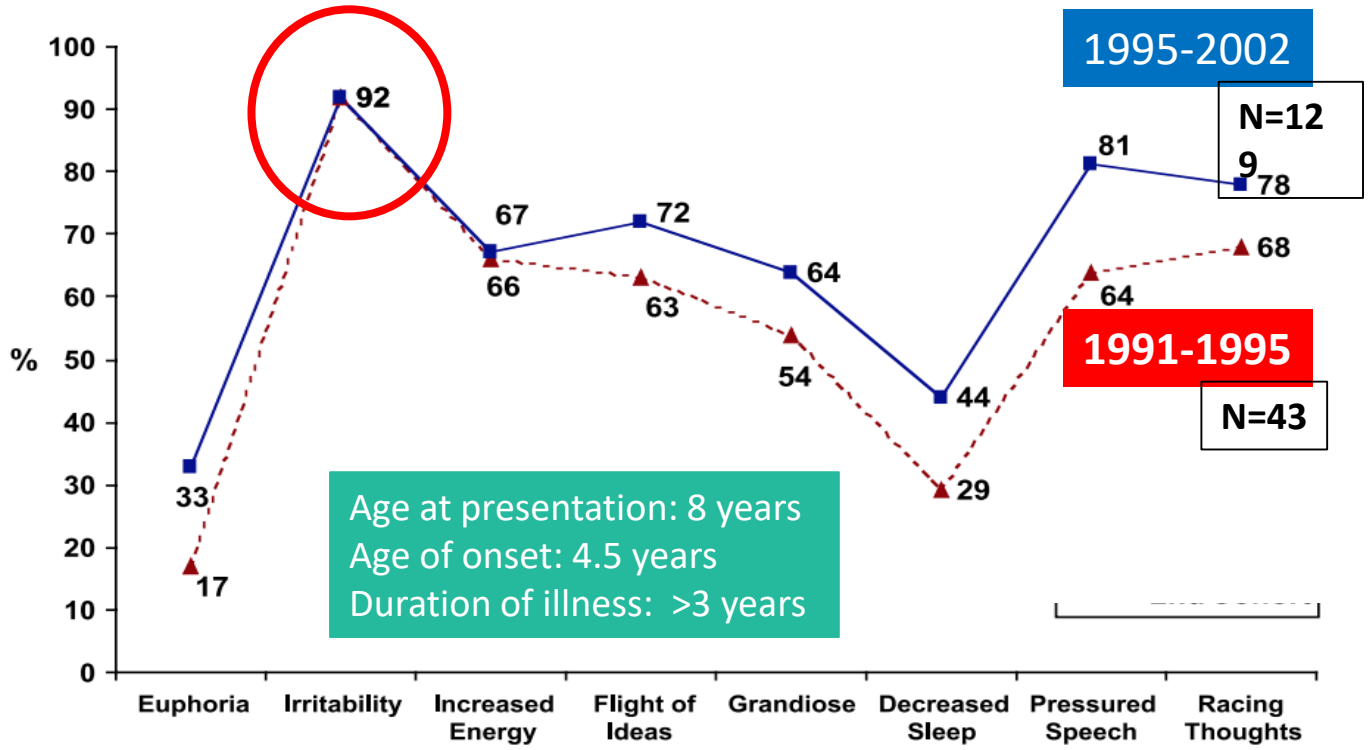
A. A *distinct period (7 days=mania; 4 days=hypomania)* of abnormally and persistently elevated, expansive, or irritable mood and persistently increased goal-directed activity or energy

B. At least 3/7 (4/7 if mood is irritable)

1) D Distractibility
2) I Increased activity/psychomotor agitation
3) G Grandiosity or inflated self-esteem
4) F Flight of ideas or racing thoughts
5) A Activities with painful consequences
6) S Sleep decreased
7) T Talkative or pressured speech

