Psychotropics - The Other Side of Stimulant Medication Dogma

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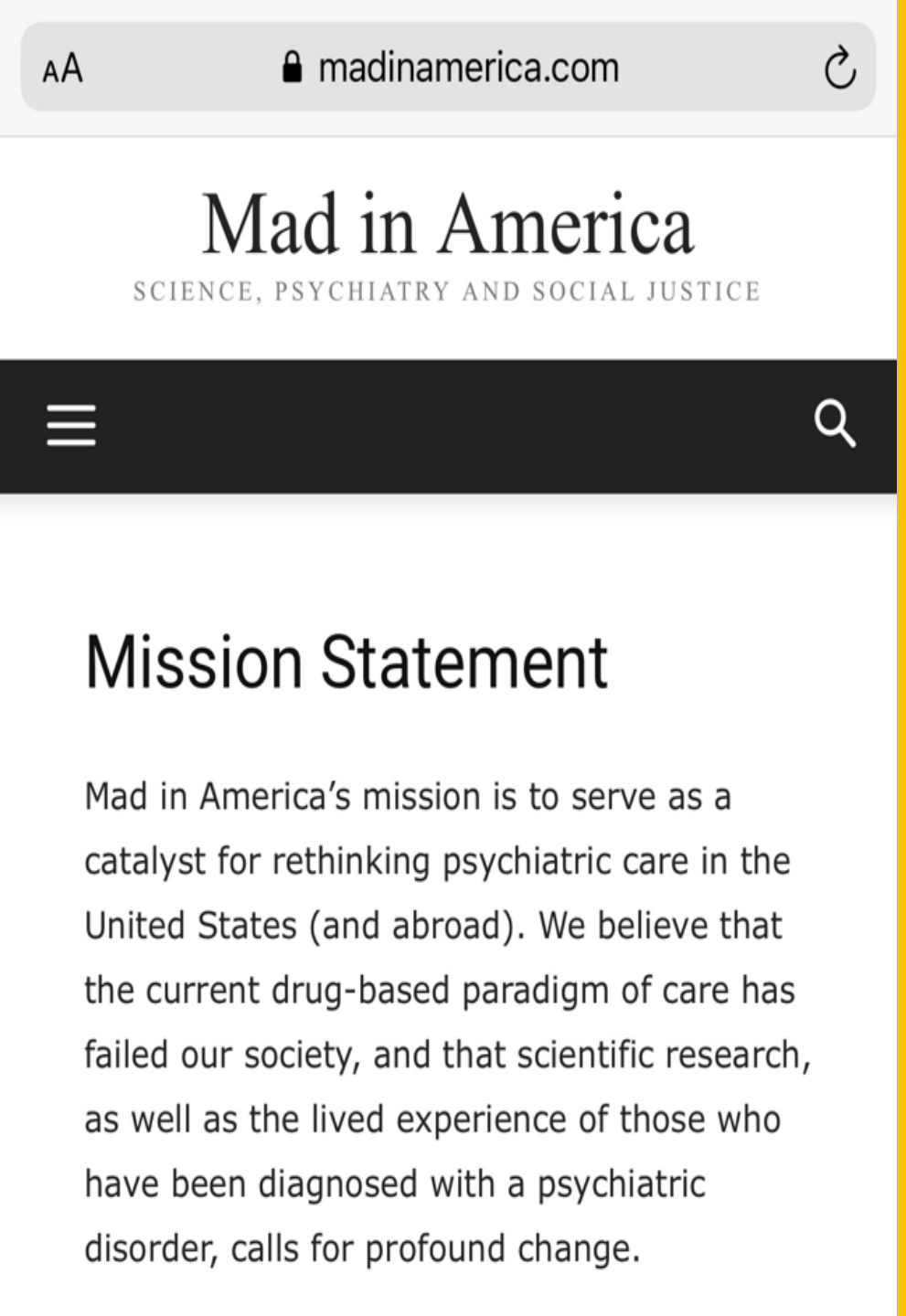

