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Diagnosis & Assessment in Pediatric Psychopharmacology

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In Tribute to Joseph Biederman, MD





Faculty Disclosure

- **Timothy Wilens, M.D. has served as a consultant, or has received grant support from the following**
 - FDA, NIH (NIDA), 3D Therapeutics
 - Licensing agreements with Ironshore (Before School Functioning Questionnaire), 3D Therapeutics
 - Clinical care: MGH, Bay Cove, Gavin, National Football League, Major/Minor League Baseball
 - (Co)Edited Straight Talk About Psychiatric Medications for Kids (Guilford); ADHD Across the Lifespan (Cambridge), Update in Pharmacotherapy of ADHD (Elsevier)
 - Some of the medications discussed may not be FDA approved in the manner in which they are discussed including diagnosis(es), combinations, age groups, dosing, or in context to other disorders (eg, substance use disorders)



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Insel's JAMA Editorial May 2014

- 50% of adults with a mental disorder reported onset by 14 years or younger
- Mental and substance use disorders remain the predominant noncommunicable disorders of young people in terms of burden of illness



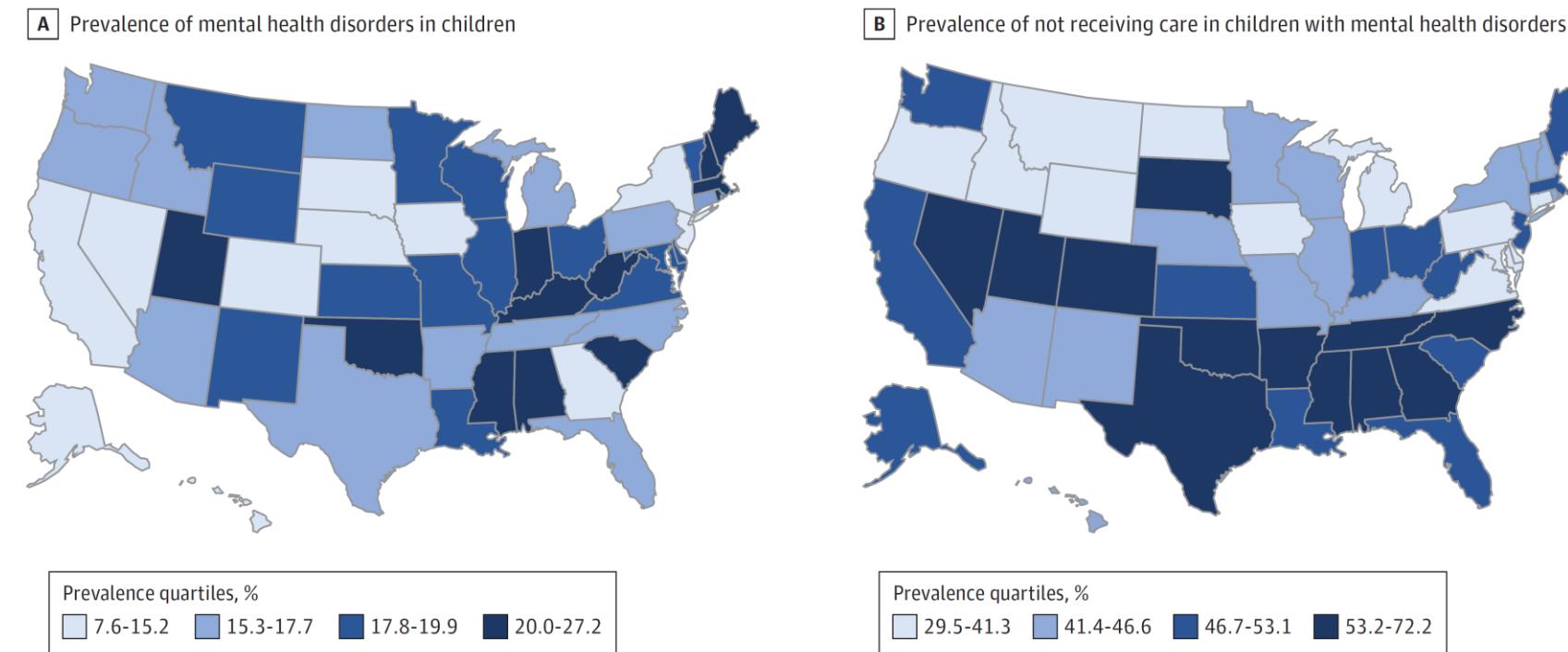
Most Prevalent Mental Illnesses in Youth