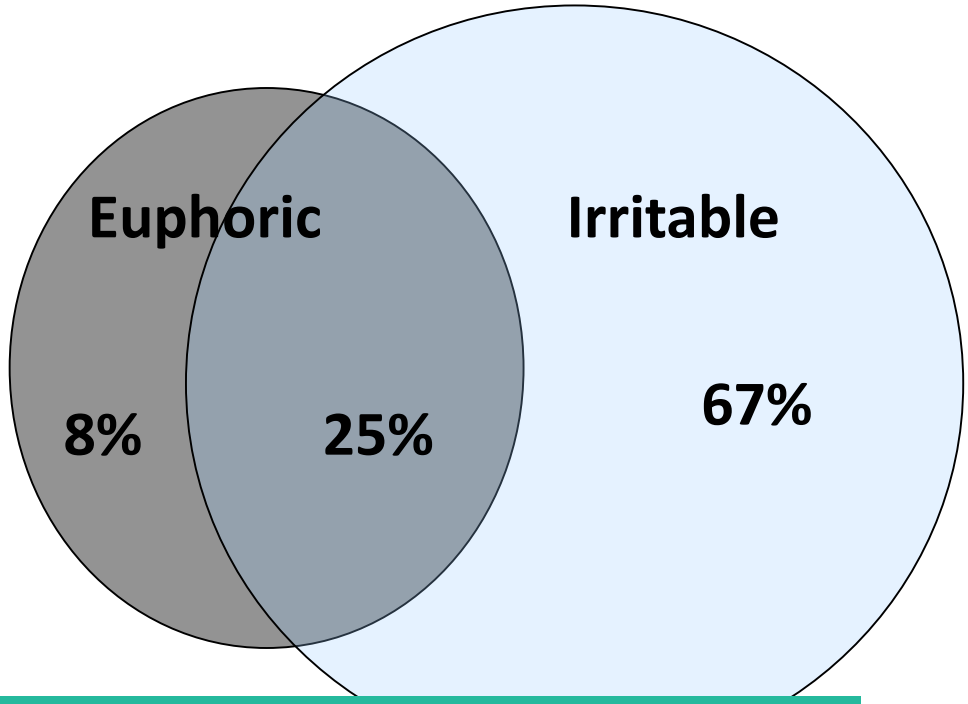
Diagnostic and Statistical Manual (DSM-5)

The symptoms of mania are the same in two cohorts of pre-adolescent age (<12 years) youth with bipolar disorder



Wozniak, 1995; Biederman, 2004

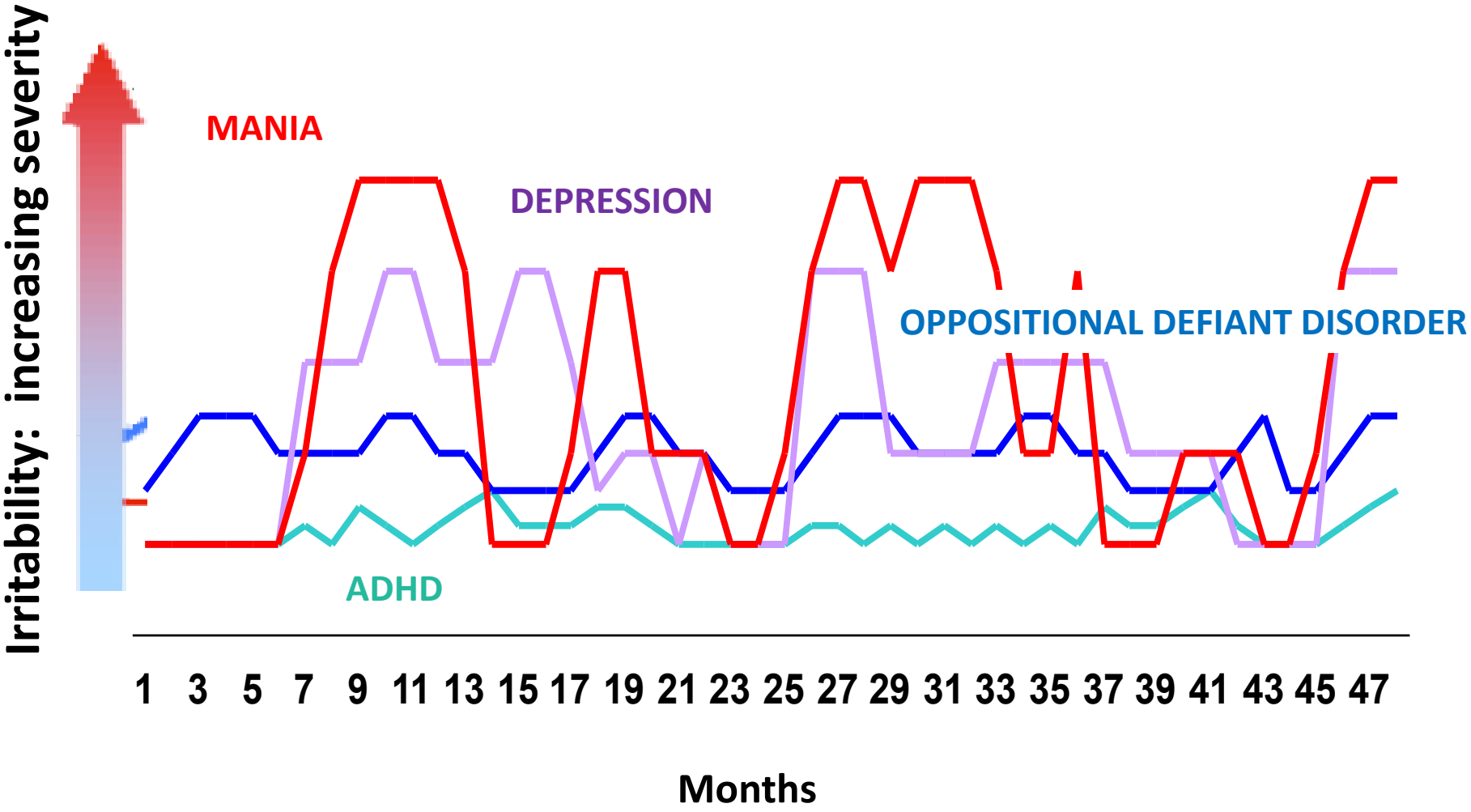
Severe aggressive and destructive irritability is a common feature of pediatric mania: kicking, hitting, biting, spitting



