MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

Diagnosis & Assessment in Pediatric Psychopharmacology

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Disclosures 2020-2021

My spouse/partner and I have the following relevant financial relationships with commercial interests to disclose:

- *Research support:* Genentech, Headspace Inc., Pfizer Pharmaceuticals, Roche TCRC Inc., Sunovion Pharmaceuticals Inc., Takeda/Shire Pharmaceuticals Inc., and Tris.
- *Consulting fees:* Akili, Avekshan LLC, Jazz Pharma, and Shire/Takeda
- *Honorarium for scientific presentation:* Tris
- *Royalties paid to the Department of Psychiatry at MGH, for a copyrighted ADHD rating scale used for ADHD diagnoses:* Biomarin, Bracket Global, Cogstate, Ingenix, Medavent Prophase, Shire, Sunovion, and Theravance
- Through Partners Healthcare Innovation, I have a partnership with MEMOTEXT to commercialize a digital health intervention to improve adherence in ADHD.

2013 CDC Major Report on Mental Illness in Youth

- 1 in 5 youth has a mental illness
- Estimated yearly cost: **$247 billion**
- Because of their high prevalence, early onset, their impact on the child, family, and community, and its associated enormous cost mental and behavioral disorders of the young represent a major public-health issue in the US (and across the world)

Most Prevalent Mental Illnesses in Youth

- ADHD (11%)
- Conduct disorder (3%)
- Anxiety disorders (3-5%)
- Depression (5%)
- Conduct Disorder (2%)
- ASD (2%)
- SUD (in prior yr 5%)
- Alcohol abuse (in prior yr 4%)
- Cigarette Dependence (prior month 3%)
- **Suicide remains a leading cause of death in youth**

Problem: Limited Manpower

- There are less than 7000 fully trained child and adolescent psychiatrists currently practicing in the US, despite estimates that over 30,000 would be required to meet the current demand.
- The need for services is projected to increase 100% by the year 2020, highlighting a growing mental health crisis.
- Increasing importance of the PCP in the management of children's mental health problems

The Potential of Tele and Digital health to Improve Access

- Improves patient access
- Geographical barriers are suspended
- Allows for access to expert care in rural and remote areas

JAMA Network Open

Original Investigation | Public Health

Effect of MyTeen SMS-Based Mobile Intervention for Parents of Adolescents

A Randomized Clinical Trial

Joanna Ting Wai Chu, PhD; Angela Wadham, BA; Yannan Jiang, PhD; Robyn Whittaker, PhD; Karolina Stasiak, PhD; Matthew Shepherd, PhD; Chris Bullen, MD