- **Autism Spectrum (1%-2%)**
- **Conduct disorder (3%)**
- **Depression (2%-4%)**
- **Anxiety disorders (3-5%)**
- **Cigarette Dependence (prior month 3%)**
- **Substance use disorders (10%)**
- **ADHD (11%)**
- **Suicide remains a leading cause of death in youth**

- Half of the estimated 7.7 million US children with a treatable mental health disorder do not receive needed treatment from a mental health professional

- This estimate varied considerably by state

Figure. Prevalence of Mental Health Disorders and Mental Health Care Use Among US Youth



A, State-level prevalence presented as quartiles of at least 1 mental health disorder (ie, depression, anxiety problems, and attention-deficit/hyperactivity disorder) in the total sample of children (weighted estimate, 46.6 million). B, State-level prevalence presented as quartiles of children with a mental health disorder not receiving needed treatment or counseling from a mental health professional (weighted estimate, 7.7 million).

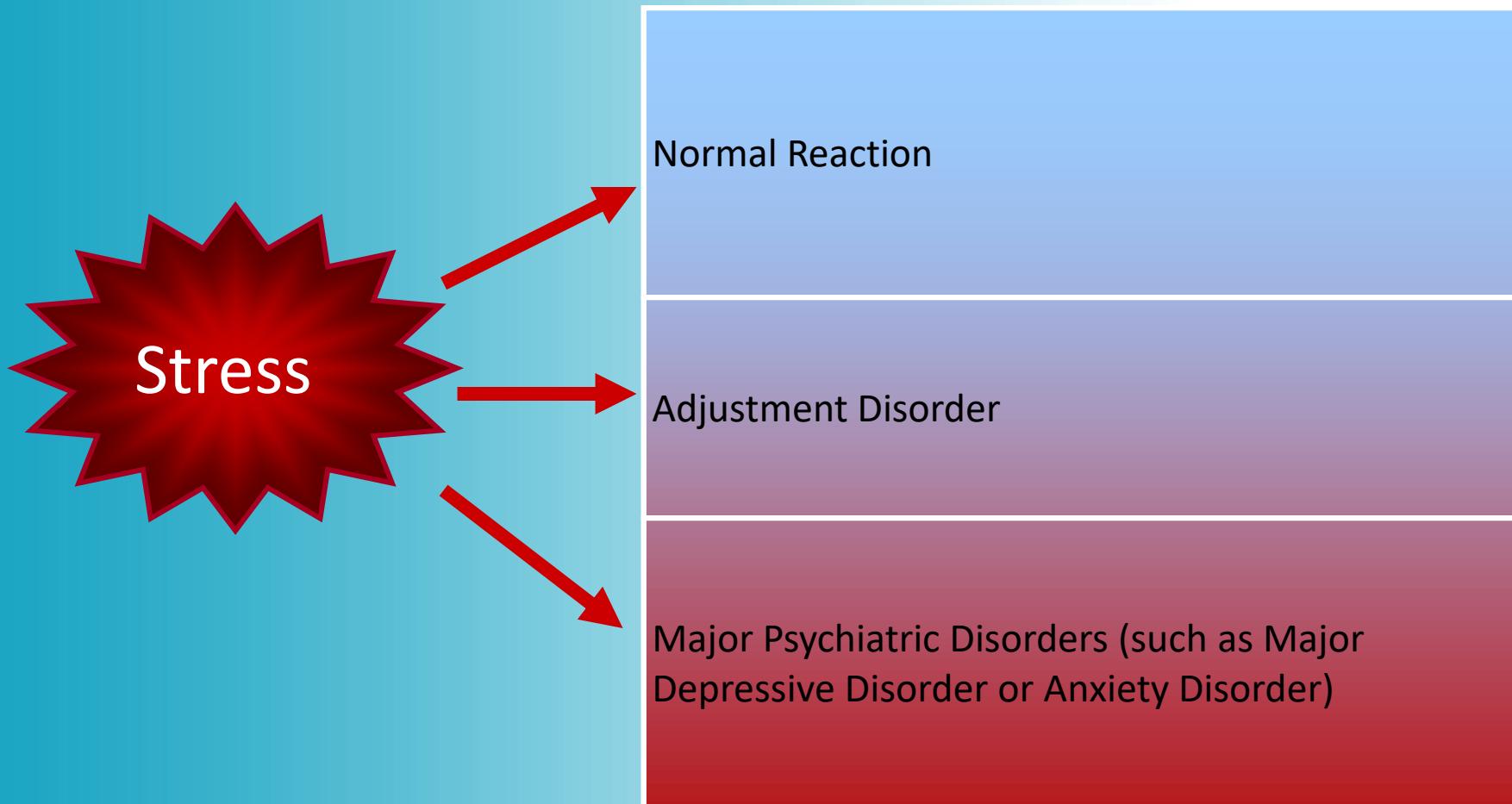


Problem: Prejudices and Misconceptions

- **Pervasiveness of psychosocial and psychological hypotheses to explain childhood mental disorders**
- **Poor public acceptance for using pharmacotherapy in children**
 - Bad Press
 - Frequent “alarming statistics” on the use of psychotropics in children
 - Diagnostic Conundrums (i.e., DSM-V Temper Dysregulation Disorder)
 - Diagnostic biases in the medical community (mental illnesses do not exist; they are accounted by other conditions; their treatment not necessary; “cosmetic” pharmacotherapy)



The Challenge of Psychopathology vs. Stress Reaction



WHAT'S NORMAL?

The difficulty of diagnosing bipolar disorder in children.

BY JEROME GROOPMAN

In April, 2000, Steven Hyman, a psychiatrist who at the time was the director of the National Institute of Mental Health, convened a meeting of nineteen prominent psychiatrists and psychologists in order to discuss bipolar disorder in children. The disorder has long been recognized as a serious psychiatric illness in adults, characterized by recurring episodes of mania and depression. (It is sometimes called manic depression.) People with bipolar disorder are often unable to hold down jobs; require lifelong treatment with powerful medications, many of which have severe side effects; and have high suicide rates. The disorder is thought to afflict between one and four per cent of Americans and tends to run in families, although no genes for it have been identified. At the time of the meeting, few children had been given a diagnosis of the illness, and it was considered to begin, typically, in adolescence or early adulthood.

