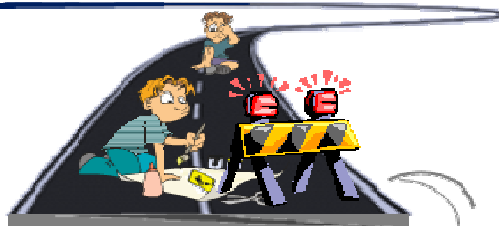


NEWSLETTER



INDICE:

1. Dalle banche dati bibliografiche

pag. 2

2. Documenti

- Clinical Practice Guideline “**ADHD: Clinical practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescent**”
Pediatrics 2011;128:1-16. pag. 38
- Summary of Current Evidence “**Guidelines and Racommendation for ADHD in Children and Adolescents**”
CADTH October 2011. pag. 54
- Zanini S. “**ADHD e genetica Uno studio e molte reazioni**”
Quaderni acp 2011;18:226. pag. 79

3. Congressi, Corsi, ...

- Convegno “**Evidence-based treatment of ADHD: Neuropsychological and psychophysiological endophenotypes**” 18 novembre 2011, Rho pag. 80
- Università degli studi di Padova. Master in genitorialità e sviluppo dei figli: interventi preventivi e Psicoterapeutici “**Corso di valutazioni cliniche con l’aiuto dell’AAI, dell’LTP, dello specchio e delle scale di sviluppo**” 18-19-20-21 gennaio 2012, Padova pag. 82
- **4° Workshop sull’ADHD** - SINPIA Sezione Regionale Sardegna e Clinica di Neuropsichiatria Infantile dell’Università degli Studi di Cagliari Dipartimento di Neuroscienze, 8-10 marzo 2012, Cagliari pag. 83

BIBLIOGRAFIA ADHD OTTOBRE 2011

Acta Med Iran. 2011;49:487-98.

ADVANCES AND CONSIDERATIONS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER PHARMACOTHERAPY.

Mohammadi M, Akhondzadeh S.

Attention-deficit/hyperactivity disorder (ADHD) is a highly heritable neuropsychiatric disorder associated with significant impairments in occupational, academic, neuropsychological, and social functioning. Central nervous system (CNS) stimulants are recommended as first-line medication therapy for children. CNS stimulants include formulations of methylphenidate and amphetamine derivatives and are available in a large variety of immediate- and extended-release preparations. Extended-release preparations are often preferred to limit drug administration during school or work and may help to limit side effects associated with rapid fluctuations in serum concentration. Stimulant medication is by far the most commonly used treatment in managing children with ADHD, 10-20% of those who take such medication do now show clinically significant improvements in their primary ADHD symptom. Even when a favorable response is obtained, some children experience side effects that are of sufficient occurrence and severity to prevent continued use of stimulant medication. In such instances or when families are unwilling to consider a stimulant, non-stimulant medications may be appealing. This review focuses on etiology, assessment and treatment of ADHD with various stimulant and non-stimulant agents.

.....

Acta Paediatr Int J Paediatr. 2011.

MOTOR EXAMINATION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND ASPERGER SYNDROME.

Pasini A, D'Agati E, Pitzianti M, et al.

Aim: Evaluating whether motor skills could differentiate drug-naïve subjects with two neurodevelopmental disorders: Attention-Deficit Hyperactivity Disorder (ADHD) and Asperger Syndrome (AS).

Methods: Thirty-six boys (12 with ADHD, 12 with AS and 12 with typical development) aged 8-12 were evaluated using the Physical and Neurological Examination for Subtle Signs. Three primary outcome variables were obtained as follows: (i) total speed of timed activities, (ii) total overflow and (iii) total dysrhythmia.

.....
Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.

Results: Children with AS performed more slowly than those with ADHD and healthy children independently of age and IQ. Total dysrhythmia differentiates ADHD and AS children from controls.

Conclusion: Dysfunction of the fronto-striatal-cerebellar networks related to motor control could be the physiopathological basis of the reported findings.

.....

Acta Paediatr Int J Paediatr. 2011;100:1468-75.

PSYCHIATRIC PROBLEMS ASSOCIATED WITH SUBTHRESHOLD ADHD AND DISRUPTIVE BEHAVIOUR DIAGNOSES IN TEENAGERS.

Malmberg K, Edbom T, Wargelius HL, et al.

Aim: To study the coexistence of subthreshold diagnoses of both attention deficit hyperactivity disorder (ADHD) and disruptive behaviour disorders (DBD) with other symptoms of child and adolescent psychiatric disorders as well as risk behaviours associated with smoking, alcohol and drug use.

Methods: A population-based sample of twins including 177 girls and 135 boys was interviewed using the Swedish version of Kiddie-SADS Present and Lifetime Version (K-SADS-PL). Subthreshold diagnoses were compiled based on the ADHD and DBD criteria, where each criterion was assessed as 'possible' or 'certain' according to K-SADS-PL. The odds ratios (OR) between the subthreshold diagnoses and each of the screening questions in K-SADS-PL were calculated.

Results: Subthreshold diagnoses of ADHD and DBD coexisted with the screening questions concerning depression, mania, panic attack, phobias, anorexia nervosa, motor tics and posttraumatic stress disorder (PTSD) in girls. In boys, these subthreshold diagnoses coexisted with symptoms of depression and PTSD. For both boys and girls, smoking and high alcohol consumption contributed to a high OR with regard to ADHD and DBD.

Conclusion: Subthreshold diagnoses of ADHD and DBD were risk factors for several other psychiatric symptoms as well as smoking and high alcohol consumption. Thus, a broad clinical assessment is needed for adolescents with such preliminary diagnoses.

.....

Acta Paediatr Int J Paediatr. 2011.

PARADIGM SHIFT IN CONSCIOUSNESS RESEARCH: THE CHILD'S SELF-AWARENESS AND ABNORMALITIES IN AUTISM, ADHD AND SCHIZOPHRENIA.

Lou HC.