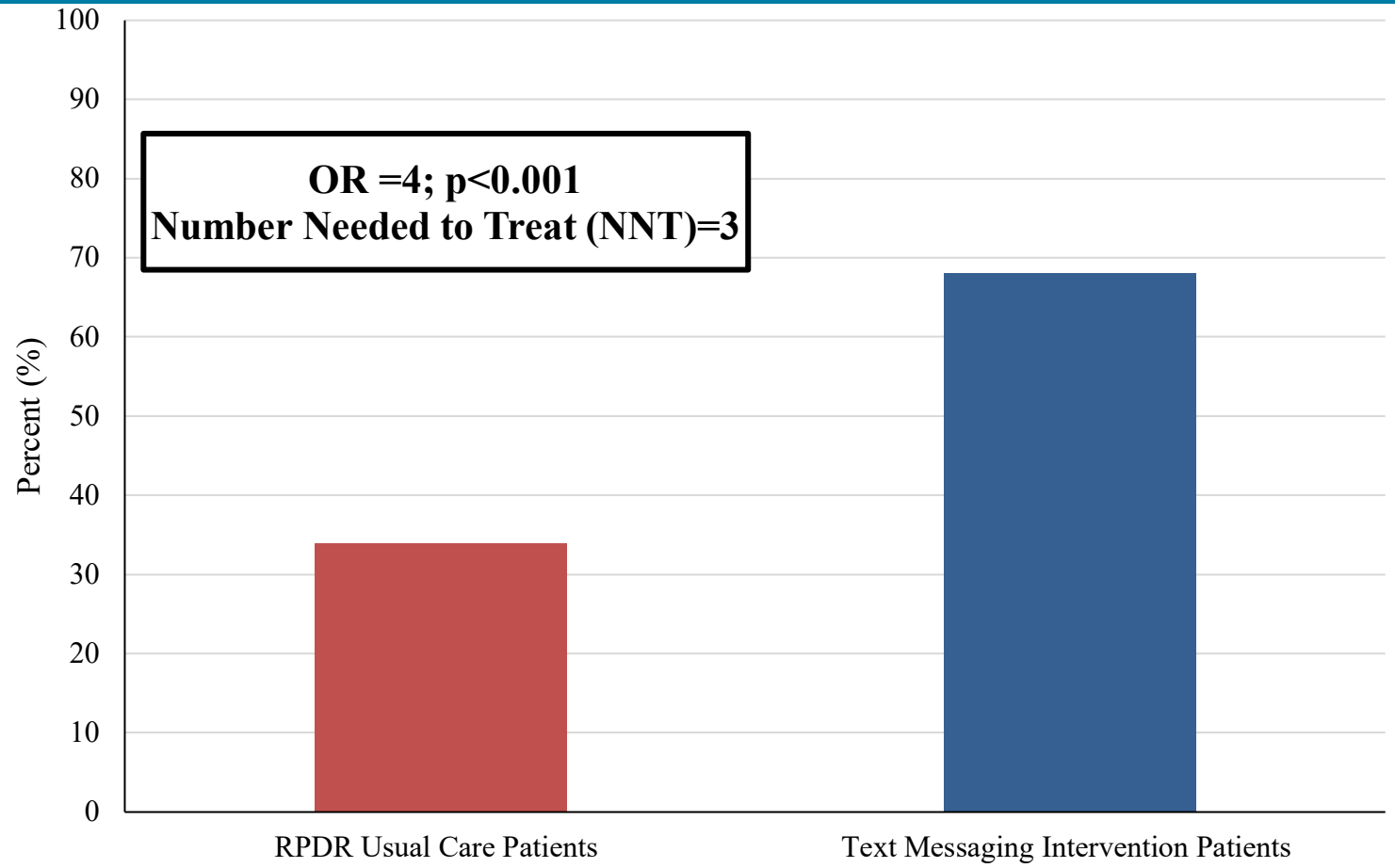
CONCLUSIONS AND RELEVANCE This text-messaging program for parents of adolescents appears to be an effective and feasible way to facilitate the implementation and delivery of evidence-based information to populations that are not easily reached with other intervention modalities. The program can be easily scaled up for delivery as an early preventive intervention and may represent a less expensive option for service delivery.

DESIGN, SETTING, AND PARTICIPANTS A parallel 2-group randomized clinical trial was conducted in New Zealand. A total of 221 parents and primary caregivers of adolescents aged 10 to 15 years were recruited from March 19 to August 17, 2018, via community outreach and social media and were randomly allocated 1:1 into the control or the intervention group. Statistical analysis was performed on the principle of intention to treat with adjustment for baseline factors and ethnicity.

messaging intervention and the control group. Participants who received the text-messaging program reported higher levels of parental competence, improved knowledge of help seeking, improved parent-adolescent communication, and lower levels of

Chu et al. *JAMA Network Open.* 2019;2(9):e1911120.

Rate of Adherence to Medication in patients receiving an SMS Intervention (N=92) vs. age- and sex-matched Controls (=460) who received treatment as usual in Partners Healthcare



Biederman et al. *J Clin Psychopharmacol* 2019;39: 351–356

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)

Groopman, J. (2007, April 9). *What's Normal? Diagnosing bipolar disorder in children.* The New Yorker, p. 28

MEDICAL DISPATCH

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 summer.) "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-

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

Newsweek Health

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.

Kalb, C. (2006, June 19). 'Off-Label' Antipsychotics—for Kids. *Newsweek Health*.