In the late nineteen-nineties, however, there was an increase in awareness of bipolar disorder in children, first in medical journals and then in places like BPParents, a Listserv founded by the mother of an eight-year-old boy who had been diagnosed with the disorder. Hyman himself had been consulted by parents of children who, he told me, were "really suffering and extremely disruptive, having violent outbursts at school and at home, and hard to contain under any circumstances." Many of the parents told Hyman that they believed their child had bipolar disorder, and they cited a book called "The Bipolar Child: The Definitive and Reassuring Guide to Childhood's Most Misunderstood Disorder." The book, which was written by Demitri Papolos, a psychiatrist affiliated with the Albert Einstein College of Medicine, in New York City, and his wife, Janice, the author of several how-to manuals, had been published in 1999. (It has sold more than 200,000 copies, and a third edition came out last sum-

mer.) "The first parents who visited me came with the Papolos book in hand," Hyman said.

The Papoloses argued that bipolar disorder was often overlooked in children. In 1998, according to "The Bipolar Child," nearly four million children were given Ritalin or other stimulants for hyperactivity; of that number, the Papoloses contended, more than a million would eventually receive a bipolar diagnosis. They also cited researchers' estimates that anywhere from a third to half of the 3.4 million children thought to suffer from depression were actually experiencing the early onset of bipolar disorder. The book detailed the negative effects of bipolar disorder on patients (disruptive behavior, drug abuse, suicide attempts) but also prominently featured what might be described as its paradoxical benefits:

This illness is as old as humankind, and has probably been conserved in the human genome because it confers great energy and originality of thought. People who have had it have literally changed the course of human history: Manic-depression has afflicted (and probably fueled the brilliance of) people like Isaac Newton, Abraham Lincoln, Winston Churchill, Theodore Roosevelt, Johann Goethe, Honoré de Balzac, George Frederic Handel, Ludwig von Beethoven, Robert Schumann, Leo Tolstoy, Charles Dickens, Virginia Woolf, Ernest Hemingway, Robert Lowell, and Anne Sexton.

(These claims are similar to those made about other serious psychiatric disorders, particularly depression.)

The Papoloses' research was based on responses to questionnaires that they distributed through BPParents, whose several hundred members are parents who suspect that their children have the disorder. "These children seem to burst into life and are on a different time schedule from the rest of the world right from the beginning," the Papoloses wrote. "Many are extremely precocious and bright—doing everything early and with gusto. They seem like magical children, their creativity can be astound-

Groopman, J. (2007, April 9). *What's Normal?* *Diagnosing bipolar disorder in children.* The New Yorker, p. 2811



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The NEW ENGLAND JOURNAL of MEDICINE

Perspective
MAY 20, 2010

Pediatric Mental Health Care Dysfunction Disorder?

Erik Parens, Ph.D., Josephine Johnston, L.L.B., M.B.H.L., and Gabrielle A. Carlson, M.D.