Bipolar disorder has ‘highs’ and ‘lows,’ with euphoric mania and melancholy depression, but irritability is common and highly impairing

Wozniak, 1995; Biederman, 2004

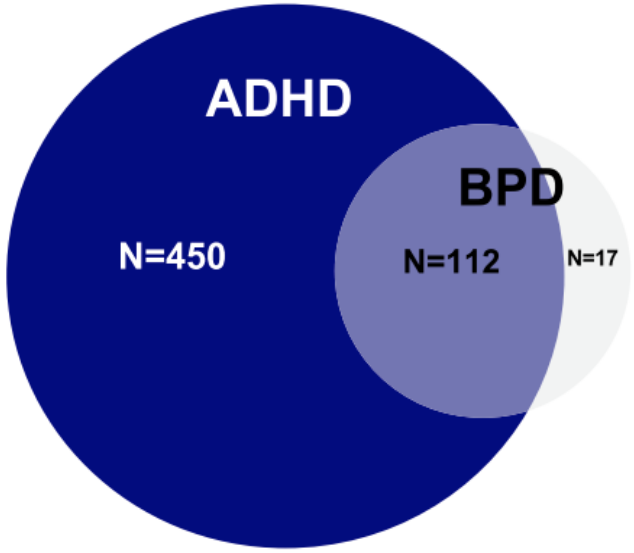
Children with bipolar disorder are seldom completely well and different types of irritability may be present



Mick 2007

Bipolar disorder + ADHD (common pediatric presentation) is a different more impairing condition from ADHD alone

	Bipolar	ADHD
Depression	86%	38%
Psychosis	**16%**	0
Defiance	88%	48%
Conduct Disorder	**37%**	15%
Anxiety	56%	26%
Hospitalization	21%	2%
Functioning	Very poor	fair
Learning Disability	42%	14%

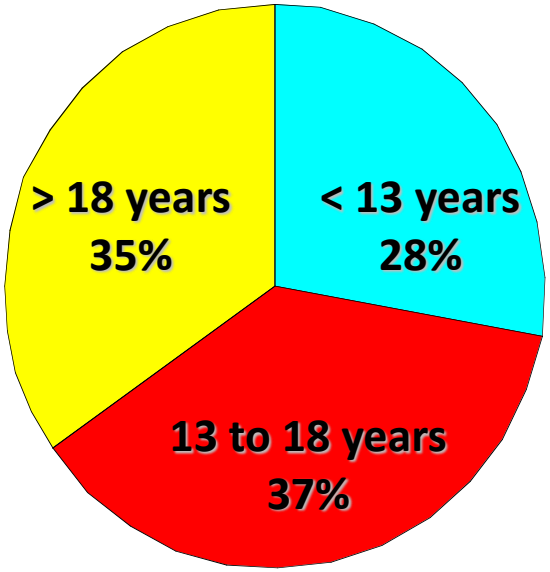


Most children with bipolar disorder also hav comorbid ADHD

Wozniak, 1995; Biederman, 2004

Adults with Bipolar Disorder + ADHD have clinical correlates similar to that seen in pediatric bipolar disorder

9.5% lifetime prevalence comorbid ADHD in adult
STEP-BD (N=983)