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

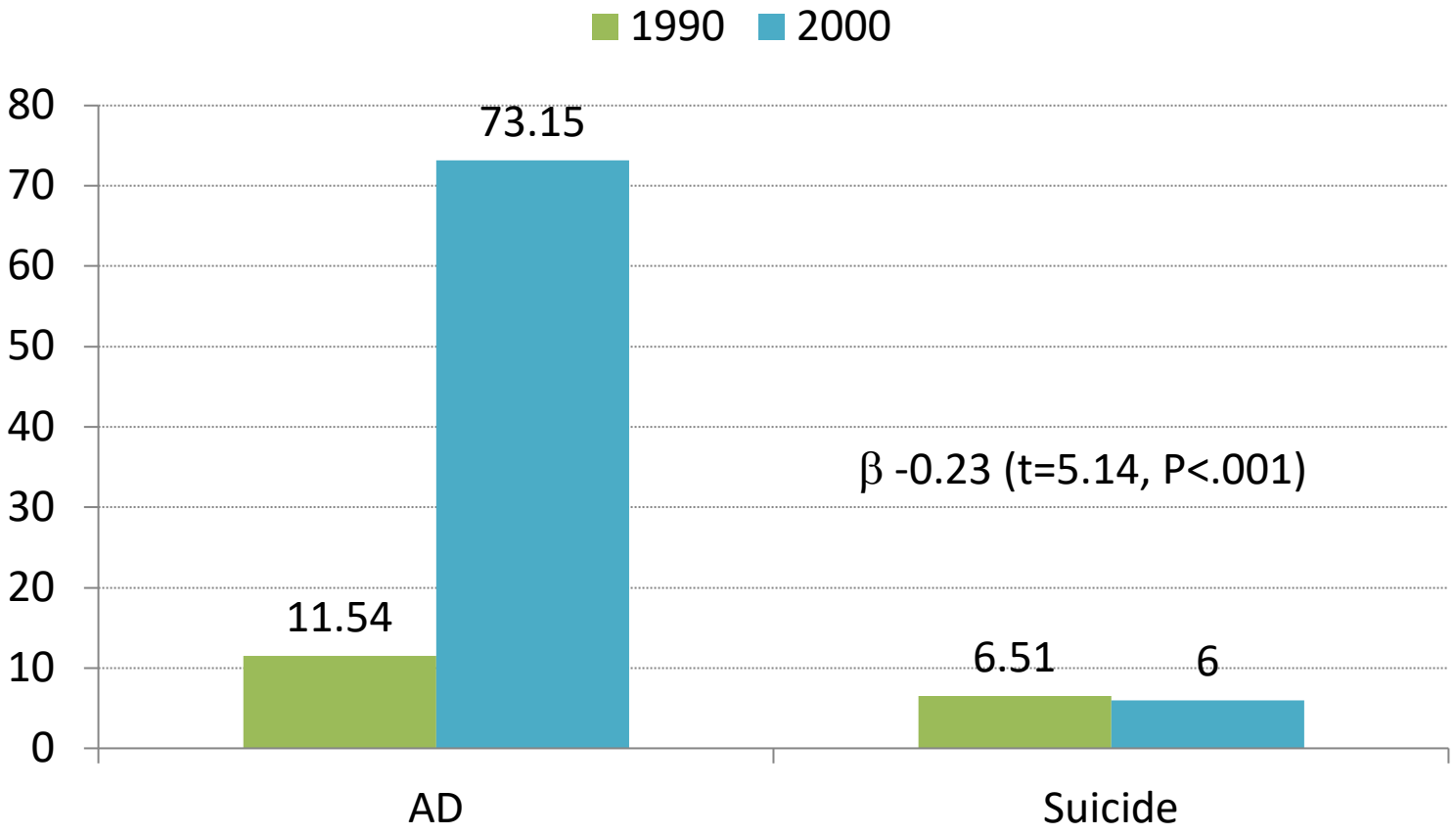
- Cardiovascular risk/sudden death for stimulants
- Suicidality/activation for antidepressants and anticonvulsants
- Metabolic syndrome/ TD for neuroleptics
- General uncertainties about long-term effects of psychotropics

FDA issues Black Box Warning: Suicide Risk with Antidepressant

- 78 out of 4,400 cases in controlled clinical trials on all antidepressants in pediatric patients suffered increases in suicidal ideation and/or self-harm
  - 52 patients (3.8%) randomized to medications
  - 26 patients (2.1%) randomized to placebo
- No patients committed suicide or seriously harmed self