In February, the American Psychiatric Association released draft revisions for the next iteration of its diagnostic manual (the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* [DSM-V]).

as reported by Moreno and colleagues,¹ the number of children with a diagnosis of bipolar disorder visiting outpatient clinics increased by a factor of 40. These children, some preschoolers, were

Parens et al. N Engl J Med. 2010 May 20;362(20):1853-5



June 19, 2006

'Off-Label' Antipsychotics—for Kids

The statistics are staggering: a sixfold spike, between 1993 and 2002, in the number of doctor visits in which kids and adolescents were prescribed antipsychotic drugs. Total tally in '02: 1.2 million. Antipsychotics are powerful drugs, typically used to treat severe mental illnesses like schizophrenia in adults—and they're not FDA-approved for children. But increasingly, doctors are prescribing newer generations of antipsychotics "off label" for a range of conditions in young people, from mood disorders to behavioral problems and ADHD.



Problem: Lack of FDA Approval for the Use of Many Psychotropics in Youth

- **Absence of FDA approval is not synonymous with proscription of use**
- **Lack of FDA approval only denotes that the drug was not adequately studied for the particular condition, at a particular dose or for a particular age group**
- **When used off-label, risks, potential benefits and informed consent should be carefully documented**



Black Box Fatigue

- **Cardiovascular risk/sudden death for stimulants**
- **Suicidality/activation for antidepressants and anticonvulsants**
- **Metabolic syndrome/ TD for neuroleptics**
- **Irritability on nonstimulants**
- **General uncertainties about long-term effects of psychotropics**



Perspective

APRIL 6, 2006

ADHD Drugs and Cardiovascular Risk

Steven E. Nissen, M.D.

On February 9, 2006, the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration (FDA) voted by a narrow margin — eight to seven — to recommend a “black-

box” warning describing the cardiovascular risks of stimulant drugs used to treat attention deficit-hyperactivity disorder (ADHD). This action was unexpected, largely because the FDA had not requested a review of current labeling for this class of drugs; it had merely asked for recommendations of approaches to studying the cardiovascular risks associated with these drugs. The committee, however, decided to take an independent course. As a consultant to this committee, I introduced two motions, one recommending the black box warning and the other proposing the development of a guide for patients, which was approved by a vote of 15 to 0. The guides are handouts that are re-

quired to be provided at the time prescriptions are dispensed; they contain information, written in nontechnical language, about the potential hazards of the medication.

The drugs under review were primarily amphetamines (Adderall and other brands) and methylphenidate (Ritalin, Concerta, and other brands). These agents are closely related members of the class of sympathomimetic amines, the structures of several of which are shown in the diagram. These compounds exert potent stimulant effects on the cardiovascular and central nervous systems. One of the oldest such agents, methamphetamine, was originally synthesized in 1891 and first widely

used during World War II in Nazi Germany to enhance the ability of Luftwaffe pilots to stay alert during extended hours of combat. Medical use of this agent is now limited, but illicit use has grown rapidly and now represents an increasing public health problem. When smoked or injected intravenously, methamphetamine (“speed”) is associated with hyperthermia, rhabdomyolysis, myocardial infarction, stroke, and sudden death — effects well known to coroners in regions of the United States where abuse is common. Beginning in the 1950s, the stereoisomer dextroamphetamine and related agents were introduced as appetite suppressants.

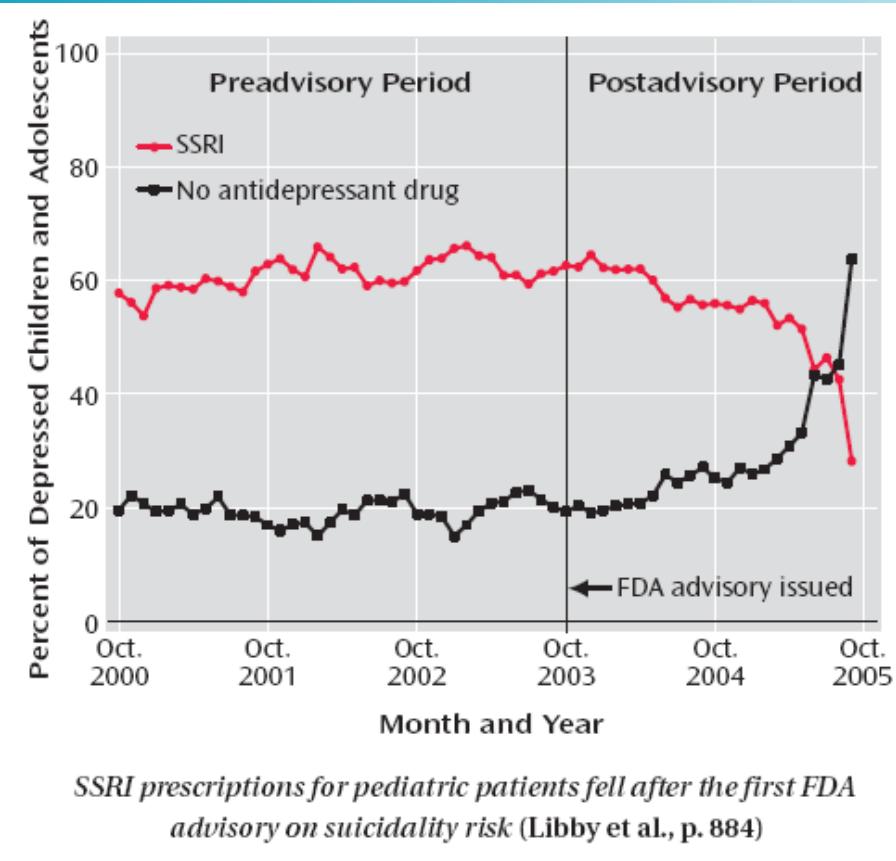
ADHD is a disorder commonly diagnosed in school-age boys (less commonly in girls) and is characterized by increased activity, an inability to concentrate, and poor school performance. The effectiveness of stimulants in