Self-awareness is a pivotal component of any conscious experience and conscious self-regulation of behaviour. A paralimbic network is active, specific and causal in self-awareness. Its regions interact by gamma synchrony. Gamma synchrony develops throughout infancy, childhood and adolescence into adulthood and is regulated by dopamine and other neurotransmitters via GABA interneurons. Major derailments of this network and self-awareness occur in developmental disorders of conscious self-regulation like autism, attention deficit hyperactivity disorder (ADHD) and schizophrenia. Conclusion: Recent research on conscious experience is no longer limited to the study of neural 'correlations' but is increasingly lending itself to the study of causality. This paradigm shift opens new perspectives for understanding the neural mechanisms of the developing self and the causal effects of their disturbance in developmental disorders.

.....

Alcohol Alcohol. 2011;46:i26.

THE IMPACT OF TEMPERAMENT, ATTENTION DEFICIT HYPERACTIVITY DISORDER AND PSYCHOSOCIAL FACTORS ON SUBSTANCE USE AND THE MOTIVATION TO CONSUME IN YOUNG ADULT MALES.

Riegler AJ, Erfurth A, Kapusta N, et al.

The consumption of alcohol, nicotine and illicit drugs is common among adolescents and young adults, and poses serious health risks. Objective. The association between dimensions of temperament, attention

deficit hyperactivity disorder (ADHD), psychosocial factors and the use of alcohol, nicotine and illicit drugs. Method. We investigated a representative sample of 18-year-old males (n = 3284) using questionnaires as well as biological markers. Due to conscription to the military service, all young men in Austria have to undergo an examination of their health status. This physical and psychological examination enabled us to investigate a representative sample of young men, independent of background, social status and education. Therefore, we could collect data regarding the prevalence of the use of alcohol, nicotine and illicit drug use, ADHD symptomatology and further aspects. We assessed different psychosocial factors such as life satisfaction, family history of drinking and smoking, leisure behaviour as well as onset, patterns and motivation of substance use. To evaluate alcohol and illicit drug use and misuse, we collected blood and urine samples, to test for smoking we measured carbon monoxide in exhaled air and we also collected some biological markers (e. g. body mass index, waist circumference). Questionnaires. We used the TEMPS-M for temperament (according to Akiskal), the ADHD checklist according to DSM IV as well as the Wender Utah Rating Scale (WURS) were used to assess the symptomatology of ADHD, the CAGE questionnaire to test for alcohol misuse and dependence and the Fagerstrom questionnaire to test for nicotine dependence. Data concerning the prevalence of ADHD symptomatology, psychosocial factors and temperament dimensions (according to Akiskal et al.) in connection with alcohol, nicotine and substance use as well as the motivation to consume will be presented. Furthermore, we will show how our findings could contribute to the development of more specific and need orientated prevention strategies of high-risk groups.

.....

Annals of General Psychiatry. 2011;25.

CLINICAL USE OF A MODIFIED RELEASE METHYLPHENIDATE IN THE TREATMENT OF CHILDHOOD ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Takon I.

Attention deficit hyperactivity disorder (ADHD) is the most commonly diagnosed neurobehavioural disorder in childhood, affecting over 5% of children worldwide. As well as the core symptoms of inattention, hyperactivity and impulsivity, patients often exhibit learning difficulties and impairment in social functioning. The frequency of referral is higher for boys than for girls (about 2:1), and girls are generally older at the time of referral. Pharmacological therapy is considered the first-line treatment for patients with severe ADHD and severe impairment. Stimulant medications are licensed in the UK for the management of ADHD in school-age children and young people, and are effective in controlling ADHD symptoms. While immediate-release preparations of methylphenidate (MPH) have proven effective in the treatment of ADHD, there are a number of problems associated with their use, most notably compliance, stigma and medication diversion. Modified release preparations are now available that overcome the need for multiple daily dosing, and which offer different MPH release profiles, thereby enabling the physician to match the medication to the patient's particular requirements. This review describes the diagnosis, referral and treatment pathways for patients with ADHD in the UK and the practical considerations when initiating pharmacological treatment. The clinical experience of treating ADHD with a modified-release MPH preparation (Equasym XL(R)) is illustrated with case studies.

.....

Behav Genet. 2011 Sep;41:668-79.

PARENTS AND TEACHERS MAKE DIFFERENT CONTRIBUTIONS TO A SHARED PERSPECTIVE ON HYPERACTIVE–IMPULSIVE AND INATTENTIVE SYMPTOMS: A MULTIVARIATE ANALYSIS OF PARENT AND TEACHER RATINGS ON THE SYMPTOM DOMAINS OF ADHD.

McLoughlin G, Rijdsdijk F, Asherson P, et al.

Attention deficit hyperactivity disorder (ADHD) is characterised by developmentally inappropriate and impairing levels of inattentive and hyperactive–impulsive behaviours. We aimed to investigate the differential effects of parent and teacher ratings on inattention and hyperactivity–impulsivity and the extent of genetic overlap between the two behavioural dimensions. Multivariate structural equation modelling was performed on DSM-IV based ADHD ratings by parents and teachers collected on a general population

sample of 672 twin pairs, at ages 7–10 years. This study is the first to simultaneously use parent and teacher ratings in twin modelling to examine the effects of different raters on the two behavioural dimensions of ADHD. The findings indicated that hyperactivity–impulsivity and inattention load on to separate latent factors that represent a common behavioural view for both parents and teachers, although there are additional aspects to the observations of these behaviours that are unique to each type of rater. The findings further indicate some shared aetiology for hyperactivity–impulsivity and inattention as measured by both parent and teacher ratings, in agreement with previous findings on the aetiology of the two symptom dimensions of ADHD.

.....

Behav Brain Funct. 2011;7.

ALTERED TRYPTOPHAN AND ALANINE TRANSPORT IN FIBROBLASTS FROM BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): AN IN VITRO STUDY.

Johansson J, Landgren M, Fernell E, et al.

Background: The catecholaminergic and serotonergic neurotransmitter systems are implicated in the pathophysiology of attention-deficit/hyperactivity disorder (ADHD). The amino acid tyrosine is the precursor for synthesis of the catecholamines dopamine and norepinephrine, while tryptophan is the precursor of serotonin. A disturbed transport of tyrosine, as well as other amino acids, has been found in a number of other psychiatric disorders, such as schizophrenia, bipolar disorder and autism, when using the fibroblast cell model. Hence, the aim of this study was to explore whether children with ADHD may have disturbed amino acid transport.