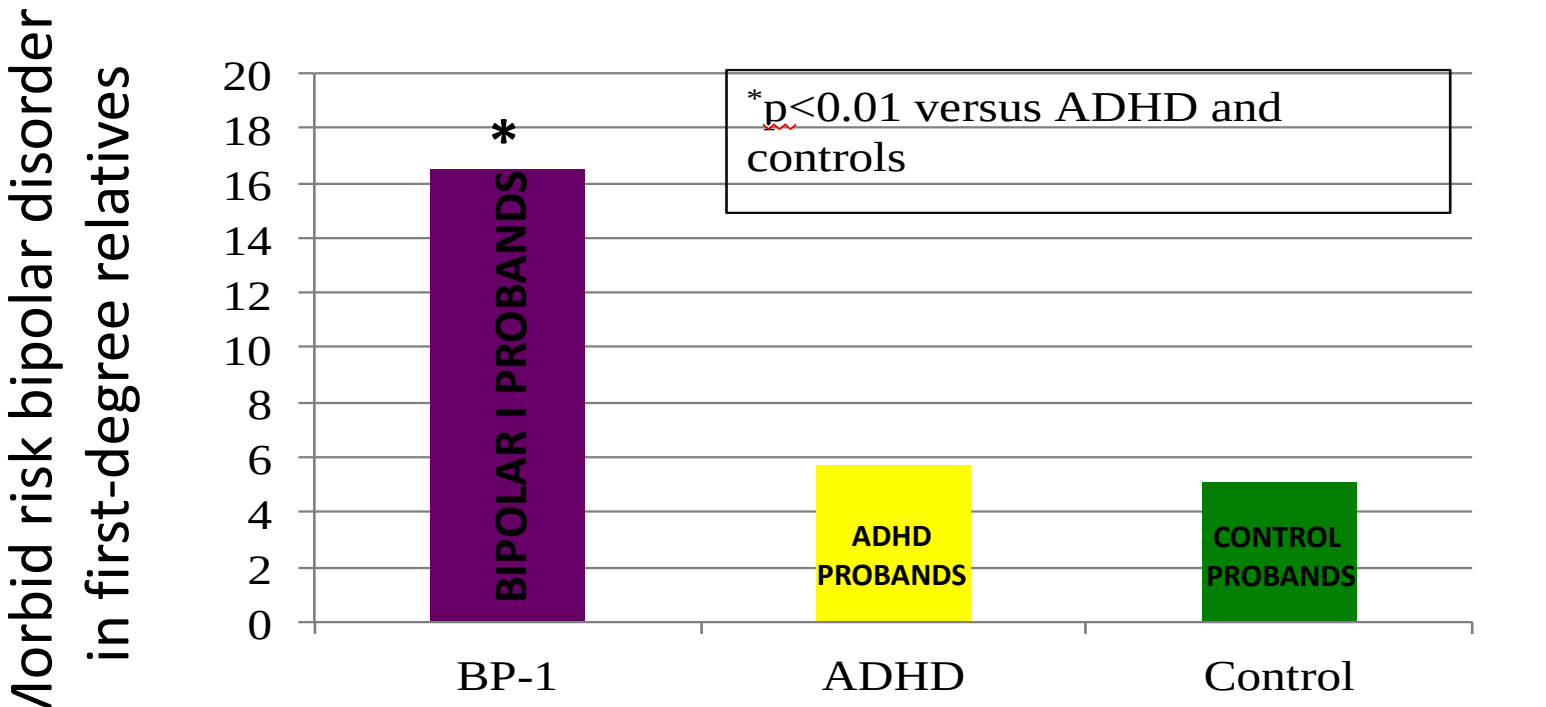
BPD+ADHD Adult patients:

- had earlier onset BPD by 5 years
- had shorter periods of wellness (chronic)
- had more comorbidity (anxiety and substance)
- were more likely to be male
- were more likely to have Bipolar I
- had more days irritable and more days elated
- had lower GAF
- more suicide attempts
- more violence
- more legal problems (conduct disorder?)

Perlis Biol Psych 2004; Nierenberg 2005

Familial risk of bipolar I disorder is greatest in first-degree relatives of BP-I versus ADHD and control probands

The MGH Pediatric Bipolar Disorder family is the largest controlled family study



239 probands
726 relatives

162 probands
511 relatives

136 probands
411 relatives

MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

Wozniak J Clin Psych 2012

Subsyndromal pediatric bipolar disorder is also familial and highly impairing

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DOI: 10.1111/bdi.12494

ORIGINAL ARTICLE

WILEY BIPOLAR DISORDERS

Similar familial underpinnings for full and subsyndromal pediatric bipolar disorder: A familial risk analysis