CONCLUSIONS

This large study showed no evidence that current use of an ADHD drug was associated with an increased risk of serious cardiovascular events, although the upper limit of the 95% confidence interval indicated that a doubling of the risk could not be ruled out. However, the absolute magnitude of such an increased risk would be low. (Funded by the Agency for Healthcare Research and Quality and the Food and Drug Administration.)

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Pediatric Depression Treatment Declines After FDA Advisory on Antidepressants

Diagnoses of new cases of major depression in children and adolescents, and their antidepressant treatment, declined sharply over the 2 years following the first Food and Drug Administration (FDA) advisory about suicidality risk for pediatric patients taking selective serotonin reuptake inhibitors (SSRIs). Decreases in SSRIs and non-SSRI antidepressants for depressed patients ages 5–18 are shown by claims in a national database of managed health care plans ana-

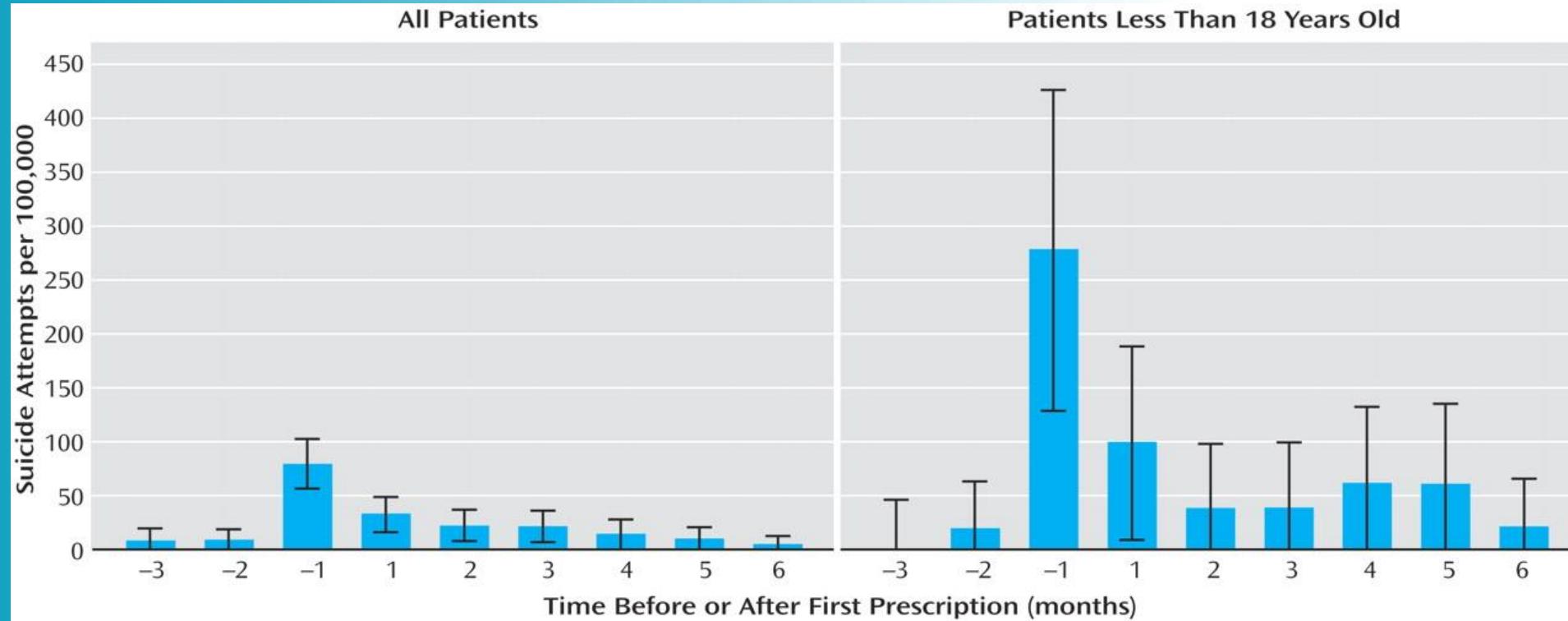
lyzed by Libby et al. (p. 884). Psychotherapy did not increase after the advisory. This comparison of the 5 years before the FDA advisory in October 2003 with the 2 years afterward encompassed more than 65,000 children and adolescents with a new diagnosis of major depressive disorder. In addition, population-level depression rates fell in 2005 after steadily increasing. Dr. Cynthia Pfeffer comments on these trends in an editorial on p. 843.

