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Medicating Children: The Enduring Controversy over ADHD and Pediatric Stimulant Pharmacotherapy

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OPINION

Medicating Children: The Enduring Controversy over ADHD and Pediatric Stimulant Pharmacotherapy

CME Test Article

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Drs. Mayes, Bagwell, and Erkulwater, University of Richmond, have disclosed that they have no financial interests in any commercial companies pertaining to this editorial content.

Attention Deficit Hyperactivity Disorder (ADHD) holds the distinction of being both the most extensively studied pediatric mental disorder and one of the most controversial.[1] This is partly due to the fact that it is also the most commonly diagnosed mental disorder among minors.[2] On average, one in every ten to 15 children in the U.S. has been diagnosed with the disorder and one in every 20 to 25 uses a stimulant medication—often Ritalin, Adderall, or Concerta—as treatment.[3,4] The biggest increase in youth diagnosed with ADHD and prescribed a stimulant drug occurred during the 1990s, when the prevalence of physician visits for stimulant pharmacotherapy increased five-fold.[5-8] This unprecedented increase in U.S. children using psychotropic medication triggered an intense public debate.[9]

This overview is drawn from our new book, *Medicating Children: ADHD and Pediatric Mental Health*, published by Harvard University Press, 2009.

Learning objectives (LO) for this issue:
1. **Assess the clinical, educational and economic factors that influence the treatment of ADHD.**
2. **Evaluate the debate over the overuse of medications in children.**
3. **Describe the ambiguities in classification and diagnosis of ADHD.**

This CME activity is intended for child and adult psychiatrists, pediatricians and other health care professionals with an interest in the psychopharmacology and treatment practices for child and adolescent psychiatric disorders.

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Ironically, neither the debate nor ADHD and stimulants were new. Methylphenidate, more commonly known by the trade name Ritalin, was first introduced in the United States in 1955, and approved by the Food and Drug Administration in 1961 for use in children with severe behavioral problems.[10] Prior to Ritalin, another stimulant (benzedrine) had been tested and used by small numbers of children as early as 1937.[11] As for ADHD, the basic symptoms of the disorder have gone by several different diagnostic labels since the early 1930s: "organic drivenness," "minimal brain damage," "hyperkinetic impulse disorder," "minimal brain dysfunction," "hyperkinesis," "hyperactive child syndrome," and "attention deficit disorder."[12] Even the core of the controversy, children using physician-prescribed psychoactive drugs, dates back almost four decades. Nevertheless, negative publicity over the "drugging of problematic children" in the early 1970s—together with another negative media blitz and a wave of lawsuits against physicians, school personnel and the American Psychiatric Association in the late 1980s—greatly reduced the prevalence of ADHD diagnoses and pharmacotherapy compared with current levels. When the 1990s began, most schools across the country had only a handful of (if any) children diagnosed with ADHD and using stimulants.[13] By 2000, most every classroom in the United States had, on average, at least one to two such students treated for the disorder.[4,14,15] Currently, almost 8% of youth aged 4 to 17 years have a diagnosis of ADHD, and approximately 4.5% have the diagnosis and are taking medication for the disorder.[16,17]

The massive increase in the number of U.S. children diagnosed with ADHD and using stimulants stemmed primarily from a confluence of trends (clinical, economic, educational, political), an alignment of incentives (among clinicians, educators, policy makers, health insurers, the pharmaceutical industry), and the sizeable growth in scientific knowledge about ADHD and stimulants that converged in the first half of the 1990s. Growing political movements advocating for children's welfare and mental health consumers,[18-24] along with the decreasing stigma associated with mental disorders, led to three seemingly minor policy changes in the early 1990s—to a federal income support program (Supplemental Security Income, SSI), a federal special education program (Individuals with Disabilities Education Act, IDEA), and a joint federal-state public health insurance program (Medicaid)—that helped trigger the surge in ADHD diagnoses and related stimulant use.[25,26]