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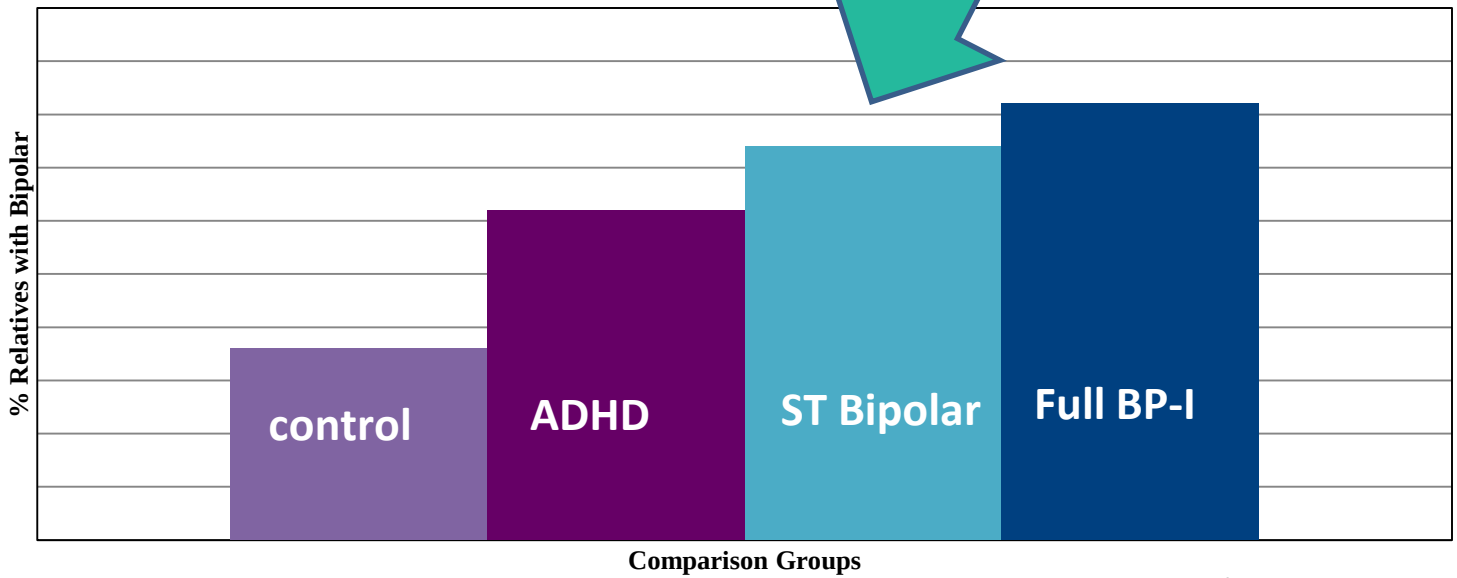
Pediatric probands with subthreshold bipolar disorder have rates of familiality similar to full syndrome probands



Wozniak 2017

Persistence of pediatric-onset bipolar disorder has been documented in St Louis and Pittsburgh samples

Geller, 2008:
WashU KSADS (modified criteria) study
In grown-up subjects with child BP-I, identified using the, the **44.4% frequency of manic episodes was 13 to 44 times higher than population prevalences**, strongly supporting continuity

Birmaher, 2009:
The Course and Outcome of Bipolar Youth (COBY) Study
25% of BPDII and 38% of BPD NOS converted to BPI
Subjects symptomatic on average for 60% of the follow-up period

Geller ArchGenPsychiatry 2008
Birmaher AmJPsychiatry 2009

We followed-up children ascertained for a family study of pediatric-onset bipolar disorder to assess persistence

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High level of persistence of pediatric bipolar-I disorder from childhood onto adolescent years: A four year prospective longitudinal follow-up study

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ABSTRACT

Objective: To examine the longitudinal course of pediatric bipolar (BP)-I disorder in youth transitioning from childhood into adolescence.

Methods: We conducted a four year prospective follow-up study of 78 youth with BP-I disorder 6–17 years old at ascertainment followed up into adolescent years (13.4 ± 3.9 years). All subjects were comprehensively assessed with structured diagnostic interviews, neuropsychological testing, psychosocial, educational and treatment history assessments. BP disorder was considered persistent if subjects met full criteria for DSM-IV BP-I disorder at follow-up.

Results: Of 78 BP-I participating youth subjects, 57 (73.1%), continued to meet full diagnostic criteria for BP-I Disorder. Of those with a non-persistent course, only 6.4% ($n = 5$) were euthymic (i.e., syndromatic and symptomatic remission) at the 4-year follow-up and were not receiving pharmacotherapy for the disorder. The other non-persistent cases either continued to have subthreshold BP-I disorder ($n = 5$, 6.4%), met full ($n = 3$, 3.8%) or subthreshold ($n = 1$, 1.3%) criteria for major depression, or were euthymic but were treated for the disorder ($n = 7$, 9.0%). Full persistence was associated with higher rates of major depression and disruptive behavior disorders at the follow-up assessment and higher use of stimulant medicines at the baseline assessment. Non-Peristent BP-I was also characterized by high levels of dysfunction and morbidity.