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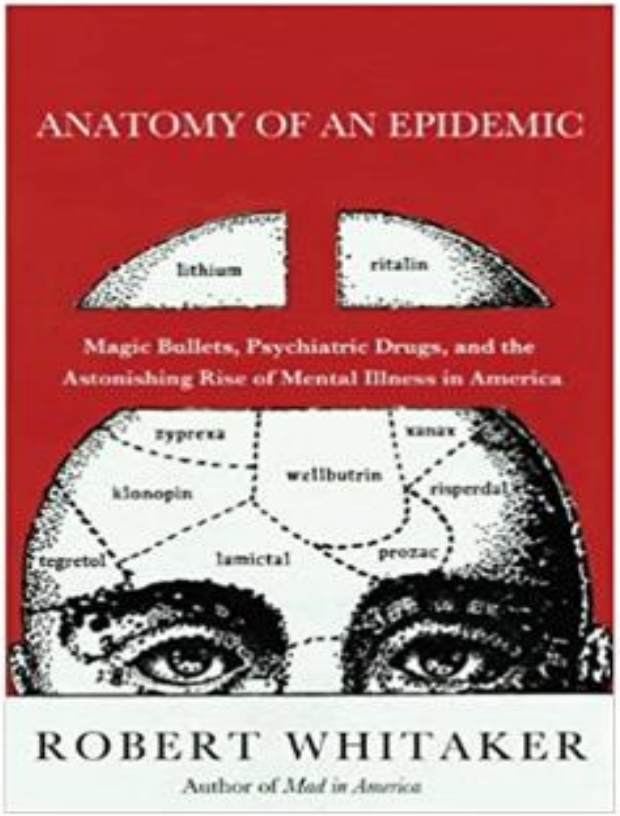
We are at a time when it is a good thing to evaluate the efficacy of psychotropic medications. This PowerPoint summarizes the work of Robert Whitaker, a medical journalist who has written and spoken about the need to re-think how we are treating mental illness, in particular, the use of psychotropics with emphasis on stimulants. Although Robert acknowledges that psychotropics have a use, he suggests that they should be used more judiciously and, in many cases, there is reason to be concerned that long-term use can have a significant and concerning downside.

Please note that I am not a prescriber, and I am not advising you to take or not take these medications. Rather, I am offering some of the research on the mechanisms and outcomes of their use to help you form your own opinion.

Please visit Robert Whitaker's website:
https://madinamerica.com

Robert Whitaker is an American journalist and author who has won numerous awards as a journalist covering medicine and science, including the George Polk Award for Medical Writing and a National Association for Science Writers' Award for best magazine article. In 1998, he co-wrote a series on psychiatric research for the Boston Globe that was a finalist for the Pulitzer Prize for Public Service. His first book, *Mad in America,* was named by *Discover* magazine as one of the best science books of 2002. *Anatomy of an Epidemic* won the 2010 Investigative Reporters and Editors book award for best investigative journalism. He is the publisher of madinamerica.com.