Methods: Fibroblast cells were cultured from skin biopsies obtained from 14 boys diagnosed with ADHD and from 13 matching boys without a diagnosis of a developmental disorder. Transport of the amino acids tyrosine, tryptophan and alanine across the cell membrane was measured by the cluster tray method. The kinetic parameters, maximal transport capacity (V_{max}) and affinity constant (K_m) were determined. Any difference between the two groups was analyzed by Student's unpaired t-test or the Mann Whitney U test.

Results: The ADHD group had significantly decreased V_{max} ($p = 0.039$) and K_m (increased affinity) ($p = 0.010$) of tryptophan transport in comparison to controls. They also had a significantly higher V_{max} of alanine transport ($p = 0.031$), but the K_m of alanine transport did not differ significantly. There were no significant differences in any of the kinetic parameters regarding tyrosine transport in fibroblasts for the ADHD group.

Conclusions: Tryptophan uses the same transport systems in both fibroblasts and at the blood brain barrier (BBB). Hence, a decreased transport capacity of tryptophan implies that less tryptophan is being transported across the BBB in the ADHD group. This could lead to deficient serotonin access in the brain that might cause disturbances in both the serotonergic and the catecholaminergic neurotransmitter systems, since these systems are highly interconnected. The physiological importance of an elevated transport capacity of alanine to the brain is not known to date.

.....

Biol Psychiatry. 2011.

DIMENSIONAL BRAIN-BEHAVIOR RELATIONSHIPS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Chabernaud C, Mennes M, Kelly C, et al.

Background: Emerging neuroscientific and genetic findings emphasize the dimensional rather than the categorical aspects of psychiatric disorders. However, the integration of dimensional approaches within the current categorical diagnostic framework remains unclear. Here, we used resting state functional magnetic resonance imaging to examine whether dimensional measures of psychiatric symptomatology capture brain-behavior relationships unaccounted for by categorical diagnoses. Additionally, we examined whether dimensional brain-behavior relationships are modified by the presence of a categorically defined illness, attention-deficit/hyperactivity disorder (ADHD).

Methods: Resting state functional magnetic resonance imaging scans were collected from 37 typically developing children (aged 10.2 (plus or minus) 2; 21 female subjects) and 37 children meeting DSM-IV

Text Revision criteria for ADHD (9.7 (plus or minus) 2; 11 female subjects). Parent-rated Child Behavior Checklist Externalizing and Internalizing scores served as dimensional measures in our analyses of default network (DN) resting state functional connectivity (RSFC).

Results: Regardless of diagnosis, we observed several significant relationships between DN RSFC and both internalizing and externalizing scores. Increased internalizing scores were associated with stronger positive intra-DN RSFC, while increased externalizing scores were associated with reduced negative RSFC between DN and task-positive regions such as dorsal anterior cingulate cortex. Several of these brain-behavior relationships differed depending on the categorical presence of ADHD.

Conclusions: Our findings suggest that while categorical diagnostic boundaries provide an inadequate basis for understanding the pathophysiology of psychiatric disorders, psychiatric illness cannot be viewed simply as an extreme of typical neural or behavioral function. Efforts to understand the neural underpinnings of psychiatric illness should incorporate both categorical and dimensional clinical assessments.

.....

BMC Psychiatry. 2011;11.

ADHD IN ADOLESCENTS WITH BORDERLINE PERSONALITY DISORDER.

Speranza M, Revah-Levy A, Cortese S, et al.

Background: The aims of this study were to assess the prevalence of a comorbid Attention Deficit Hyperactivity Disorder (ADHD) diagnosis in Borderline Personality Disorder (BPD), and its impact on the clinical presentation of BPD in adolescents, and to determine which type of impulsivity specifically characterizes adolescents with BPD-ADHD.

Methods: ADHD diagnoses were sought in a sample of 85 DSM-IV BPD adolescents drawn from the EURNET BPD. Axis-I and -II disorders were determined with the K-SADS-PL and the SIDP-IV, respectively. Impulsivity was assessed with the BIS-11.

Results: 11% (N = 9) of BPD participants had a current ADHD diagnosis. BPD-ADHD adolescents showed higher prevalence of Disruptive disorders ($\chi^2 = 9.09$, $p = 0.01$) and a non-significant trend for a higher prevalence of other cluster B personality disorders ($\chi^2 = 2.70$, $p = 0.08$). Regression analyses revealed a significant association between Attentional/Cognitive impulsivity scores and ADHD (Wald $Z = 6.69$; $p = 0.01$; Exp(B) = 2.02, CI 95% 1.19-3.45).

Conclusions: Comorbid ADHD influences the clinical presentation of adolescents with BPD and is associated with higher rates of disruptive disorders, with a trend towards a greater likelihood of cluster B personality disorders and with higher levels of impulsivity, especially of the attentional/cognitive type. A subgroup of BPD patients may exhibit developmentally driven impairments of the inhibitory system persisting since childhood. Specific interventions should be recommended for this subsample of BPD adolescents.

.....

Chronobiology International. 2011 Aug;28:630-37.

SALIVARY MELATONIN RHYTHM AS A MARKER OF THE CIRCADIAN SYSTEM IN HEALTHY CHILDREN AND THOSE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Nováková M, Paclt I, Ptáček R, et al.

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood. Problems with sleep structure, efficiency, and timing have been reported in some, but not all, studies on ADHD children. As the sleep-wake cycle belongs to circadian rhythms, the timekeeping circadian system might be involved in ADHD. To assess whether the circadian system of ADHD children differs from that of controls, the rhythm of the pineal hormone melatonin was used as a reliable marker of the system. Saliva from 34 ADHD and 43 control 6- to 12-yr-old children was sampled at 2-h intervals throughout the entire 24-h cycle, and the melatonin profiles of the ADHD and control children were compared. The nocturnal melatonin peaks of the ADHD and control group did not differ significantly. The high nocturnal interindividual variability of the peaks seen in adulthood was present already in the studied children. The 24-h melatonin profiles of all the ADHD subjects did not differ significantly from those of the control

subjects. Categorization of subjects according to age, into groups of 6- to 7-yr-old (9 ADHD, 5 control), 8- to 9-yr-old (16 ADHD, 26 control), and 10- to 12-yr-old (9 ADHD, 12 control) children, revealed significant differences between the ADHD and control group in the melatonin rhythm waveform, but not in nocturnal melatonin peaks; the peaks were about the same in both groups and did not change significantly with increasing age. In the oldest, but not in the younger, children, the melatonin signal duration in the ADHD group was shorter than in the control group. The difference might be due to the fact that whereas in the control group both the evening melatonin onset and the morning offset phase delayed in the oldest children relative to those in the youngest children, in the ADHD group only the onset, but not the offset, phase delayed with increasing age. The data may indicate subtle differences between the circadian system of ADHD and control children during development.