Conclusions: This four year follow-up shows that the majority of BP-I disorder youth continue to experience persistent disorder into their mid and late adolescent years and its persistence is associated with high levels of morbidity and disability. Persistence of subsyndromal forms of bipolar disorder was also associated with dysfunction and morbidity

78 of 105 youth with Bipolar I Disorder participating in family study followed-up after 4 years

- **Baseline age 10 years**
- **76% male**
- **Age of onset bipolar disorder: 5 years**
- **Duration of BPD at baseline: 7 years**

Wozniak JPsychiatrRes 2011

A one-year period at follow-up and nuanced definition of persistence are clinically meaningful

BASELINE

PREVIOUS ONE YEAR PREVALENCE

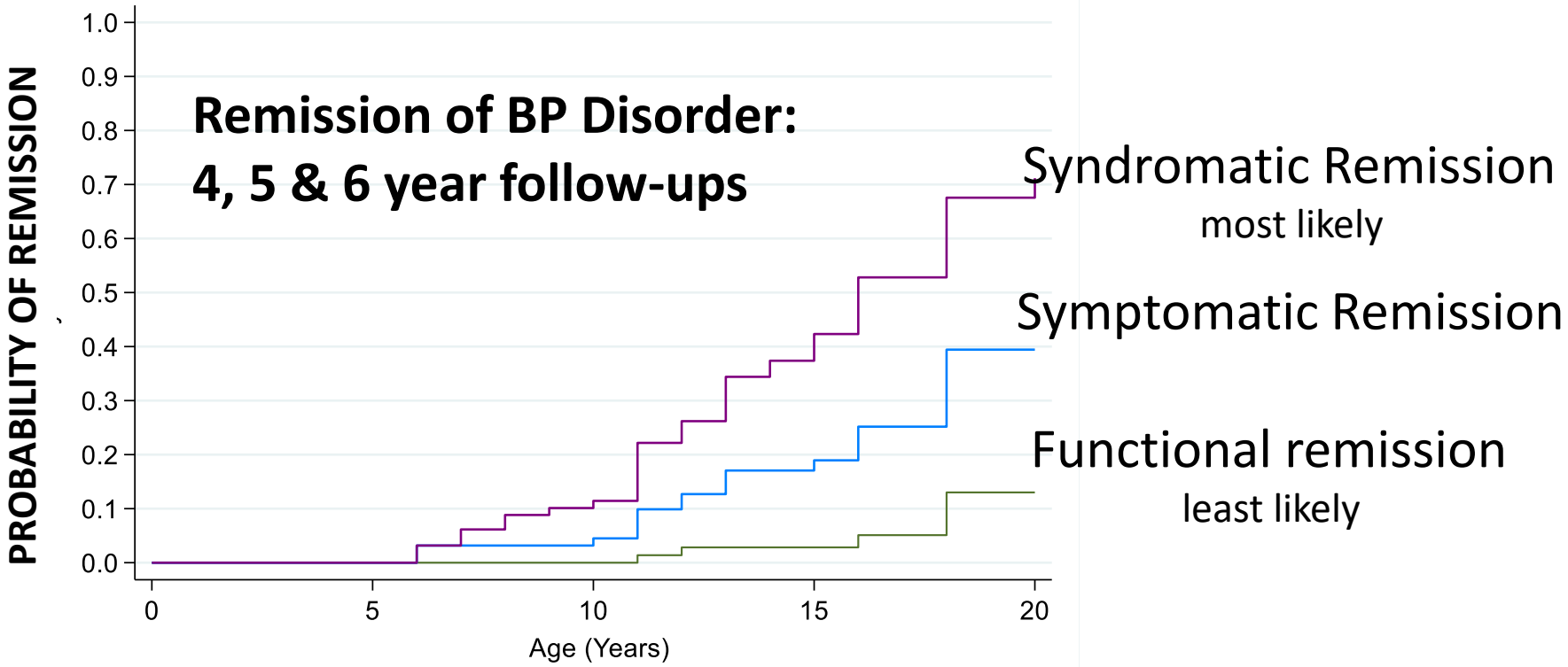
full or subthreshold mania
full or subthreshold depression
treatment for mood disorder
global assessment of functioning
comorbidity assessed