Rates of Suicide Attempts During the 3 Months Before and the 6 Months After Initial Antidepressant Prescription



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Simon et al. (2006) Am J Psychiatry (163):41-47

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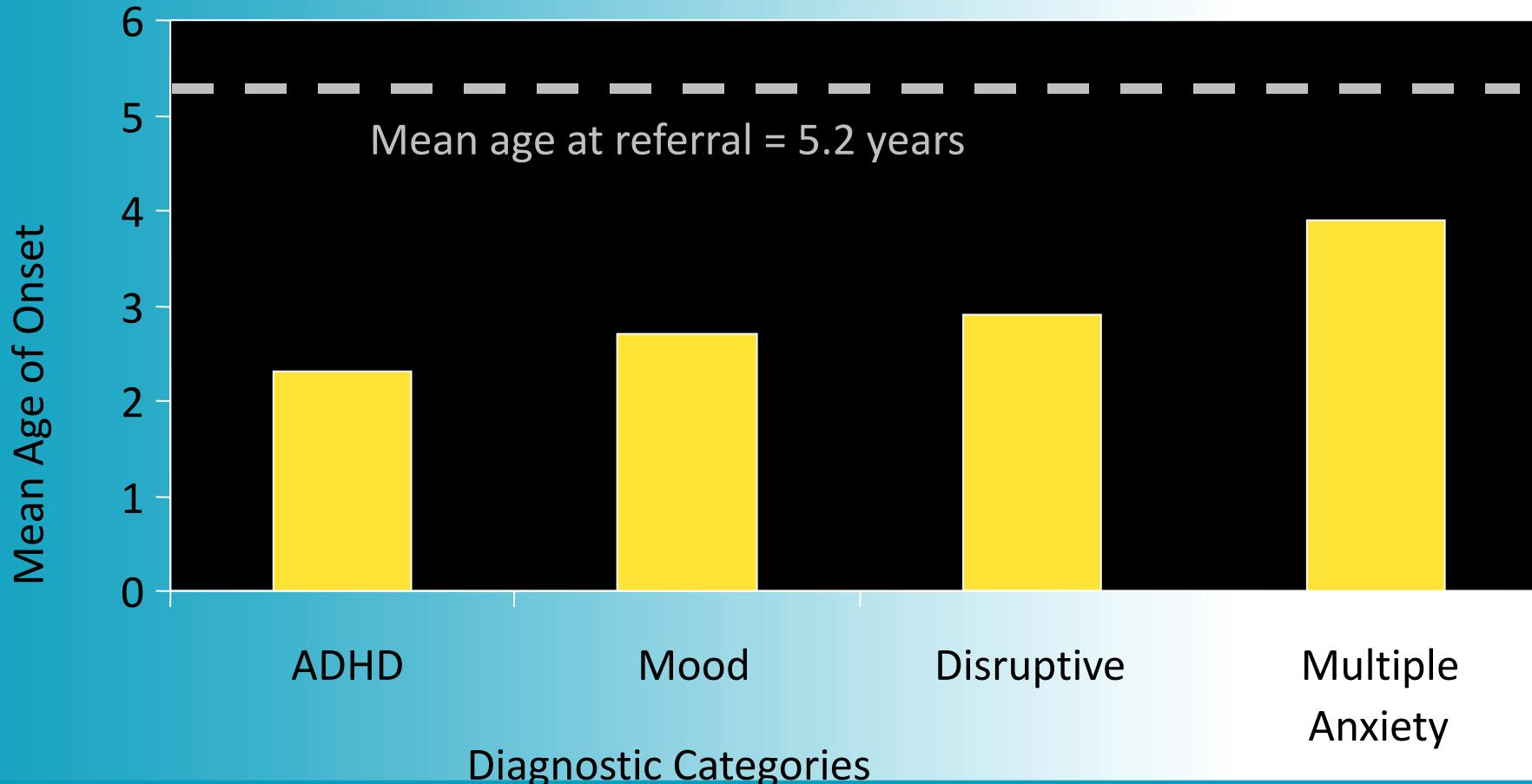