Clin Genet. 2010;78:98.

THE ROLE OF MTHFR GENE POLYMORPHISMS IN ETIOLOGY OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD).

Gokce C, Kocak N, Ozen F.

Introduction: Attention-Deficit Hyperactivity Disorder (ADHD) is a common childhood neurobehavioural disorder defined by symptoms of developmentally inappropriate inattention, impulsivity and hyperactivity. A recent meta-analysis estimated the worldwide prevalence of ADHD to be 5.29% (1), making it the most prevalent psychiatric disorder of childhood. Although the exact aetiology of ADHD has not been determined, the related factors include familial and hereditary factors, prenatal or perinatal factors, chemotoxic factors, sociopsychological stress, structural and functional abnormalities of the brain, and developmental neurobiological factors in the regions of the brain related to ADHD. Folates seem to be of fundamental importance in brain growth, differentiation, development, repair, mood, cognition, and ageing. Neuropsychological studies have found general and specific impairments of intellectual function-including attention, episodic and visuospatial memory, and abstract reasoning-that were attributed to folate deficiency. The methylenetetrahydrofolate reductase (MTHFR) gene polymorphism is associated with a reduction in the bioavailability of folate and folate metabolites and nullmimicsnull low dietary folate intake. Therefore, we aimed to investigate the role of MTHFR gene polymorphisms in etiology of ADHD.

Material and methods: Forty patients with ADHD and 30 healthy volunteers were included in the study. A semi-structured diagnostic interview designed to assess current and past episodes of psychopathology in children and adolescent according to DSM-IV (and DSM-III-R) criteria, administered to clinically diagnosed patients with ADHD and their parents for verification of the diagnosis. Genomic DNA of patients and controls was isolated from peripheral blood samples using the QIAamp DNA Blood Mini Kit (Qiagen, Valencia, CA, USA). The PCR products for the base pair 677 and 1298 mutations underwent restriction enzyme digestion. PCR products for each base pair (677 and 1298) were loaded onto 2% or 3% ultra-pure agarose gel.

Results: There were no statistically significant differences in genotype distributions of the C677T alleles between the ADHD and control groups ($p = 0,678$). The genotypic pattern of the distributions of the A1298C alleles was different between the ADHD patients and the controls ($p = 0,033$).

Compr Psychiatry. 2011;52:644-49.

IS THERE A RELATIONSHIP BETWEEN ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND MANIC SYMPTOMS AMONG CHILDREN WITH MENTAL RETARDATION OF UNKNOWN ETIOLOGY?

Fidan T, Kirpinar I, Oral M, et al.

Mental retardation (MR) is common and lifelong. In children and adolescents with MR, the rate of attention deficit/hyperactivity disorder (ADHD) and bipolar disorder is higher than that in the general population. However, there are no previous sufficient data that exist in establishing a relationship between ADHD and manic symptoms. The aim of the present study was to examine the relationship between manic symptoms and ADHD as well as oppositional-defiant disorder (ODD) and conduct disorder (CD) in children with MR of unknown etiology (MR-UE). A total of 167 children with MR-UE attending a rehabilitation and training

school in Erzurum, Turkey, were included in the study. We administered the Child Disruptive Behavior Screening and Rating Scale related to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition and the Young Mania Rating Scale-Parent Version (P-YMRS) to parents. The age range of children and adolescents with MR-UE was between 5 and 21 years, with a mean age of 11.13 (plus or minus) 3.75 years. In total, 5.8% of children and adolescents with MR-UE showed a border intelligence quotient (IQ), with 58.4% having a mild IQ, 29.2% having a moderate IQ, and 6.6% having severe IQ. According to the Child Disruptive Behavior Screening and Rating Scale related to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, 40.1% of children and adolescents with MR-UE had inattention, 19.9% had hyperactivity, 28.7% had ODD, and 13.3% had CD. A total of 7.2% of the children and adolescents with MR-UE had probable mania, and 1.8% had mania according to Young Mania Rating Scale-Parent Version. A positive correlation existed between the mean scores of Young Mania Rating Scale-Parent Version and the mean scores of inattention, hyperactivity, ODD, and CD ($P = .000$). Hyperactivity and ODD were predictors of being manic/probably manic. Diagnosing psychiatric disorders in children and adolescents with MR-UE is difficult but essential for better functioning. Manic symptoms and disruptive behaviors as well as ADHD symptoms were prevalent among children and adolescents with MR-UE and hyperactivity, and oppositional-defiant symptoms were predictors of manic symptoms in these patients.

.....

Curr Med Res Opin. 2011;27:45-52.

EFFECT OF ATOMOXETINE ON TANNER STAGE SEXUAL DEVELOPMENT IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: 18-MONTH RESULTS FROM A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL.

Trzepacz PT, Spencer TJ, Zhang S, et al.

Objective: To determine the effects of long-term atomoxetine treatment on sexual development in children and adolescents with attention-deficit/ hyperactivity disorder (ADHD) as compared with placebo and with a national US survey in non-Hispanic white children and adolescents.

Methods: This double-blind, placebo-controlled, relapse prevention, multicenter trial was conducted in pediatric patients (615 years) with DSM-IV diagnosed ADHD and lasting for ~18 months. All patients received 10 weeks of open-label atomoxetine treatment (0.51.8mg/kg/day). Patients responding in the last 2 weeks of treatment were randomized to double-blind treatment with either placebo or atomoxetine for up to 9 months, after which atomoxetine patients were re-randomized to either continued atomoxetine treatment or to placebo for up to another 6 months. Patients randomized to placebo at first randomization remained on placebo. The Tanner stage was assessed by the investigator at baseline and at approximately 6, 12, and 18 months, and the rate of sexual development (change in the Tanner stage) was compared between treatment groups.