ADHD and stimulant use have been and remain controversial, in part because most children are diagnosed and medicated as the result of decisions made by their parents and clinicians. In short, the treatment is ordinarily decided for them instead of by them, a scenario that invites criticism that a patient's autonomy is being compromised to some extent.[27,28,29] Yet many medical decisions involving children are made this way and are not controversial. Mental disorders such as ADHD, however, are different. They are regularly diagnosed based mainly, if not solely, on the presence of behavioral symptoms—inattentiveness, hyperactivity, and impulsiveness—that are common—this despite the fact that the DSM-IV outlines a far more extensive and rigorous approach to making a proper diagnosis of ADHD than relying exclusively on rating an individual's symptoms. The key difference is one of degree. Children with ADHD are significantly more inattentive, impulsive, distractible, and/or fidgety than their peers, such that their symptoms cause major personal impairment and interfere with daily human functioning.[30]

At the same time, mental disorders usually involve matters of degree, so why has ADHD been more controversial than other mental disorders? One of the main reasons has to due with the disorder's dominant educational aspect. The majority of ADHD diagnoses originate with the observations of a child's

teacher,[31] and many of the disorder's symptoms—rated on behavioral scales—require teacher reports to make a diagnosis. The child

> "often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities,"
>
> "often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace,"
>
> "often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort [such as school work or homework],"
>
> "often leaves seat in classroom or in other situations in which remaining seated is expected,"
>
> "often blurts out answers before questions have been completed")."[32-35]

With ADHD, teachers are typically the primary source of diagnostic information.[36] Only a minority of children with the disorder exhibit symptoms during a physician's office visit.[37,38]

Similar to all mental disorders, however, there is no definitive medical test (blood, urine, radiological) to verify an ADHD diagnosis. Therefore, the diagnosis contains a large element of unavoidable subjectivity, which leaves it open to competing definitions of what is considered "normal" childhood behavior.[39] The United States, for example, consumes the majority of the world's production of stimulants with school-age children using as much as three times more psychiatric medication than children in the rest of the world combined.[40,41] In some European countries, only a child psychiatrist can prescribe a stimulant for a minor diagnosed with ADHD, while in other countries the drugs can only be prescribed if approved by three independent professionals.[42] These regulations have precluded a similar growth in stimulant use in other developed countries, despite the fact that international studies suggest that the prevalence of ADHD is similar across different Western countries when clinicians use roughly the same diagnostic procedures.[43,44]

For these and other reasons, people debate whether the ADHD and stimulant phenomenon in the U.S. is more the story of medical science making progress on a long misunderstood disorder or if ADHD has largely been "socially constructed," under the biological vision of mental health, as a response to non-medical problems such as under-performing schools, increased academic demands and expectations, and higher poverty and divorce rates than existed before the 1970s.[46] What makes this question so contentious is that the debate is political and philosophical in nature because ADHD and stimulants do not exist in a clinical vacuum.[47,48] All mental disorders and mental health care, notes medical anthropologist Byron Good, are "social, psychological and cultural to the core," powerfully influenced by public opinion and varying expectations of what is considered normal and abnormal behavior by girls and boys of very different ages and stages of development.[49] Meanwhile, teachers, parents, clinicians, health plans, and policy-makers are all trying to determine—within their separate but overlapping spheres of influence—what is in the best interests of literally millions of children.

The Core of the Controversy over ADHD and Stimulants

It seems virtually impossible to give a presentation on or even just talk about ADHD and stimulants without being asked if the drugs are overused in the United States. We assume that many readers of this paper will have the same curiosity. The answer is "yes" and "no." In some geographic areas and among specific childhood populations, ADHD appears to be over-diagnosed and the drugs overused. However, several of the same research findings that identify this overuse also identify areas and populations in which ADHD is very likely underdiagnosed and the drugs underused with serious personal and public health consequences.[50-54]

This more complicated and nuanced reality of both over- and under-use of stimulants is rarely presented in the popular press, but it reflects two key factors. First, while a valid (real, genuine) disorder, ADHD is also—similar to many mental disorders—one that primary care physicians often diagnose in a less than strictly thorough manner due to the intense economic and time constraints they face, as well as to their training (or lack thereof) in the area of mental disorders.[55,56,57] This reality is important, because primary care physicians make the majority of ADHD diagnoses and stimulant drug prescriptions.[58,59] In addition, it is not clear to clinicians, researchers or the general public if ADHD is primarily a medical disorder, a behavioral problem manifesting primarily in schools, a mental illness, or an evolutionary disorder of human adaptation.[60,61] It is also not self-evident how hyper, inattentive, and/or impulsive a child has to be to warrant a diagnosis, because the benchmark of comparison for diagnosing a child is whatever is considered "normal" for his or her peer age-group.