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MGH Study of Preschoolers: Preliminary Study of Psychopathology

Age of Onset of Psychopathology





General Principles: Assessment

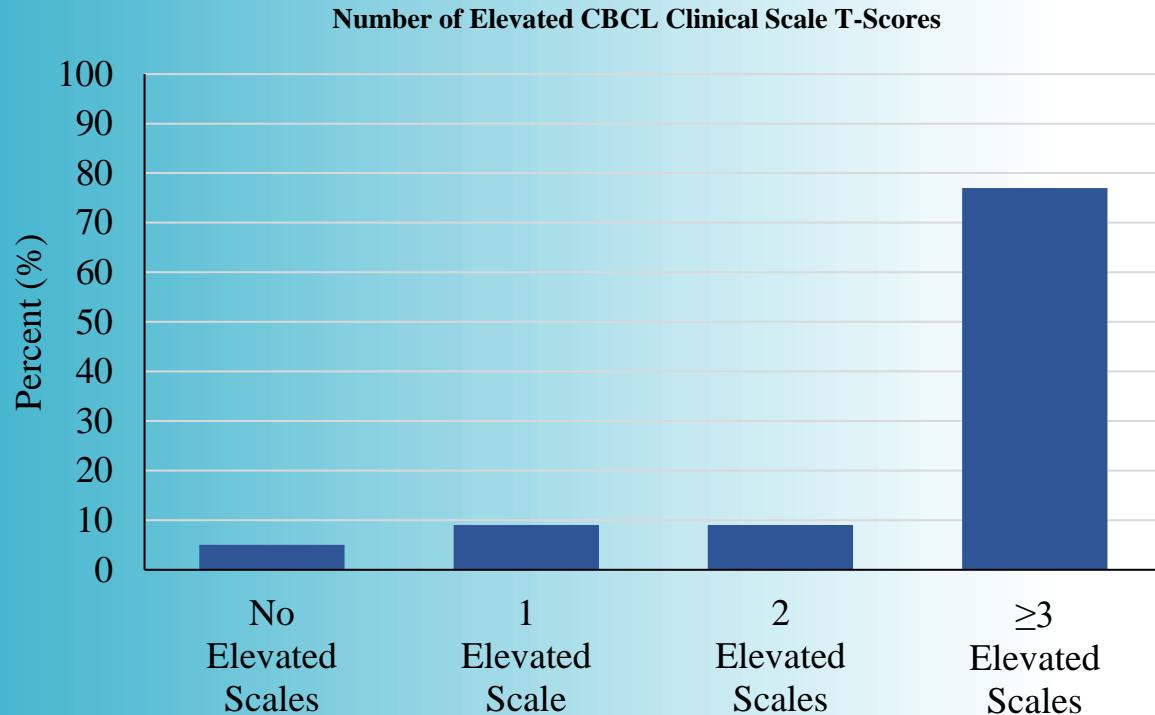
- The critical importance of attention to comorbidity and differential diagnosis
- Most children are affected with multiple disorders
- Some disorders can complicate the management of other disorders
- Prioritize: the most serious disorder should be addressed first

Characterizing Referral to a Public Child Psychiatry Clinic (N=450 Youth)