ANATOMY OF AN EPIDEMIC
lithium
ritalin
Magic Bullets, Psychiatric Drugs, and the Astonishing Rise of Mental Illness in America
zyprexa
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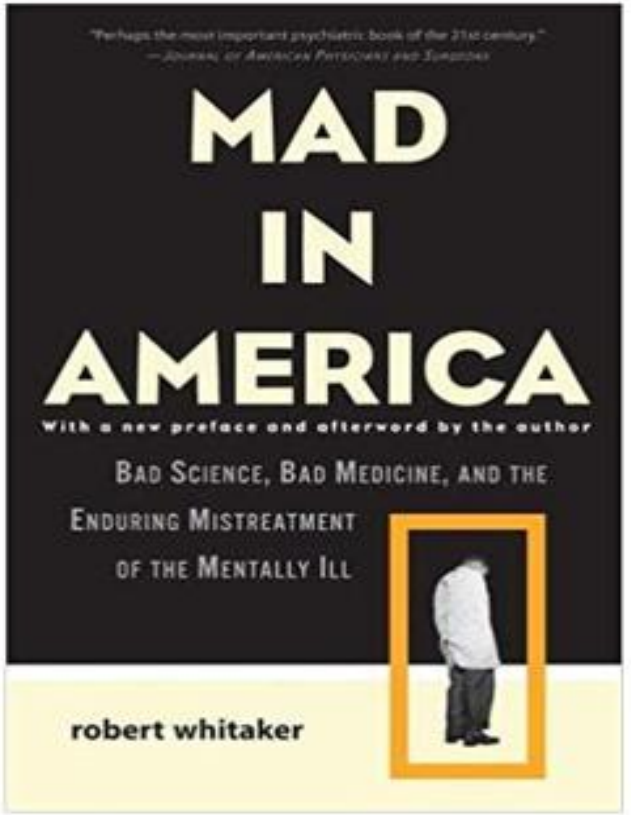
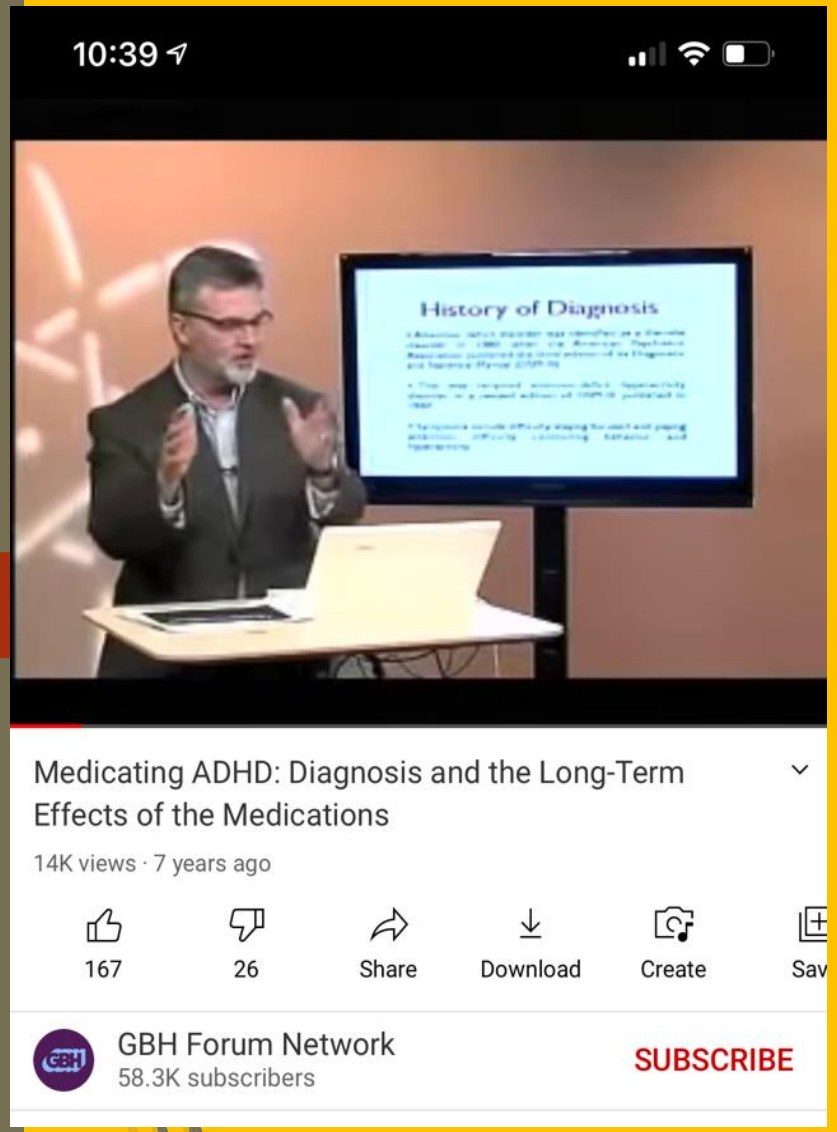
prozac
ROBERT WHITAKER
Author of Mad in America


MAD IN AMERICA
With a new preface and afterword by the author
Bad Science, Bad Medicine, and the Enduring Mistreatment of the Mentally Ill
robert whitaker



The content of this PowerPoint is largely from Robert Whitaker's excellent YouTube videos:

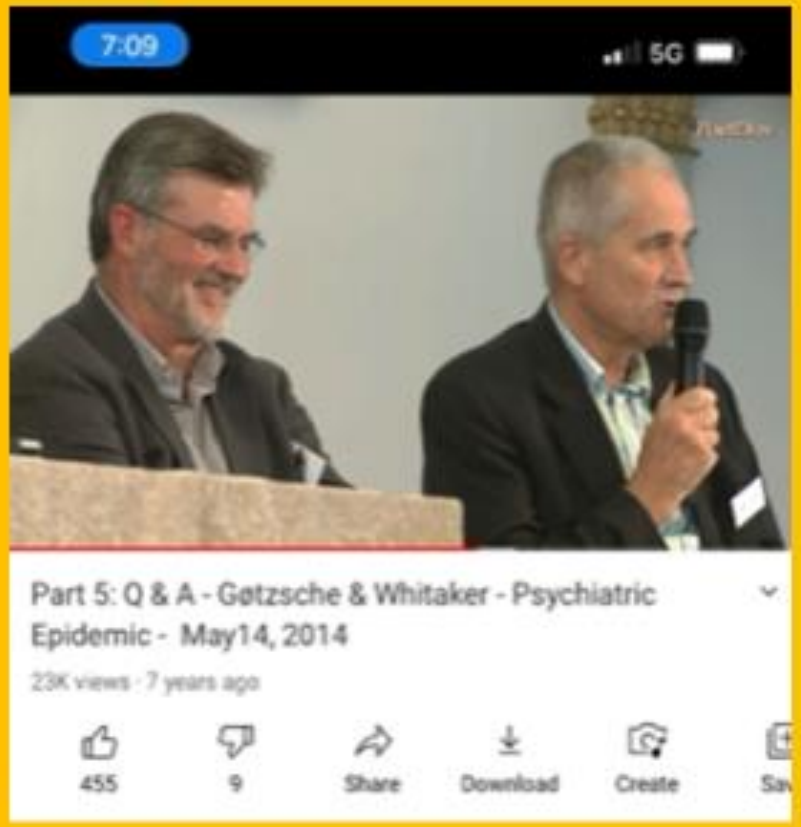
https://youtu.be/2fvTmyjHXlg
Accessed July 18, 2021

https://www.youtube.com/watch?v=x1NYmZxZL_g
Accessed July 18, 2021

https://www.youtube.com/watch?v=gigZD4RIXhg
Accessed July 18, 2021

Medical journalist Robert Whitaker and Danish physician Dr. Peter Gotzsche:

Leading the way in investigating the other side of dogma of psychotropics



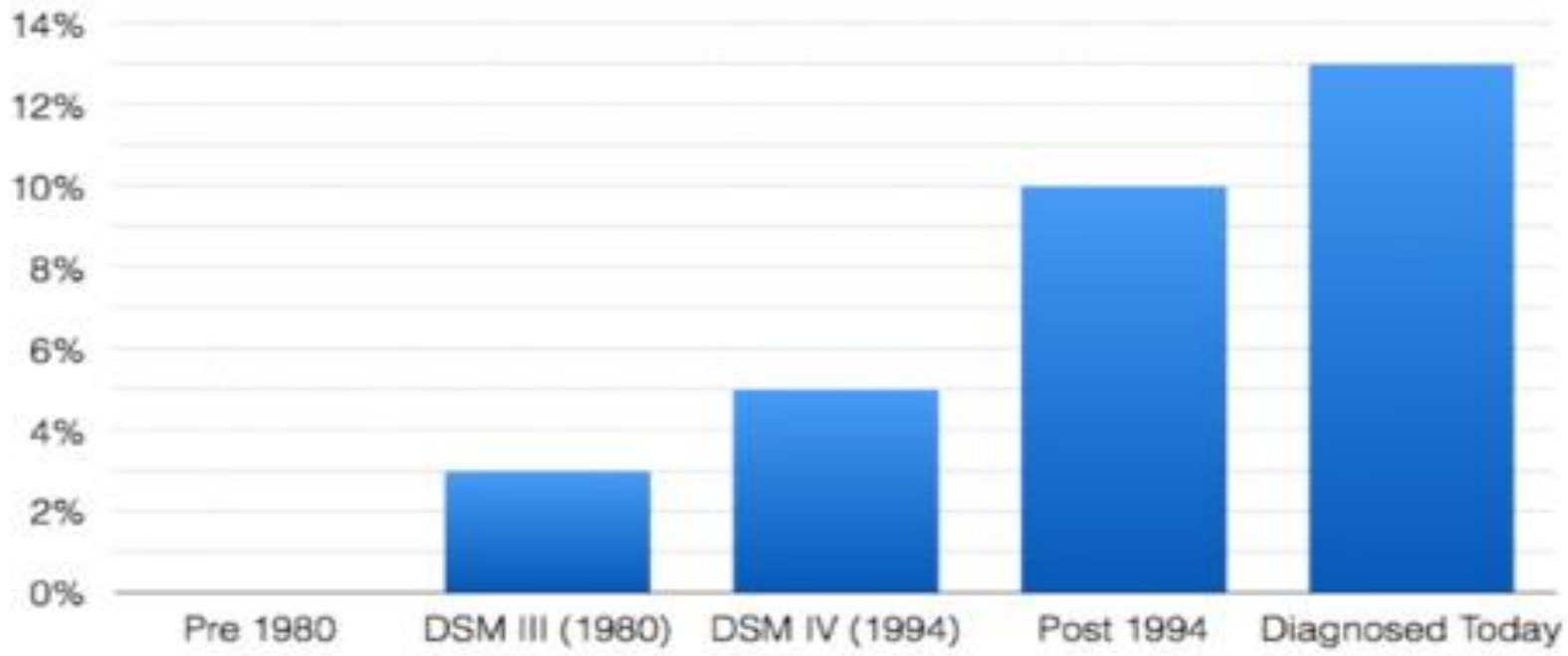
History of Diagnosis

- Attention deficit disorder was first created as a discrete disorder in 1980, when the American Psychiatric Association published the third edition of its Diagnostic and Statistical Manual (DSM-III).

- There was no new scientific discovery that led the APA to create this diagnosis.

- Diagnostic criteria include difficulty staying focused and paying attention, difficulty controlling behavior, and hyperactivity. A child who "often fails to finish things he or she starts," or "often acts before thinking" is said to be a candidate for this diagnosis.

The Growth of ADHD in U.S.



Diagnosis arises primarily from teacher complaints, as "only a minority of children with the disorder exhibit symptoms during a physician's office visit." (*Harvard Review of Psychiatry*, 2009).

The youngest children in a classroom are 50% more likely to be diagnosed than the oldest children.

The Biology of ADHD

- 1991: "Attempts to define a biological basis for ADHD have been consistently unsuccessful. The neuroanatomy of the brain, as demonstrated by imaging studies, is normal."

--Gerald Gordon, pediatric neurologist.

- 1997: "Efforts to identify a selective neurochemical imbalance (in ADHD children) have been disappointing."

--*Textbook of Neuropsychiatry.*

- 1998: "After years of clinical research and experience with ADHD, our knowledge about the cause or causes of ADHD remain largely speculative."

  --NIH Consensus Development Conference statement

- 2012: "The vast majority of neuroimaging studies to date demonstrate relative, quantitative differences between ADHD and typically developing controls that are neither sufficiently large nor specific enough to be useful on a case-by-case basis as a diagnostic or treatment biomarker."

  --Consensus report of the APA Work Group on Neuroimaging Markers of Psychiatric Disorders, 2012.

On confound of medication:

"Notably absent from structural neuroimaging literature examining biomarkers of ADHD are treatment studies which contrast morphometric differences before and after medication treatment. To our knowledge, no controlled trials have examined the effect of stimulant medication on structural brain abnormalities in youth with ADHD, suggesting a critical area for future research."

Consensus report of the APA Work Group on Neuroimaging Markers of Psychiatric Disorders.

How Stimulants Work

1. Stimulants increase dopamine activity in the brain.

2. For instance, at a therapeutic dose, methylphenidate (Ritalin) blocks the transporters that remove dopamine from the synaptic cleft between neurons and bring it back into the presynaptic neuron.

3. Cocaine acts on the brain the same way, and with similar potency.

4. Methylphenidate clears more slowly from the brain than cocaine, and thus it blocks dopamine reuptake for hours, as opposed to cocaine's relatively brief disruption of this function.