AACAP Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee September 28, 2004

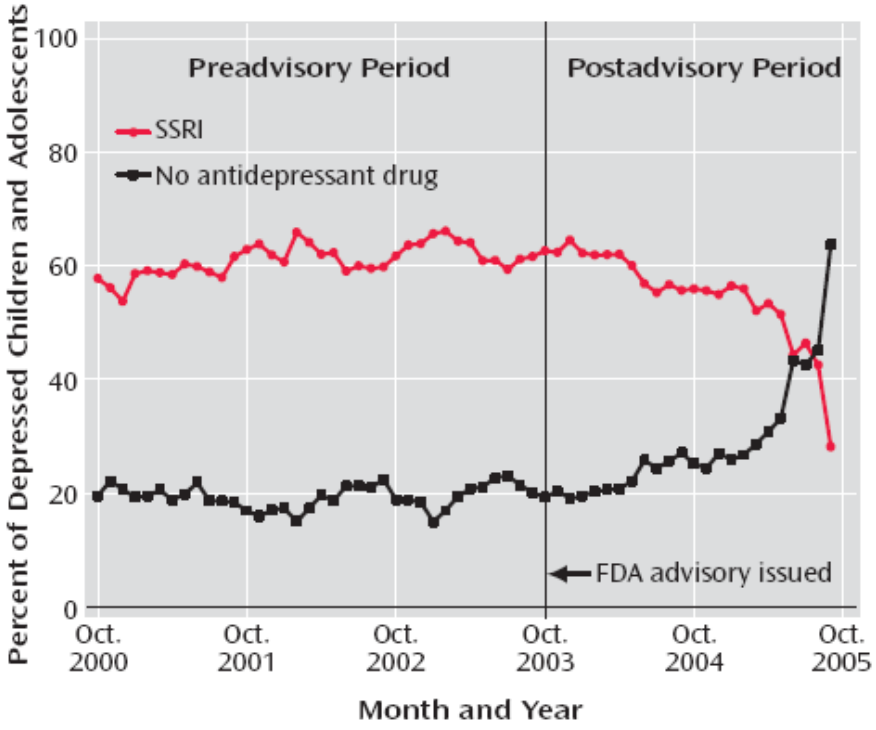
Antidepressant Medication and Suicide in Adolescents



AD= Antidepressant rate per 1000 Medication Users

Olfson et al., (2003) AGP 60 (10): 978-982

In This Issue
THE AMERICAN JOURNAL OF
PSYCHIATRY



SSRI prescriptions for pediatric patients fell after the first FDA advisory on suicidality risk **(Libby et al., p. 884)**

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 analyzed 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.

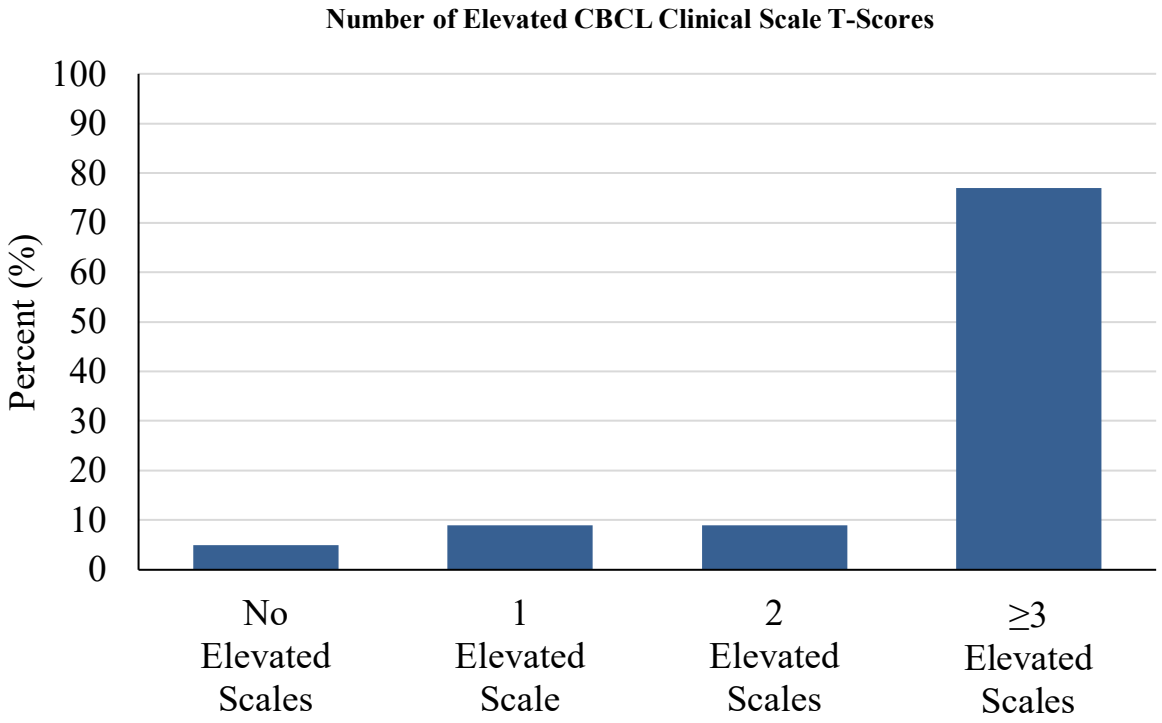
General Principles

- 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: 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 Using the CBCL (N=450 Youth)