The ambiguity over ADHD's classification, and the manner in which it is regularly diagnosed, contributes to significant variation in diagnostic and treatment styles by clinicians: prevalence rates for the disorder range from as low as 2% to as high as 18% in different communities across the United States.[62,63] This variation results in a serious mismatch between the need for and provision of pharmacotherapy, with both "under-treatment" of ADHD[64] and the "over-use" of stimulants by many children who do not meet full ADHD diagnostic criteria (as well as some children who exhibit no symptoms of ADHD at all).[53]

The second factor that fuels the debate is that stimulants are heavily regulated Schedule II drugs, which are effective in helping individuals with or

without ADHD.[65,66] In other words, they enhance most individuals' ability to sustain their level of concentration.[67,68] This is not the way the public understands medical interventions to operate. The general view of medicines is that they treat people with a chronic or acute episode of illness or a disorder, but that they would either have no effect or possibly be harmful to someone who did not have an illness or a disorder. Consequently, when stimulants help those with ADHD and enhance the performance of individuals without the disorder, they often invite skepticism about the appropriateness of stimulant use by millions of children.[68]

Even as scientific understanding of ADHD advances, it is hard to imagine the social and political controversy over ADHD abating. As a diagnosis and form of treatment, ADHD and stimulant pharmacotherapy illustrate both the success that science is capable of producing—when applied to the study of mental disorders—and its limitations. Researchers have made tremendous progress over the last three decades in increasing our understanding of ADHD, but when it comes to diagnosing most mental disorders our system is still far behind other branches of medicine, notes E. Jane Costello, a professor of psychiatry and behavioral sciences at Duke University. "On an individual level, for many parents and families, the experience can be a disaster; we must say that." For these families, the search for a diagnosis is best seen as a process of trial and error that may not end with a definitive answer. If a family can find some combination of treatments that help a child improve, Costello adds, "then the diagnosis may not matter much at all."[69] ADHD is more straightforward and easier to diagnosis in children than, for example, bipolar disorder or autism. Yet, as previously noted, diagnosing ADHD still relies on some combination of interviews with children (who often do not exhibit symptoms in a clinician's office or are reluctant or unable to talk about themselves the way an adult would), behavioral checklists, less-than-precise rating scales (that measure the existence and severity of ADHD symptoms along the lines of "never," "occasionally," "often," "very often"), and reports from teachers and parents.

Clinical Uncertainty and Boundary Drawing

Ultimately, then, diagnosing and treating ADHD is still partially an art, despite the fact that the science applied to it has improved dramatically in recent decades. At the heart of the controversy over ADHD were questions of boundary drawing. Children exhibit symptoms of inattentiveness, hyperactivity, and impulsiveness along a continuum. Despite the fact that scientific research can inform our choices, where the boundary between ADHD and typical childhood behavior is located is ultimately a political and social choice, not a scientific one. No amount of clinical research, therefore, can resolve this question for us. Moreover, to the extent that the boundary between sickness and health is, in the case of mental disorders such as ADHD, demarcated without the ability to reference objective clinical signs or indicators of illness, debates about underdiagnosis or overdiagnosis invariably tap into society's ambivalence about mental disorders. The DSM was designed to identify children with the severest symptoms, those with the lowest levels of functional ability. Yet the DSM is not applied in a vacuum: Social, political, and economic forces impinge on where physicians, educators, program administrators, and others decide to locate the boundaries of medical dysfunction. Criticisms of ADHD are criticisms both of the limits of clinical knowledge and of the extra-clinical forces that influence diagnostic decision-making.

ADHD, of course, is not alone; the diagnoses of all mental disorders are subject to influences outside of clinical medicine. ADHD, however, is unique in the extent to which it elicits intense reactions from people. Because the symptoms of ADHD are often most evident in the school setting, where adults make sometimes tremendous demands on children, some critics worry that the identification of children with the disorder is driven more by the wants and expectations of teachers, parents, and school administrators than by the needs of the students. More important, because ADHD can be treated with pharmaceutical medication produced by major companies, other critics worry (for good reason) about the influence of corporate profit-seeking motives on the diagnosis of children. ADHD is among the most visible and controversial mental disorders, in short because it is a vehicle through which many controversial social and political trends can be criticized.