How the Brain Is Changed by Methylphenidate

- The presynaptic neurons may begin releasing less dopamine.

- The density of dopamine receptors on the postsynaptic neurons declines.

- Methylphenidate also acts on serotonin and norepinephrine neurons, and that causes similar compensatory changes in those two pathways.

These Compensatory Changes May Not Be Reversible

In a study of prepubertal rats exposed to methylphenidate for two weeks, there was a dramatic decrease in the density of dopamine receptors in the striatum that persisted into adulthood.

Source: G. Moll, "Early methylphenidate administration to young rats causes a persistent reduction in the density of striatal dopamine transporters." *J of Child and Adolescent Psychopharmacology* 11 (2001): 15-24

Three-Year Results from NIMH's MTA Study

At the end of 36 months, "medication use was a significant marker not of beneficial outcome, but of deterioration. That is, participants using medication in the 24-to-36 month period actually showed increased symptomatology during that interval relative to those not taking medication." Medicated children were also slightly smaller, and had higher delinquency scores.

Source: Jensen, "A 3-year follow-up of the NIMH MTA study," *J Amer Academy of Child & Adolescent Psychiatry* 46 (200&):989-1002.

Analyzing the Results

"The findings . . . were not consistent with views and expectations about medication effects held by many investigators and clinicians in the field. That is, long term benefits from consistent treatment were not documented; selection bias did not account for the loss of relative superiority of medication over time; there was no evidence for "catch up" growth; and early treatment with medication did not protect against later adverse outcomes."

Source: J. Swanson. "Evidence, interpretation and qualification from multiple reports of long-term outcomes in the multimodal treatment study of children with ADHD Part II." *J of Attention Disorders* 12 (2008):15-43.

Six-Year Results from MTA Study

At end of six years, medication use was "associated with worse hyperactivity-impulsivity and oppositional defiant disorder symptoms," and with greater "overall functional impairment."

Source: Molina, "MTA at 8 years," *J Amer Academy of Child & Adolescent Psychiatry 48 (2009)*:484-500.

MTA Study Conclusion

"We had thought that children medicated longer would have better outcomes. That didn't happen to be the case. There were no beneficial effects, none. In the short term, [medication] will help the child behave better, in the long run it won't. And that information should be made very clear to parents."

--MTA Investigator William Pelham, University at Buffalo

Daily Telegraph, "ADHD drugs could stunt growth," Nov. 12, 2007.

Canadians Review the Literature, 2002

In a review of 14 studies that lasted a minimum of three months, involving 1,379 youth, Canadian investigators concluded that there is "little evidence for improved academic performance" with stimulants.

Source: R. Sachar, "Attention-deficit hyperactivity disorder," *Canadian Journal of Psychiatry* 47(2002):337-348.

A Meta-Analysis of the Literature, 2005

In a review of 2,287 studies:

There is "no good quality evidence on the use of drugs to affect outcomes relating to global academic performance, consequences of risky behaviors, social achievements, etc."

-- Drug Effectiveness Review Project
Oregon Health and Science University, 2005

Source: McDonagh, "Drug class review on pharmacologic treatment for ADHD," 2006. http://www.ohsu.edu/drugeffectiveness

Spanish Investigators: Time To Rethink Use of Stimulants

"These drugs are the same stimulants whose harmful consequences are well known in other uses in adults. In this paper we have carried out an exhaustive review of the sources from scientific evidence regarding the short and long term effectiveness of the medication . . . The result is disappointing and should lead to a modification of the [Clinical Practice Guidelines] to the use of drugs as tools of last resort, in a small number of cases and limited and short periods of time."

--Miguel Valverde Eizaquirre

Source: M. Valverde. "Outreach and limitations of the pharmacological treatment of Attention Deficit Disorder with Hyperactivity (ADHD) in children and adolescents and Clinical Practice Guidelines: A literature review." *Rev Asoc Esp. Neuropsiq* 34 (2014):37-74.