Biederman et al 2020

SJCAPP

Scandinavian Journal of Child and Adolescent Psychiatry and Psychology
Vol. 8:157-165 (2020) DOI 10.21307/sjcapp-2020-016

Research Article **Open Access**

Conclusions: The CBCL can aid in the identification of individual and comorbid mental disorders affecting youth seeking mental health services by providing specific information about the presence and the severity of specific suspected disorder. These findings have implications for prioritizing scarce resources in child mental health and for improved consideration of the complexity of clinical presentations to pediatric psychiatry programs of any type.

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Abstract

Background: Little is known about the scope of problems driving referrals to child and adolescent psychiatry services. Identifying the full range of mental disorders affecting a particular child can help triage the child to a clinician with the

Biederman et al. *Scand J Child Adolesc Psychiatr Psychol*. 2020 Oct 31;8:157-165.
doi: 10.21307/sjcapp-2020-016.

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 Issues: Adverse Effects

- Certain adverse effects can be anticipated based on known pharmacologic properties of the drug (i.e.., the anticholinergic effects of tricyclic antidepressants), while others, generally rare, are unexpected (idiosyncratic) and are difficult to anticipate

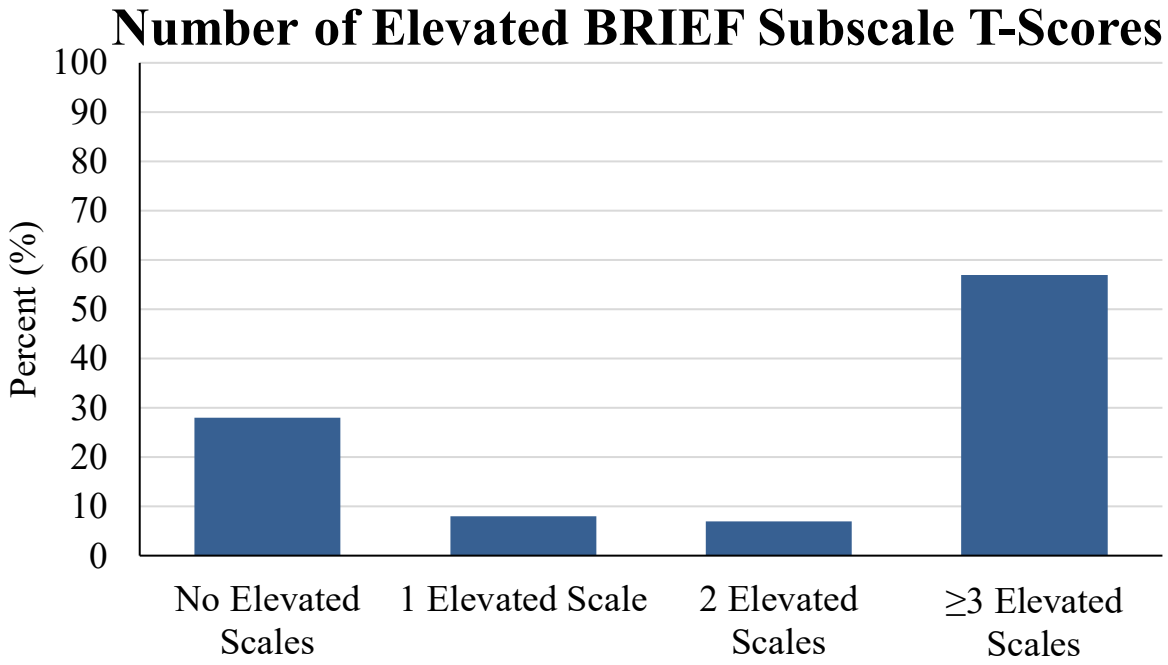
Components of the Diagnostic Process

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

Diagnostic Process: Cognitive Assessment

- Estimates of IQ
- Estimates of EFDs (i.e, working memory, processing speed) (Rating scales/testing)
- Estimates of academic performance
- Search for discrepancies between expected and actual functioning
- **Distinguish Low achievement from Underachievement**
  - Example: a brilliant child that is performing averagely in school may be underachieving