In the middle of this confusion are the parents of children with ADHD. They must decide whether to accept the label of the disorder, and they must choose which of the many forms of treatment and school-based interventions to pursue: behavioral therapy alone, medication alone, medication in combination with behavioral therapy, which medication, which kinds of behavioral therapy. The path to choose is far from evident, and choices are constrained by healthcare financing arrangements and the attitudes of teachers and physicians toward their children's ADHD. In addition, critics like Peter Breggin and Phyllis Schlafly write for a broad audience with colorful anecdotes and pithy phrases, and they publish their work in places that are easily accessible to the general public. Meanwhile, most researchers write for an expert audience in specialized journals and in language filled with clinical and scientific jargon that lay readers might find difficult to comprehend. As a result, even with the advances in our understanding of the nature of ADHD and especially in our knowledge of effective treatments brought about by extensive research (including the Multimodal Treatment Study of Children with ADHD and numerous carefully designed medication trials), parents often have easier access to the vocal, and sometimes extreme, views of critics of stimulant treatment via the Internet and news re-

ports than to the research published in scientific journals. It is little surprise, then, that despite the growth of scientific knowledge of ADHD and stimulants, parents are swayed by the extremists and unsure about which treatment to pursue; the misinformation that fills the public debate over ADHD only serves to heighten parents' fear that they will choose the wrong path. Thus, even if parents decide to medicate their child, it is a decision that can be fraught with guilt and anxiety. Although other mental disorders are difficult to diagnose with accuracy, although rates of childhood depression and other disorders are also on the rise, and although the growing pediatric use of psychotropic drugs is not limited to stimulants, no other disorder touches upon so many vexing social and political questions, a situation that amplifies the ambivalence that parents feel about medicating their children.