Results: No statistically significant differences were observed between treatment groups either in sexual development (mean time, in days, to the first Tanner stage change: atomoxetine, 464.3(plus or minus)23.0; placebo, 433.1(plus or minus)14.4; $p=0.33$) or in the duration of treatment exposure (atomoxetine, 315.3 days; placebo, 315.1 days; $p=0.90$). Similar proportions of patients had at least one Tanner stage increase (atomoxetine: 27.1%; placebo: 31.9%; $p=0.39$). Proportions of patients in each baseline Tanner stage group moving to higher stages were not statistically significantly different ($p=0.88$, $p=0.18$, $p>0.99$, $p=0.68$ for baseline Tanner stages 14, respectively). The puberty onset age was similar across treatment groups and consistent with US normative data.

Conclusions: Long-term atomoxetine treatment was not associated with any appreciable impact on or delay in sexual maturation in children with ADHD compared with US normative data.

Limitations: Study limitations include the relatively short duration of exposure to atomoxetine treatment, and the fact that half of the patients had been previously treated with stimulants. In addition, the Tanner stage data were collected as a secondary measure.

Clinical trial registration: Trial was completed prior to the requirement to post trials at initiation and therefore does not have a registration number.

.....

Curr Med Res Opin. 2011;27:35-44.

EFFECT OF TRANSITIONING FROM EXTENDED-RELEASE METHYLPHENIDATE ONTO OSMOTIC, CONTROLLED-RELEASE METHYLPHENIDATE IN CHILDREN/ADOLESCENTS WITH ADHD: RESULTS OF A 3-MONTH NON-INTERVENTIONAL STUDY.

Wolff C, Alfred A, Lindermiller A, et al.

Background: To explore the clinical outcomes of children/adolescents with ADHD who transitioned from extended-release methylphenidate (ER MPH, Medikinet Retard*) to osmotic release oral system (OROS) MPH (Concerta(dagger)). *Medikinet Retard is a registered trade name of Medice, Bad Iserlohn, Germany. (dagger)Concerta is a registered trade name of JanssenCilag GmbH, Neuss, Germany.

Methods: This prospective, non-interventional study included patients aged 6 to 18 years with a confirmed diagnosis of ADHD who experienced insufficient clinical response and/or poor tolerability on ER MPH. Patients transitioned onto OROS MPH and were followed for 12 weeks. Symptoms, functional outcome, health-related quality of life, safety and tolerability were assessed.

Results: 180 patients were included in the intention-to-treat analysis. The mean ER MPH dose before switching was 28.2mg/day; mean OROS MPH starting dose was 38.1mg/day, increasing to 41.2mg/day at the final visit. Mean treatment duration was 79.49(plus or minus)24.22 days (median 85; range 7136). Several symptomatic and functional outcomes under OROS MPH treatment changed from baseline and included the Conners' Parent Rating Scale (CPRS;-11.7(plus or minus)11.3; $p<0.0001$), C-GAS (12.3(plus or minus)15.2; $p<0.0001$) and ILC-LQ0-28 (parents' rating 2.9(plus or minus)4.3 and patients' rating 2.8(plus or minus)3.8; both $p<0.0001$). Improvements in social interactions, playing with other children, doing household chores, or school homework, going to bed, and behavior towards visitors/at visits were noted ($p<0.0001$). Approximately 40% of patients reported better sleep quality and appetite ($p<0.0001$), and 72.8% expressed satisfaction with OROS MPH therapy compared to previous ER MPH. OROS MPH was well tolerated; the most common AEs after switching, with an incidence $>2\%$ and possibly related to therapy, were involuntary muscle contractions (tics; 8.9%), insomnia (7.2%) and anorexia (5.0%). No relevant changes in body weight or vital signs were observed. Three patients reported four serious AEs, but none were considered related to OROS MPH. Limitations included those associated with the uncontrolled, open-label design, possible inclusion bias and non-validation of the CPRS in a German population.

Conclusions: Transitioning onto OROS MPH improved functionality, symptom control and decreased burden of disease in patients with ADHD who had insufficient response to, and/or poor tolerability of ER MPH. Similarly, care givers benefited from patients' treatment and reported significant reduction in their burden of disease and improvement of their quality of life upon the child's transition onto OROS MPH.

.....

Curr Med Res Opin. 2011;27:53-62.

TREATMENT OUTCOMES WITH METHYLPHENIDATE FORMULATIONS AMONG PATIENTS WITH ADHD: RETROSPECTIVE CLAIMS ANALYSIS OF A MANAGED CARE POPULATION.

Hodgkins P, Sasane R, Christensen L, et al.

Objective: Describe treatment patterns, resource use, and predictors of methylphenidate (MPH) switch among children (612 years), adolescents (1317 years), and adults (a(per mille)(yen) 18 years) with attention-deficit/ hyperactivity disorder (ADHD).

Methods: This retrospective U.S. managed care database study used medical, pharmacy, and enrollment data to examine treatment patterns among patients with a(per mille)(yen) 1 ADHD diagnosis code (ICD-9 314.00-314.9), MPH pharmacy claims during 01/01/200409/30/2006, and no ADHD pharmacy claims in prior 6 months. Patients were followed for 1 year for dosage change, switch (change to non-MPH treatment), augmentation, persistence (number days on index medication) and adherence (days supplied/days persistent). End points were assessed by age group and MPH formulation. Cox proportional hazards modeling was conducted to determine predictors of MPH switch.