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

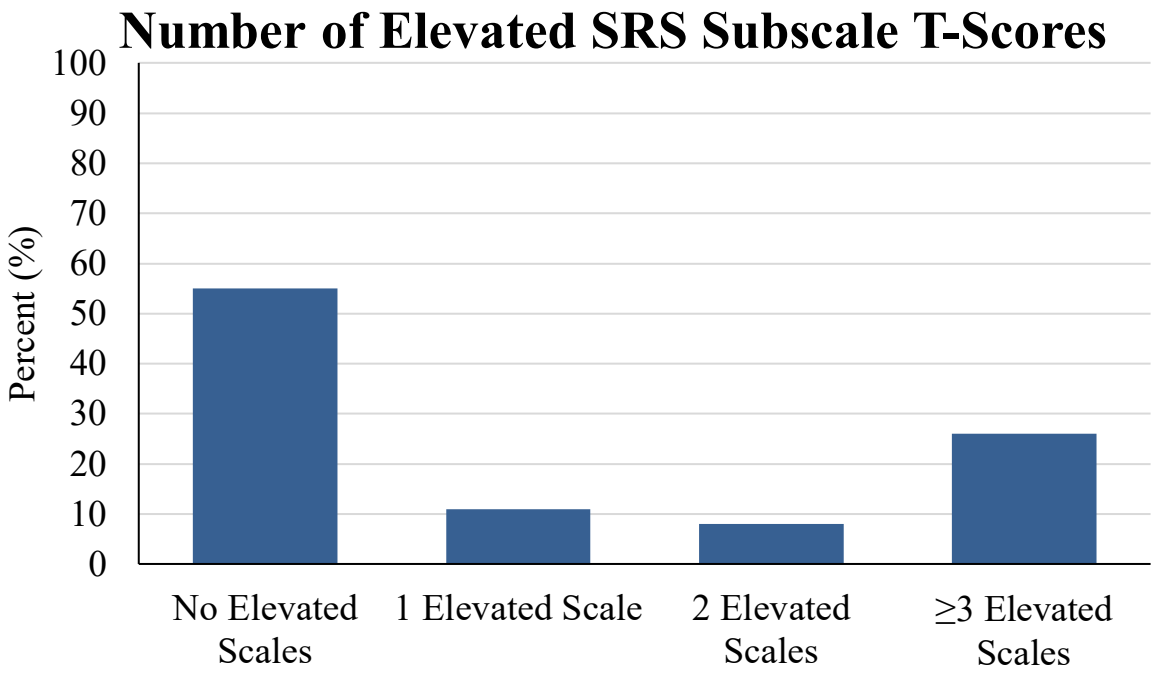


Biederman et al 2020

Diagnostic Process: Psychosocial Evaluation

- Evaluation of the family environment
  - Marital discord
  - Parenting difficulties
  - Separation and divorce
  - Custodial parent
  - Guardianship
  - Potential issues of abuse and neglect