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References

1. Wolraich M. Attention deficit hyperactivity disorder: the most studied and yet the most controversial diagnosis. *Mental Retard Dev Disabil Res Rev* 1999;5:163-8.
2. Williams J., Klinepeter K. Palmes G., Pulley A., Foy J. Diagnosis and treatment of behavioral health disorders in pediatric practice. *Pediatrics* 2004;114:601-6.
3. Rappley M. Attention-deficit hyperactivity disorder. *N Engl J Med* 2005;352:165-73.
4. Zuvekas S., Vitiello B., Norquist G. Recent trends in stimulant medication use among u.s. children. *Am J Psychiatry* 2006;163:579-85.
5. Bhatara V., Feil M., Hoagwood K., Vitiello B., Zima B. National trends in concomitant psychotropic medication with stimulants in pediatric visits: practice versus knowledge. *J Atten Disord* 2004;7:217-26.
6. Robison L., Sclar D., Skaer T. Datapoints: trends in ADHD and stimulant use among adults, 1995-2002. *Psychiatric Serv* 2005;56:1497.
7. Thomas C., Conrad P., Casler R., Goodman E. Trends in the use of psychotropic medications among adolescents, 1994 to 2001. *Psychiatric Serv* 2006;57:63-9.
8. Olfson M., Gameroff M., Marcus S., Jensen P. National trends in the treatment of attention deficit hyperactivity disorder. *Am J Psychiatry* 2003;160:1071-77.
9. Eberstadt M. Why ritalin rules. *Policy Review* 1999;94:24-44.
10. Chiarello R., Cole J. The use of psychostimulants in general psychiatry: a reconsideration. *Arch Gen Psychiatry* 1987;44:286-95.
11. Bradley C. The behavior of children receiving Benzedrine. *Am J Psychiatry* 1937;94:577-8.
12. Barkley R. *Attention-deficit hyperactivity disorder: A handbook for diagnosis and treatment*. New York: The Guilford Press, 1990.
13. Swanson J., Lerner M., Williams L. More frequent diagnosis of attention-deficit hyperactivity disorder. *N Engl J Med* 1995;333:944.
14. Schneider H., Eisenberg D. Who receives a diagnosis of attention-deficit/hyperactivity disorder in the united states elementary school population? *Pediatrics* 2006;117:601-9.
15. Spencer T., Biederman J., Mick E. Attention-deficit/hyperactivity disorder: diagnosis, fifespan, comorbidities, and neurobiology. *Ambul Pediatr* 2007;7:73-81.
16. Visser S., Lesesne C., Perou R. National estimates and factors associated with medication treatment for childhood attention-deficit/hyperactivity disorder. *Pediatrics Suppl* 2007;119:S99-S106.
17. Centers for Disease Control and Prevention. Mental health in the united states: prevalence of diagnosis and medication treatment for attention-deficit/hyperactivity disorder. *MMWR Morb Mortal Wkly Rep* 2005;54:842-7.
18. Scotch R. Politics and policy in the history of the disability rights movement. *Milbank Q* 1989;67:380-400.
19. Sommer R. Family advocacy and the mental health system: the recent rise of the alliance for the mentally ill. *Psychiatric Q* 1990;61:205-21.
20. Tomes N. The patient as a policy factor: a historical case study of the consumer/survivor movement in mental health. *Health Aff* 2006;25:720-9.
21. McLean A. Empowerment and the psychiatric consumer/ex-patient movement in the united states: contradictions, crisis and change. *Soc Sci Med* 1995;40:1053-71.
22. Hatfield A. The national alliance for the mentally ill: a decade later. *Community Mental Health J* 1991;27:95-103.
23. Minow M., Weissbourd R. Social movements for children. *Daedalus* 1993;122:1-29.
24. Pfeiffer D. Overview of the disability movement: history, legislative record, and political implications," *Policy Studies Journal* 1993;21:724-34.
25. Perrin J., Kuhlthau K., McLaughlin T., Ettner S., Gortmaker S. Changing patterns of conditions among children receiving supplemental security income disability benefits. *Arch Pediatr Adolesc Med* 1999;153:80-84.
26. Reid R., Maag J., Vasa S. Attention deficit hyperactivity disorder as a disability category: a critique. *Exceptional Children* 1994;60:198-214.
27. Hickey K., Lyckholm L. Child welfare versus parental autonomy: medical ethics, the law, and faith-based healing. *Theor Med Bioeth* 2004;25:265-76.
28. Kuther T. Medical decision-making and minors: issues of consent and assent. *Adolescence* 2003;38:343-58.
29. Sherer D. The capacities of minors to exercise voluntariness in medical treatment decisions. *Law Hum Behav*1991;15:431-49.
30. Goldman L., Genel M., Bezman R., Slanetz P. Diagnosis and treatment of attention-deficit/hyperactivity disorder in children and adolescents: council on scientific affairs, american medical association. *JAMA* 1998;279:1100-07.
31. Sax L., Kautz K. Who first suggests the diagnosis of attention-deficit/hyperactivity disorder? *Ann Fam Med* 2003;1:171-4.
32. DuPaul G., Stoner G. *ADHD in schools: assessment and intervention strategies*. New York: Guildford Press, 2003.
33. Stein M., Marx N., Beard J., Lerner M., Levin B., Glascoe F., et al. ADHD: The diagnostic process from different perspectives. *J Dev Behav Pediatr* 2004;25:53-8.
34. Biederman J., Faraone S., Monuteaux M., Grossbard J. How informative are parent reports of attention-deficit/hyperactivity disorder symptoms for assessing outcome in clinical trials of long-acting treatments? a pooled analysis of parents' and teachers' reports. *Pediatrics* 2004;113:1667-71.
35. Biederman J., Gao H., Rogers A., Spencer T. Comparison of parent and teacher reports of attention-deficit/yperactivity disorder symptoms from two placebo-controlled studies of atomoxetine in children. *Biol Psychiatry* 2006;60:1106-10.
36. Havey J., Olson J., McCormick C., Cates G. Teachers' perceptions of the incidence and management of attention-deficit hyperactivity disorder. *Appl Neuropsychol* 2005;12:120-7.
37. Sleator E., Ullmann R. Can the physician diagnose hyperactivity in the office? *Pediatrics* 1981:67:13-7.
38. Johnson T. Evaluating the hyperactive child in your office: is it ADHD? *Am Fam Physician* 1997;56:155-70.
39. Luhrmann T. *Of two minds: the growing disorder in american psychiatry*. New York: Vintage, 2001.
40. Buitelaar J., Rothenberger A. Foreword—ADHD in the scientific and political context. *Eur Child Adolesc Psychiatry Suppl*. 2004;13:11-6.
41. Hick H., Kaye J., Black C. Incidence and prevalence of drug-treated attention deficit disorder among boys in the UK. *Br J Gen Pract* 2004;54:345-7.
42. P. Jensen quoted in PBS Frontline's "Medicating Kids," available at http://www.pbs.org/wgbh/pages/frontline/shows/medicating/experts/explosion.html (accessed 9 December 2007).
43. Rohde L., Szobot C., Polanczyk G., Schmitz M., Martins S., Tramontina S. Attention-deficit/hyperactivity disorder in a diverse culture: do research and clinical findings support the notion of a cultural construct for the disorder? *Biol Psychiatry* 2005;57:1436-41.