Animal Studies of Stimulants

- Preadolescent rats exposed to methylphenidate turned into anxious, depressed adult rats, with a "deficit in sexual behavior." Researchers concluded that "administration of methylphenidate" while the rat brain is still developing "results in aberrant behavioral adaptations during adulthood."
- In an overview of animal studies, researchers concluded that adolescent exposure to methylphenidate provokes "persistent neurobehavioral consequences," including less tolerance of stress and decreased sensitivity to natural rewards.
- In monkeys, repeated exposure to low doses of amphetamines caused monkeys to exhibit "aberrant behaviors" that remained long after drug exposure stopped.

Source: S. Castner, "Long-lasting psychotomimetic consequences of repeated low-dose amphetamine exposure in rhesus monkeys," *Neuropsychopharmacology* 20 (1999):10-28; E. Marco, "Neurobehavioral adaptations to methylphenidate," Neuroscience and Behavioral Reviews 35 (2011):1722-1739.W. Carlezon, "Enduring behavioral effects of early exposure to methylphenidate in rats," *Biological Psychiatry* 54 (2003):1330-37; C. Bolanos, "Methylphenidate treatment during pre-and periadolescence alters behavioral responses to emotional stimuli at adulthood," *Biological Psychiatry* 54(2003):1317-29.

Summary of Animal Studies

"Adolescent exposure to methylphenidate seems to provoke persistent neurobehavioral consequences: long-term modulation of self-control abilities, decreased sensitivity to natural and drug reward, and enhanced stress-induced emotionality."

E. Marco. "Neurobehavioral adaptations to methylphenidate." *Neuroscience and BioBehavioral Reviews* 35 (2011):1722-1739.

Stimulants Can Induce Mood Swings That Are Basis for Bipolar Diagnosis

Stimulant-induced symptoms		Bipolar Symptoms	
Arousal	Dysphoric	Arousal	Dysphoric
Increased energy Intensified focus Hyperalertness Euphoria Agitation, anxiety Insomnia Irritability Hostility Hypomania Mania Psychosis	Somnolence Fatigue, lethargy Social withdrawal Decreased spontaneity Reduced curiosity Constriction of affect Depression Emotional lability	Increased energy Intensified goal-directed activity Agitation Severe mood change Decreased need for sleep Irritability Destructive outbursts Increased talking Distractibility Hypomania Mania	Sad mood Loss of energy Loss of interest in activities Social isolation Poor communication Feelings of worthlessness Unexplained crying

Conversion to Bipolar Illness

Stimulants can induce mania and psychosis

- In Canadian study, six percent of ADHD children treated with stimulants for average of 21 months developed psychotic symptoms.
- In a study of 195 bipolar children, Demitri Papolos found that 65% had "hypomanic, manic and aggressive reactions to stimulant medications."
- University of Cincinnati reported that 21 of 34 adolescent patients hospitalized for mania had been on stimulants "prior to the onset of an affective episode."

Source: Cherland, "Psychotic side effects of psychostimulants," *Canadian Journal of Psychiatry* 44 (1999):811-13. Papolos, "Bipolar disorder, co-occuring conditions, and the need for extreme caution before initiating drug treatment." *Bipolar Child Newsletter* 1 (Nov. 1999). DelBello, "Prior stimulant treatment in adolescents with bipolar disorder," *Bipolar Disorders* 3 (2001):53-57.

Long-Term Risks With Stimulants

- Desensitized brain-reward system?
- Conversion to bipolar diagnosis: 10% to 25% now convert (in U.S.)

Harm-Benefit Ratio of Stimulants

Benefits	Harms
Short-term improvement of ADHD symptoms	No long-term benefit on any domain of functioning
Possible short-term improvement in reading	Physical, emotional and psychiatric adverse effects
Possible reduction in criminality in teenagers	Risk that the brain's dopaminergic system will become desensitized
	Risk of drug-induced conversion to juvenile bipolar disorder

The Hippocratic Oath

In order for a treatment to do no harm, it must improve on natural recovery rates.

In Conclusion

- To restate my opening comment, I am not recommending that you or your child take or not take any medication. Rather, I suggest that you apprise yourself of the outcome research as best you can before you take any psychotropic medication. Empower yourself to ask your prescriber about any concerns you might have to include the content of this PowerPoint. Robert Whitaker has done us a great service in offering the other side of medication dogma and I believe that we owe him much gratitude for his courage in challenging us on the need for thoughtful consideration before we embark down the medication highway.