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

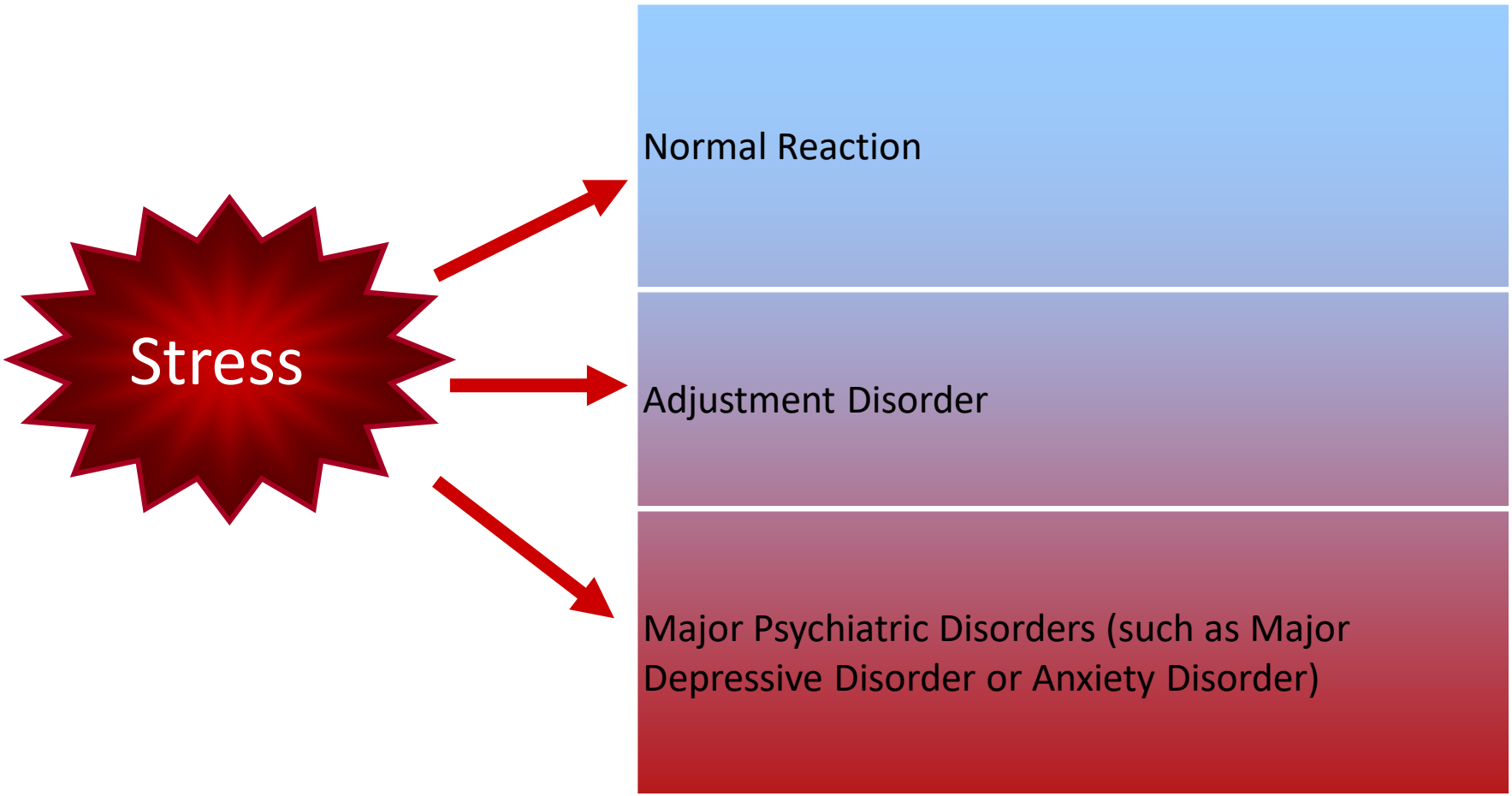


Biederman et al 2020

Psychosocial Adversity

- Low SES (poverty)
- Family conflict
- Single parent homes
- Parental psychopathology

The Challenge of Psychopathology vs. Stress Reaction



Diagnostic Process: Psychosocial Evaluation

- Social Functioning
  - Relationship with peers
  - Relationship with parents
  - Use of leisure time

Diagnostic Process: School Functioning

- School Functioning
  - School and grade placement
  - Teacher information
  - Parent-based school information

Diagnostic Process: School Functioning

- Parent-based school information
  - Parent-teacher conferences
  - Teacher reports
  - Teacher complaints
  - Observation

Indications for Major Drug Classes

- Stimulants
- Antidepressants
- Antipsychotics
- Mood stabilizers
- Anxiolytics
- Alpha adrenergic compounds
- Beta blockers