(continued on page 9)

Bupropion SR and Individual Counseling

Efficacy of bupropion SR and individual counseling as smoking cessation treatments was assessed in a randomized, placebo-controlled clinical trial among adult daily smokers. Intent-to-treat analyses indicated that bupropion SR increased abstinence rates at the end of treatment. Bupropion SR treatment also improved latency to lapse and relapse in survival analyses. Counseling was not associated with increases in the likelihood of abstinence at any time point.

McCarthy et al, A randomized controlled clinical trial of bupropion SR and individual smoking cessation counseling. Nicotine Tob Res. 2008 Apr;10(4):717-29.

Effect of Genetic Polymorphisms

Even though bupropion is a first line pharmacological agent for smoking cessation, not all smokers successfully quit smoking by using bupropion. It means other factors such as genetic predisposition could contribute to the therapeutic outcome.

Objectives: The aim of this study is to elucidate the question of whether abstinence rates in a bupropion trial would be different depending on genotypes.

Six candidate genes, thought to be involved in the interaction of nicotine and bupropion (for example, the dopamine receptor type 2, dopamine transporter, norepinephrine transporter, serotonin transporter, catecholamine-O-methyltrasferase) and the clinical outcomes of smoking behavior were investigated. The participants were 225 male smokers to whom 150mg of bupropion SR was administered for 4 weeks.

Main Results: (1) the frequencies of A1/A2 genotype of the dopamine receptor type 2 TaqI A gene and the SLC6A3-9 genotype of the dopamine transporter1 gene were higher in he non-abstinence group than in the abstinence group. The frequencies of COMTH/COMTH and A/G genotypes of the norepinephrine transporter gene were higher in the abstinence group than in non-abstinence group. (2) Participants having specific genotypes such as homozygotes (A1/A1 or A2/A2) of DRD2 TaqI A, COMTH/COMTH, AG of NET-8 and LL of 5-HTTLPR showed higher abstinence rate than other participants.

Conclusions: It can be concluded that genetic diversity might determine the effects of bupropion on smoking cessation.

Han DH et al, Effect of genetic polymorphisms on smoking cessation: trial of bupropion in Korean male smokers. Psychiatric Genet. 2008 Feb; 18(1): 11-6.