Results: Among 23,860 MPH users, 51.4% had a dosing change, 14% switched to a non-MPH agent, and 4% augmented MPH therapy. Among those prescribed long-acting (LA) MPH (N=14,681), switching rates were 14% for children, 13% for adolescents, and 16% for adults. Augmentation rates for LA MPH were $<5\%$. Overall, 53% of patients were adherent with mean persistence of 219 days. For the subgroup of patients prescribed LA MPH (n=14,681), adherence ranged from 49% (adolescents) to 59% (children);

persistence varied between 183 days (adults) to 256 days (children). During the 1-year follow-up, office/clinic visits were the major driver of health care resource use in MPH patients (mean 9.7 visits/patient). Patients with psychiatric comorbidity utilized significantly greater services. Predictors of MPH switch included psychiatric comorbidity (hazards ratio [HR] 1.37; 95% confidence interval [CI]=1.261.48; $p<0.0001$) and specialty prescribers (HR 1.19, 95% CI=1.041.35; $p=0.011$). Potential limitations of this study include use of claims data for definition of drug usage; inclusion of medications approved for use in ADHD; assessment of switching that may not have captured short-term augmentation; absence of economic, clinical and other variables from the claims dataset that may have influenced treatment selection, and outcomes. The 6-month baseline period to determine newly treated patients may not guarantee exclusion of all previously treated patients who restart therapy after an extended period.

Conclusions: Children exhibited the highest persistence of MPH users. ADHD patients on MPH therapy with a psychiatric comorbidity may require additional follow-up to help improve adherence and reduce health care resource use.

.....

Curr Med Res Opin. 2011;27:13-22.

ADHD MEDICATION USE, ADHERENCE, PERSISTENCE AND COST AMONG TEXAS MEDICAID CHILDREN .

Barner JC, Khoza S, Oladapo A.

Objectives: (1) Describe ADHD medication use, adherence and persistence. (2) Determine factors (e.g., medication type, demographics, concomitant medication use) associated with ADHD medication adherence and persistence. (3) Compare ADHD medication costs.

Methods: Continuously enrolled Texas Medicaid children (318 years) with a(per mille)(yen) 2 ADHD prescription claims (July 2002December 2008) were included. Prescription claims were grouped by medication type (i.e., immediate-release, extended-release, prodrug, non-stimulant); medication class (i.e., stimulant, non-stimulant); and duration of action (i.e., long-acting, short-acting). Adherence, using medication possession ratio, was measured continuously and dichotomously (80% cut-off). Persistence was days of continuous therapy without a 30-day gap and medication costs were reimbursement amount paid to dispensing pharmacies.

Results: The study sample ($n=62,789$) was primarily 612 years (61.7%) and male (69.2%). The majority of the subjects were prescribed extended-release agents (70.3%), stimulant agents (86.4%), and long-acting agents (84.5%). Adherence and persistence (adherence mean(plus or minus)SD; adherence dichotomous; persistence mean(plus or minus)SD) varied among medication type and was highest for non-stimulants (52.5(plus or minus)30.9; 25.8%; 153.3(plus or minus)124.3), followed by extended-release stimulants (52.1(plus or minus)30.2; 24.1%; 143.7(plus or minus)120.8), prodrug stimulants (47.6(plus or minus)30.9; 21.1%; 113.3(plus or minus)100.5) and immediate-release stimulants (37.2(plus or minus)27.1; 9.8%; 95.4(plus or minus)92.6). Logistic regression showed immediate-release stimulant users were 67% less adherent than non-stimulant users ($p<0.0001$) and linear regression showed immediate-release, extended-release and long-acting users ($p<0.0001$) were significantly less persistent than non-stimulant users. Females, increase in total number of medications, and comorbid medications were associated with better adherence and persistence. Non-stimulant agents (\$\$4.04(plus or minus)\$\$2.15) had the highest mean medication cost per patient per day and immediate-release stimulants had the lowest (\$\$1.24(plus or minus)\$\$0.97).

Conclusions: ADHD medication adherence and persistence was suboptimal. Although there was no difference in adherence between long-acting stimulant and non-stimulant users, non-stimulant users were more persistent compared to stimulant users. This study was limited due to the use of retrospective prescription claims data, which cannot capture actual patient use patterns, ICD-9 diagnoses, family history and support, or side effect profiles. Because ADHD can be effectively treated with pharmacotherapy, providers should be proactive in identifying patients with poor adherence and intervene to address barriers to medication adherence and persistence.

.....

Developmental Medicine & Child Neurology. 2011 Jul;53:630-35.

HOW DOES EXERCISE BENEFIT PERFORMANCE ON COGNITIVE TESTS IN PRIMARY-SCHOOL PUPILS?

Hill LJB, Williams JHG, Aucott L, et al.

Aim: We have previously demonstrated improved cognitive performance after a classroom-based exercise regime. In this study, we examined the reproducibility of this effect in a more socio-economically diverse sample and also investigated whether cognitive benefits of exercise were moderated by body mass index (BMI) or symptoms of attention-deficit-hyperactivity disorder (ADHD).

Method: A crossover design trial (2 wks in duration) randomized 552 children (mean age 9y 8mo, SD 1y 2mo; range 8-12y) by their school into two counterbalanced groups. Children were eligible to participate provided that they did not receive any additional support. One group received a classroom-based programme of physical exercise on week 1 and then no programme on week 2, and this order was reversed for the other group. Each week, all participants completed a cognitive test battery that was delivered in one part per day at the end of each school day.

Results: On the cognitive tests, a significant interaction between counterbalance group and exercise was observed ($p < 0.001$). Benefits occurred only for participants who exercised during the second week (mean improvement mean 3.85, standard error 1.39). Although test scores were affected by age, sex, and level of ADHD symptoms, the effect of exercise was not moderated by either these factors or BMI.

Interpretation: Exercise interventions have a positive effect (with variable magnitude) on cognitive performance, possibly by facilitating practice effects. These effects are not moderated by sex, ADHD symptom level, or BMI.

.....

Drug Alcohol Depend. 2011;118:470-74.

INTRAUTERINE CANNABIS EXPOSURE LEADS TO MORE AGGRESSIVE BEHAVIOR AND ATTENTION PROBLEMS IN 18-MONTH-OLD GIRLS.

Marroun HE, Hudziak JJ, Tiemeier H, et al.

Background: The development of the fetal endocannabinoid receptor system may be vulnerable to maternal cannabis use during pregnancy and may produce long-term consequences in children. In this study, we aimed to determine the relationship between gestational cannabis use and childhood attention problems and aggressive behavior.