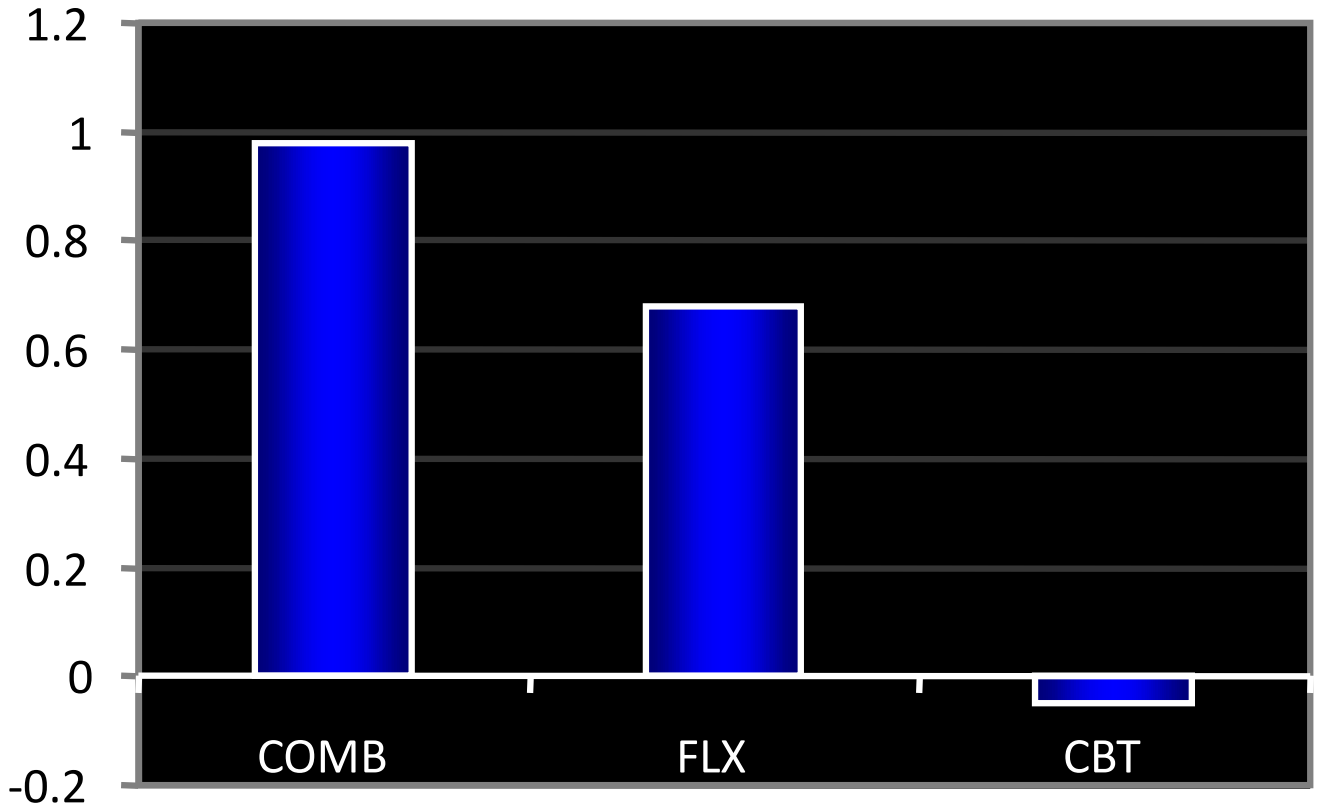
Indications for Major Drug Classes

- Stimulants
  - ADHD
  - Narcolepsy
  - Tx resistant depression

Indications for Major Drug Classes

- Antidepressants
  - Depressive disorders
  - Anxiety disorders
  - OCD (serotonergic)
  - ADHD (noradrenergic, dopaminergic)
  - Enuresis (TCAs)

Treatment of Adolescent Depression Effect Size for CDRS (ITT)



March et al. *JAMA*. (2004) 292 (7):807-820.

Indications for Major Drug Classes

- Antipsychotics (atypical)
  - Psychotic disorders
  - Tourette's disorder
  - Bipolar disorder
  - Dysphoric dyscontrol
  - Augmentation of antidepressants

Indications for Major Drug Classes

- Mood stabilizers
  - Bipolar disorder
  - Tx refectory depression
  - Dysphoric dyscontrol

Indications for Major Drug Classes

- Anxiolytics
  - Anxiety disorders
  - Augmentation of treatments for other disorders (BPD, depression, TS)
  - Severe situational anxiety
  - Tourette's syndrome (high potency BZDs)
  - Stimulant induced anxiety
  - Insomnia

Indications for Major Drug Classes

- Alpha Adrenergic Compounds (clonidine, guanfacine)
  - TS/Tics
  - ADHD
  - Dyscontrol
  - SIB
  - Augmentation
  - Treatment emergent adverse effects (I.e., stimulant-induced insomnia

Indications for Major Drug Classes

- Beta Blockers
  - Akathisia
  - Stage fright
  - Tremor
  - Dyscontrol
  - SIB

Indications for Combined Pharmacotherapy

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

Wilens et al. JAACAP. 1995 Jan;34(1):110-2

Combined Pharmacotherapy

- Simple cases: monotherapy could be sufficient and should be preferred
- Complex cases: monotherapy may be insufficient and combined pharmacotherapy needs to be considered