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44. Faraone S., Sergeant J., Gillberg C., Biederman J. The worldwide prevalence of ADHD: is it an american condition? *World Psychiatry* 2003;2:104-13.
45. Polanczyk G., de Lima M., Horta B., Biederman J., Rohde L. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *Am J Psychiatry* 2007;164:942-8.
46. Hinshaw S., Cicchetti D. Stigma and mental disorders: conceptions of illness, public attitudes, personal disclosure, and social policy. *Dev Psychopathol* 2000;12:555-98.
47. Bussing R., Schoenberg N., Perwien A. Knowledge and information about ADHD: evidence of cultural differences among african-american and white parents. *Soc Sci Medicine 1*998;46:919-28.
48. McLeod J., Fettes D., Jensen P., Pescosolido B., Martin J. Public knowledge, beliefs, and treatment preferences concerning attention-deficit hyperactivity disorder. *Psychiatr Serv* 2007;58:626-31.
49. Good B. Studying mental illness in context: local, global or universal? *Ethos* 1997;25:230-48.
50. Gross J. Checklist for camp: bug spray, sunscreen, pills. New York Times, July 16, 2006, 1.
51. Bokhari F., Mayes R., Scheffler R. An analysis of the significant variation in stimulant use across the U.S. *Pharmacoepidemiol Drug Saf* 2005;14:267-75.
52. Cox E., Motheral B., Henderson R., Mager D. Geographic variation in the prevalence of stimulant medication use among children 5 to 14 years old: results from a commercially insured US sample. *Pediatrics* 2003;111:237-43.
53. Angold A., Erkanli A., Egger H., Costello J. Stimulant treatment for children: a community perspective. *J Am Acad Child Adolesc Psychiatry* 2000;39:975-984.
54. Jensen P., Kettle L., Roper M., Sloan M., Dulcan M., Hoven C., et al. Are stimulants overprescribed? treatment of adhd in four U.S. communities. *J Am Acad Child Adolesc Psychiatry* 1999;38:797-804.
55. Kwasman A., Tinsley B., Lepper H. Pediatricians' knowledge and attitudes concerning diagnosis and treatment of attention deficit and hyperactivity disorders: a national survey approach. *Arch Pediatr Adolesc Med* 1995;149:1211-16.
56. Williams J., Klinepeter K., Palmes G., Pulley A., Foy J. Diagnosis and treatment of behavioral health disorders in pediatric practice. *Pediatrics* 2004;114:601-6.
57. Rushton J., Fant K., Clark S. Use of practice guidelines in the primary care of children with attention-deficit/hyperactivity disorder. *Pediatrics* 2004;114:23-8.
58. Culpepper L. Primary care treatment of attention-deficit/hyperactivity disorder. *J Clin Psychiatry Suppl.* 2006;67:51-8.
59. Zito J., Safer D., dosReis S., Magder L., Gardner J., Zarin D. Psychotherapeutic medication patterns for youths with attention-deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med* 1999;153:1257-63.
60. Pellegrini A., Horvat M. A developmental contextualist critique of attention deficit hyperactivity disorder. *Educational Researcher* 1995;24:13-9.
61. Jensen P., Mrazek D., Knapp P., Steinberg L., Pfeffer C., Schowalter J., et al. Evolution and revolution in child psychiatry: ADHD as a disorder of adaptation. *J Am Acad Child Adolesc Psychiatry* 1997;36:1672-81.
62. Rowland A., Umbach D., Catoe K., Stallone L., Long S., Rabiner D., et al. Studying the epidemiology of attention-deficit hyperactivity disorder: screening method and pilot results. *Can J Psychiatry* 2001;46:931-40.
63. Jensen P. *Epidemiological research on ADHD: what we know and what we need to learn*. presented at the conference, "ADHD: A Public Health Perspective," CDC, available at http://www.cdc.gov/ncbddd/adhd/confepi.htm (accessed 9 July 2007).
64. Guevara J., Lozano P. Wickizer T., Mell L., Gephart H. Psychotropic medication use in a population of children who have attention-deficit/hyperactivity disorder. *Pediatrics* 2002;109:733-9.
65. Rapoport J., Buchsbaum M., Zahn T., Weingartner H., Ludlow C., Mikkelsen J. Dextroamphetamine: cognitive and behavioral effects on normal prepubertal boys. *Science* 1978;199:560-3.
66. Rapoport J., Buchsbaum M., Weingartner H., Zahn T., Ludlow C., Mikkelsen E. Dextroamphetamine: the cognitive and behavioral effects in normal and hyperactive boys and normal men. *Arch Gen Psychiatry* 1980;37:933-43.
67. Zahn T., Rapoport J., Thompson C. Autonomic and behavioral effects of dextroamphetamine and placebo in normal and hyperactive prepubertal boys. *J Abnorn Child Psychol* 1980;8:145-160.
68. Safer D. Are stimulants overprescribed for youths with ADHD? *Ann Clin Psychiatry* 2000;12:55-62.
69. Carey B. What's wrong with a child? Psychiatrists often disagree. New York Times, November 11, 2006, A1.