Methods: Using a large general population birth cohort, we examined the associations between parental prenatal cannabis and tobacco use and childhood behavior problems at 18 months measured using the Child Behavior Checklist in $N = 4077$ children. Substance use was measured in early pregnancy.

Results: Linear regression analyses demonstrated that gestational exposure to cannabis is associated with behavioral problems in early childhood but only in girls and only in the area of increased aggressive behavior ($B = 2.02$; 95% CI: 0.30-3.73; $p = 0.02$) and attention problems ($B = 1.04$; 95% CI: 0.46-1.62; $p < 0.001$). Furthermore, this study showed that long-term (but not short term) tobacco exposure was associated with behavioral problems in girls ($B = 1.16$; 95% CI: 0.20-2.12; $p = 0.02$). There was no association between cannabis use of the father and child behavior problems.

Conclusions: Our results suggest that intrauterine exposure to cannabis is associated with an increased risk for aggressive behavior and attention problems as early as 18 months of age in girls, but not boys. Further research is needed to explore the association between prenatal cannabis exposure and child behavior at later ages. Our data support educating future mothers about the risk to their babies should they smoke cannabis during pregnancy.

.....

Environ Health Perspect. 2011;119:1466-71.

SERUM PERFLUORINATED COMPOUND CONCENTRATION AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN 5-18 YEARS OF AGE.

Stein CR, Savitz DA.

Background: Perfluorinated compounds (PFCs) are persistent environmental pollutants. Toxicology studies demonstrate the potential for perfluorooctanoic acid (PFOA) and other PFCs to affect human

growth and development. Attention deficit/hyperactivity disorder (ADHD) is a developmental disorder with suspected environmental and genetic etiology. Objectives: We examined the cross-sectional association between serum PFC concentration and parent or self-report of doctor-diagnosed ADHD with and without current ADHD medication.

Methods: We used data from the C8 Health Project, a 2005-2006 survey in a Mid-Ohio Valley community highly exposed to PFOA through contaminated drinking water, to study non-Hispanic white children 5-18 years of age. Logistic regression models were adjusted for age and sex.

Results: Of the 10,546 eligible children, 12.4% reported ADHD and 5.1% reported ADHD plus ADHD medication use. We observed an inverted J-shaped association between PFOA and ADHD, with a small increase in prevalence for the second quartile of exposure compared with the lowest, and a decrease for the highest versus lowest quartile. The prevalence of ADHD plus medication increased with perfluorohexane sulfonate (PFHxS) levels, with an adjusted odds ratio of 1.59 (95% confidence interval, 1.21-2.08) comparing the highest quartile of exposure to the lowest. We observed a modest association between perfluorooctane sulfonate and ADHD with medication.

Conclusions: The most notable finding for PFOA and ADHD, a reduction in prevalence at the highest exposure level, is unlikely to be causal, perhaps reflecting a spurious finding related to the geographic determination of PFOA exposure in this population or to unmeasured behavioral or physiologic correlates of exposure and outcome. Possible positive associations between other PFCs and ADHD, particularly PFHxS, warrant continued investigation.

.....

Eur Child Adolesc Psychiatry. 2011;1-10.

RISK FACTORS OF AUTISTIC SYMPTOMS IN CHILDREN WITH ADHD.

Kroger A, Hanig S, Seitz C, et al.

Autistic symptoms are frequently observed in children with attention-deficit/hyperactivity disorder (ADHD), but their etiology remains unclear. The main aim of this study was to describe risk factors for increased autistic symptoms in children with ADHD without an autism or autism-spectrum diagnosis. Comorbid psychiatric disorders, developmental delay, current medication, prenatal biological and postnatal psychosocial risk factors as well as parental autistic traits were assessed in 205 children with ADHD. Linear regression models identified maternal autistic traits, current familial risk factors and hyperactive symptoms as predictors of autistic symptoms in children with ADHD. Findings are indicative of possible genetic as well as environmental risk factors mediating autistic symptoms in children with ADHD. An additional validity analysis by ROC, area under the curve (AUC), suggested a cut-off of 11 to differentiate between ADHD and high-functioning ASD by the Social Communication Questionnaire (SCQ).

.....

Eur Psychiatry. 2011 Sep;26:370-74.

TIC DISORDERS: ADMINISTRATIVE PREVALENCE AND CO-OCCURRENCE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN A GERMAN COMMUNITY SAMPLE.

Schlander M, Schwarz O, Rothenberger A, et al.

Coexistence of tics and attention-deficit/hyperactivity disorder (ADHD) has important clinical and scientific implications. Existing data on the co-occurrence of tic disorders, Tourette Syndrome (TS), and ADHD are largely derived from small-scale studies in selected samples and therefore heterogeneous. The Nordbaden project captures the complete outpatient claims data of more than 2.2 million persons, representing 82% of the regional population in 2003. Based upon the number of diagnosed cases of tic disorders, TS, and ADHD, we determined 12-months administrative prevalence rates as well as rates of co-occurrence. Both tic disorders and ADHD were diagnosed most often in the age group 7–12 years (any tic disorder: 0.8%; ADHD: 5.0%). With increasing age, the administrative prevalence difference in favor of males disappeared, with tic disorders being somewhat more frequently reported in females than males in the age groups above 30 years. The highest rate of ADHD co-occurring with tic disorders was found in adolescents (age 13–18 years, 15.1%). Tic disorders were observed in 2.3% of patients with ADHD. Administrative prevalence rates of tic disorders and TS were substantially lower compared to rates found in community-based

epidemiological studies, suggesting that a large number of cases remain undetected and untreated under present conditions of routine outpatient care.

Int Clin Psychopharmacol. 2011;26:e37.

THE ABNORMAL BRAIN BLOOD PERFUSION AND IMPAIRED FUNCTIONS IN ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER CO MORBID BIPOLAR DISORDER.

Yeh CB, Lo MC, Chang CJ, et al.

Objective: Co morbid bipolar disorder (BD) symptoms in adolescents with attention deficit hyperactivity disorder (ADHD) interfere with early recognition of ADHD. Our aim, was to identify regional cerebral blood flow (rCBF) patterns specifically associated with these symptoms and the impact of these symptoms on adolescents with ADHD.