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Biederman et al 2020



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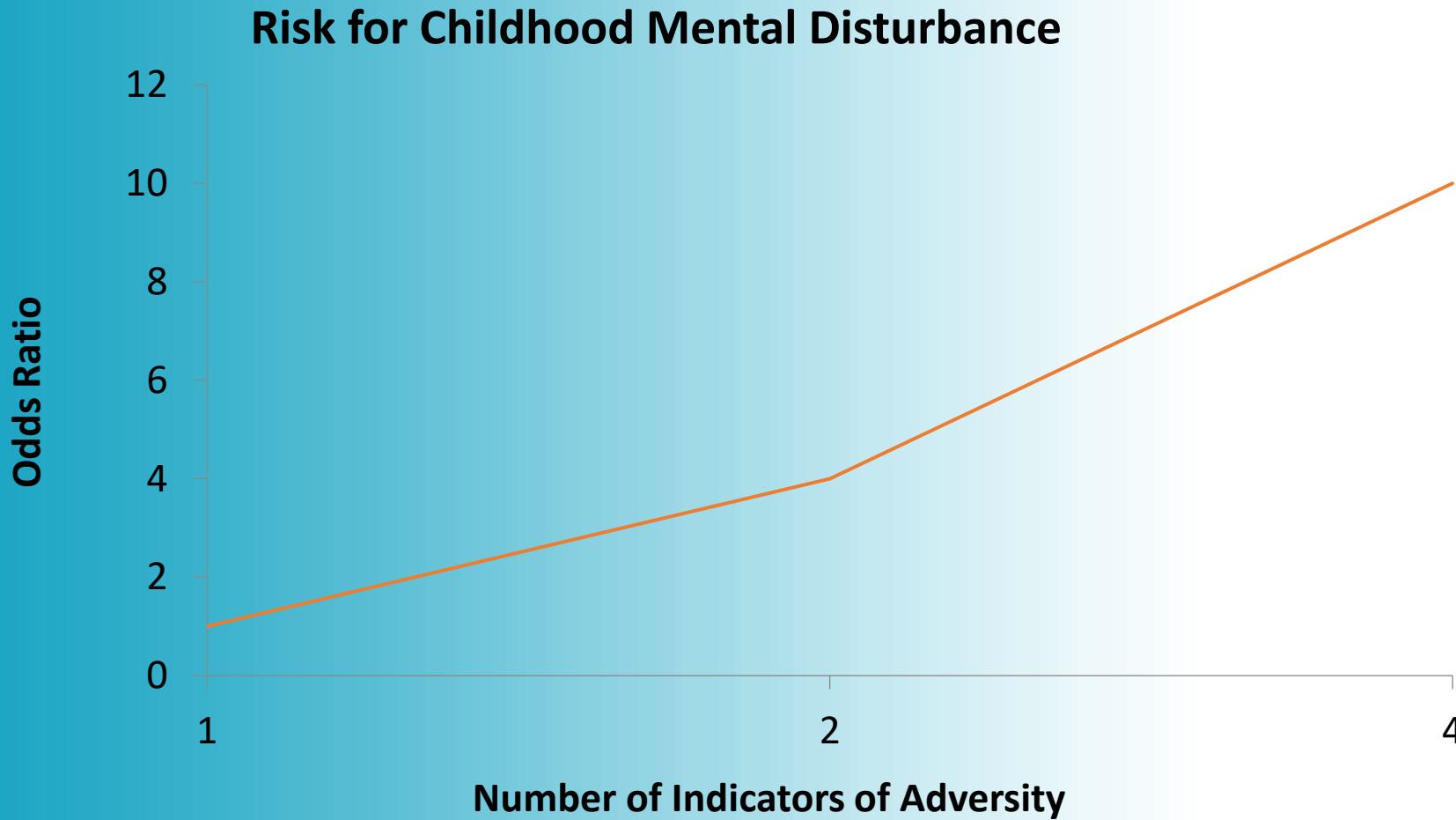
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Components of the Diagnostic Process

- **Psychiatric Assessment**
- **Cognitive Assessment**
- **Assessment of School Functioning**
- **Psychosocial Assessment**
- **Laboratory Assessments (when indicated)**



Psychopathology is Linked to Adversity





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General Principles

- The use of psychotropics should follow a careful evaluation of the child and the family
- Before beginning treatment, the family and the child need to be familiarized with the risks and benefits of such an intervention



General Principles

- Treatment should be started at the lowest possible dose with frequent reevaluation during the initial phase of treatment
- Following a sufficient period of clinical stabilization (i.e.... 6-12 months) it is prudent to reevaluate the need for continued psychopharmacologic intervention
- This approach need to be considered when the clinical picture has fully stabilized



General Principles

- A successful pharmacotherapeutic intervention requires realistic expectations and initial diagnostic hypotheses with careful definition of target symptoms
 - i.e., the treatment of insomnia is very different if driven by existential concerns, mania, psychosis or depression
- While psychotropics can be highly beneficial, their use is not always successful



Indications for Combined Pharmacotherapy

- Comorbidity
- Treatment resistant cases: Augmentation
- Treatment emergent adverse effects
- Poor tolerability with therapeutic doses of individual medicines



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Summary

- Behavioral health issues are common in young people
- Diagnostics are critical as a first step
- Pharmacotherapy can be a critical component of the treatment
- Welcome to the course!