FOLLOW-UP

Functional Remission
(no symptoms, good functioning) is less likely than

Symptomatic Remission
(no symptoms, functioning impaired) which is less likely than

Syndromatic Remission
(symptoms persist, functioning impaired)

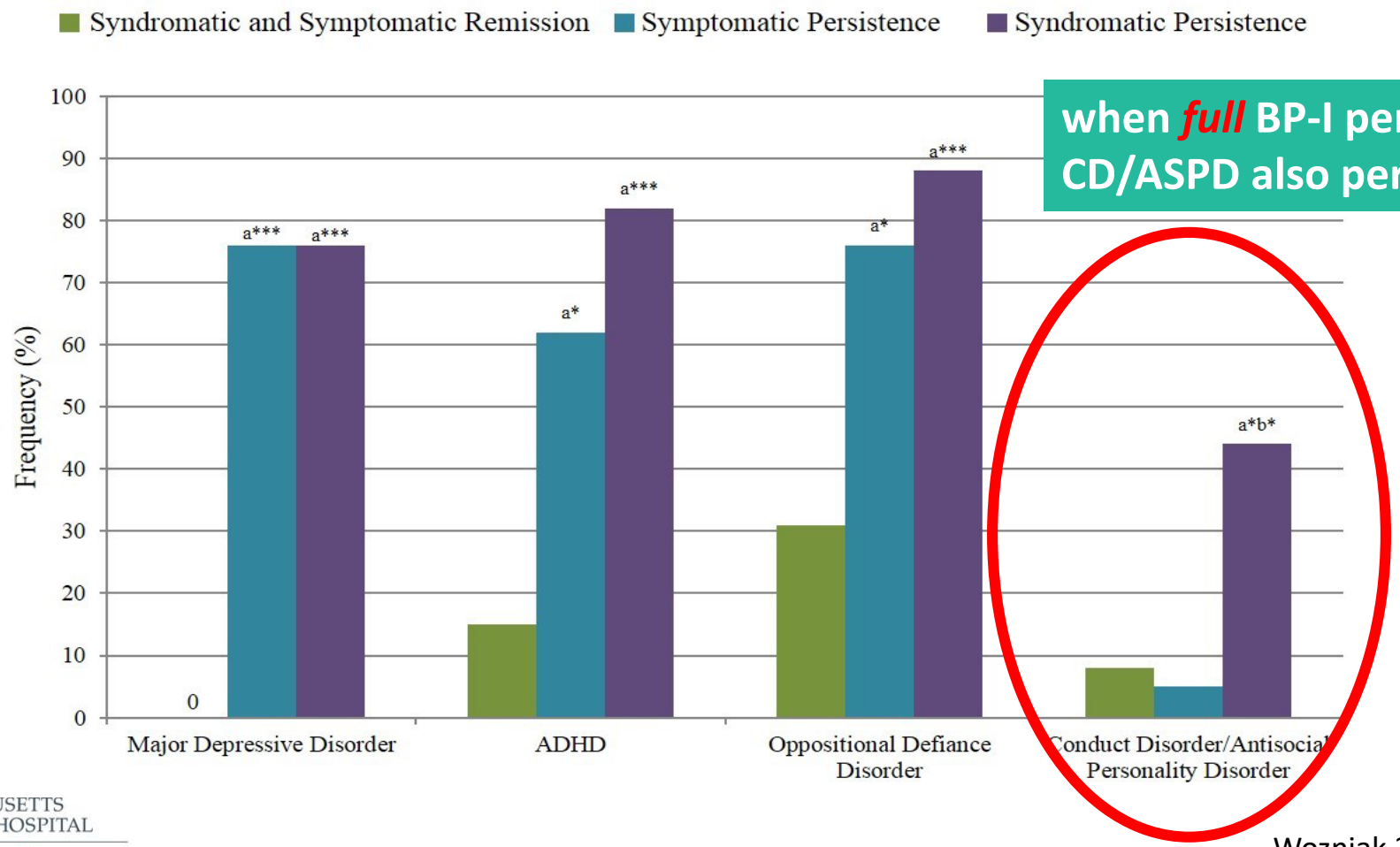


Symptoms and poor functioning found at follow-up

Wozniak 2020

Comorbid diagnoses at 5-year follow-up are high and similar in both persistent groups versus full remission (except CD/ASPD)

Figure 2. One-year prevalences of comorbid psychiatric disorders.
[a] Compared to syndromatic and symptomatic remission. [b] Compared to symptomatic persistence. *P<0.05, **P<0.005, ***P<0.001



when *full* BP-I persists, CD/ASPD also persists

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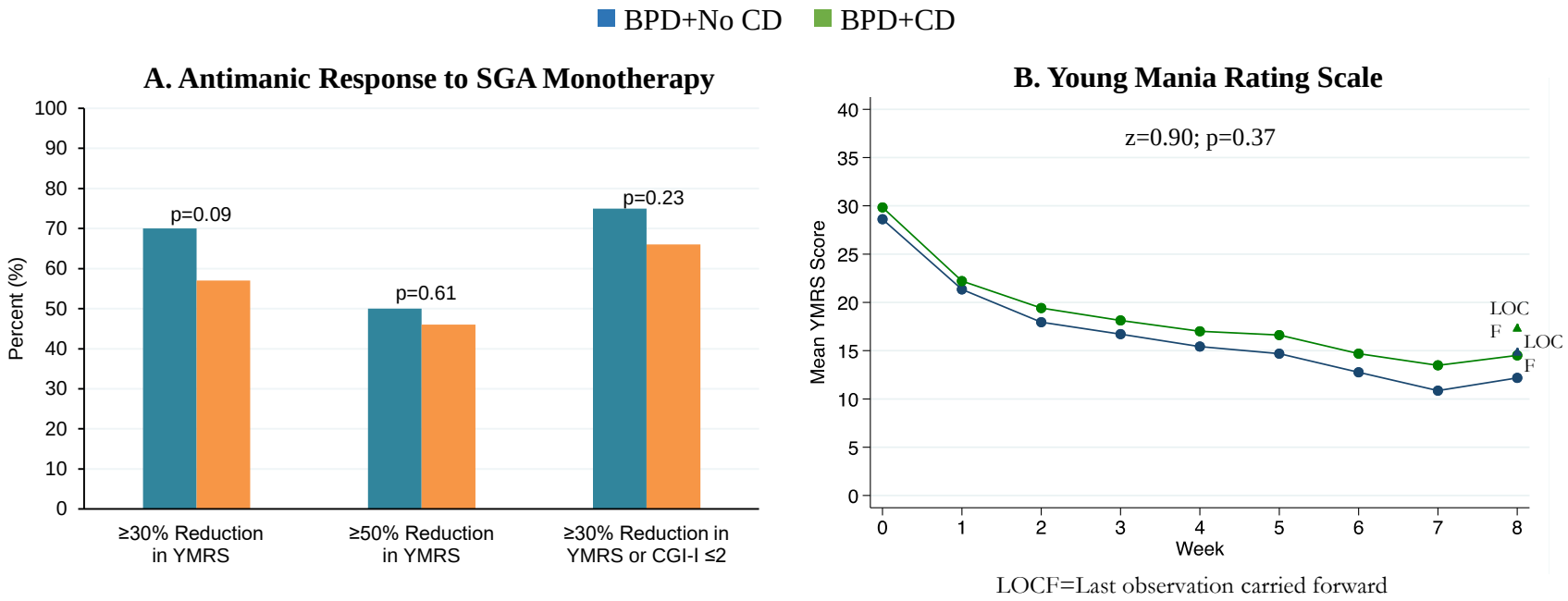
Wozniak 2018

SGAs can successfully treat bipolar disorder even in the setting of CD comorbidity (and CD remits for many subjects only when BPD remits)

Figure 1. (A) Antimanic response to SGA monotherapy and (B) YMRS scores over the course of the 8-week trials in youth with bipolar disorder with and without comorbid conduct disorder.



Of the 57 BP + CD with antimanic response to SGA treatment,

18 (32%) had CGI-CD-I scores ≤ 2 at endpoint (very much or much improved)

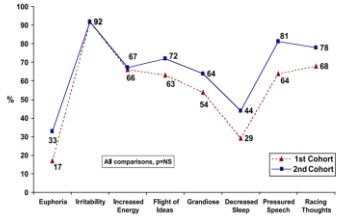
Of the 32 BP + CD with no antimanic response to SGA treatment,

3 (9%) had CGI-CD-I scores ≤ 3 at endpoint (very much or much or improved)

Overview: Switch from pediatric depression to bipolar disorder is common. Pediatric-onset bipolar disorder is a severely impairing disorder which persists into late adolescence.

Antipsychotic medications are most effective for pediatric mania, and comorbid conditions must be addressed. Natural treatments hold promise

Children with MDD often switch: Early depression is a predictor of bipolar disorder



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Treatment: Pharmacologic treatment with SGAs is generally required for pediatric bipolar disorder and comorbidities need separate treatment: use antidepressants with caution

Natural Treatments hold promise in the treatment of pediatric bipolar disorder

QUESTIONS?