Methods: Questionnaires were completed and interviews were carried out using the Kiddie-Schedule for Affective Disorders and Schizophrenia-epidemiology version (K- SADS-E) in 39 ADHD patients, who were then divided into a group with co morbid bipolar disorder (ADHD + BD, N = 14) and a group with ADHD only (N = 25). Each subject underwent single photon emission computed tomography (SPECT) using technetium-99 m ethyl cysteinate dimer (99mTc-ECD), and between-group differences in rCBF were evaluated using the statistical parametric mapping (SPM99) analysis software package.

Results: The ADHD +BD group had decreased blood perfusion in the right dorsolateral prefrontal lobe, right ventromedial prefrontal lobe, right hypothalamus, and increased blood perfusion in the left ventral medial pre-frontal, bilateral superior frontal lobe, premotor cortex, and supplementary motor area, more severe ADHD symptoms, but equally severe depressive or anxiety symptoms.

Conclusion: Our findings help physicians to recognize the underlying psychopathology (cognitive deficit) earlier and provide treatment sooner, and describe the impact of comorbid bipolar disorder on adolescents with ADHD.

Int J Med Sci. 2011;8:523-28.

METHYLENETETRAHYDROFOLATE REDUCTASE GENE POLYMORPHISMS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Gokcen C, Kocak N, Pekgor A.

Objective: The purpose of this study was to evaluate the relationship between 5,10-methylenetetrahydrofolate reductase (MTHFR) polymorphisms and Attention Deficit Hyperactivity Disorder (ADHD) in a sample of Turkish children.

Study Design: MTHFR gene polymorphisms were assessed in 40 patients with ADHD and 30 healthy controls. Two mutations in the MTHFR gene were investigated using polymerase chain reactions and restriction fragment length polymorphisms.

Results: Although there were no statistically significant differences in genotype distributions of the C677T alleles between the ADHD and the control groups ($p=0,678$) but the genotypic pattern of the distributions of the A1298C alleles was different between the ADHD patients and the controls ($p=0,033$).

Conclusions: Preliminary data imply a possible relationship between A1298C MTHFR polymorphisms and the ADHD.

Isr Med Assoc J. 2011;13:530-33.

Iron deficiency in children with attention deficit hyperactivity disorder.

Lahat E, Heyman E, Livne A, et al.

Background: Several studies have suggested that iron deficiency may be related to the pathophysiology of attention deficit hyperactivity disorder (ADHD) due to the role of iron in the production of dopamine and

noradrenaline. Objectives: To evaluate the status of iron deficiency in ADHD children, using ferritin levels, a reliable measure of iron storage in body tissue, as an iron status marker, and to investigate a possible correlation between ferritin levels and the diagnosis of ADHD. Methods: The study group included 113 newly referred ADHD children aged 5-15 years (mean age 8.8 (plus or minus) 2.7). Results: Ferritin levels were below 20 ng/ml in 67 children (59%) and above 20 ng/ml in 46 (41%). There was a very low inverse statistical correlation between scores on Conners' Rating Scale and ferritin levels, probably without clinical significance. Conclusions: Our findings suggest that low iron stores may be related to ADHD pathophysiology; therefore, ferritin should be included in the overall evaluation of children with ADHD.

.....

Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2011 Oct;39:1025-34.

PREDICTORS OF PARENT-REPORTED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AGED 6–7 YEARS: A NATIONAL LONGITUDINAL STUDY.

Sciberras E, Ukoumunne OC, Efron D.

This study examined the prenatal, postnatal and demographic predictors of parent-reported attention-deficit/hyperactivity disorder (ADHD) in an Australian population-based sample. Participants were families participating in the Longitudinal Study of Australian Children. There were approximately even numbers of males (51%) and females (49%) in the sample. Predictors of parent-reported ADHD status at Wave 2 (children aged 6–7 years) which were measured at Wave 1 (children aged 4–5 years) included cigarette smoking and alcohol use during pregnancy (prenatal factors); maternal postnatal depression, intensive care at birth, birth weight, and gestation (postnatal factors); and child gender, primary caregiver education, income, family composition, and maternal age at childbirth (socio-demographic factors). We found that male gender, cigarette smoking during pregnancy, and maternal postnatal depression were the only significant predictors (at the 5% level) of ADHD in the adjusted analysis (N = 3,474). Our results are consistent with previous findings that male gender and cigarette smoking during pregnancy are risk factors for ADHD. In addition, we found that postnatal depression was predictive of parent-reported ADHD.

.....

Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2011 Oct;39:1059-71.

THE MODERATING ROLE OF VERBAL AGGRESSION ON THE RELATIONSHIP BETWEEN PARENTAL FEEDBACK AND PEER STATUS AMONG CHILDREN WITH ADHD.

Jack A, Mikami AY, Calhoun CD.

We examined associations between children's sociometric status and (a) observed parental feedback as well as (b) child aggression. Participants were 94 children ages 6–10 (64 male; 44 with ADHD) and their parents. Children's peer status, parental feedback to their children, and child aggression were all assessed during lab-based playgroups of four children and their parents. Parent criticism in front of the child's peers was associated with the child receiving more negative ("disliked") and fewer positive ("liked") nominations, but only for children who displayed aggression; this interaction applied almost exclusively to children with ADHD. Parent praise in front of peers was associated with fewer negative nominations when children displayed low levels of aggression, but more at higher levels. Additional analyses revealed that relationships did not exist in the full sample between privately-given parental feedback and children's peer status. Processes by which peers use overheard adult feedback to inform their assessments of children are discussed.

.....

Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2011 Oct;39:1073-83.

SEVERITY OF CHILDREN'S ADHD SYMPTOMS AND PARENTING STRESS: A MULTIPLE MEDIATION MODEL OF SELF-REGULATION.

Graziano PA, McNamara JP, Geffken GR, et al.

The goal of the current study was to determine the extent to which the perceived self-regulation deficits across behavioral, cognitive, and emotional domains seen in children with ADHD explain the association between the severity of ADHD symptoms and parenting stress. Participants for this study included 80 children (mean age = 10 years, 9 months) with a DSM-IV diagnosis of ADHD confirmed by a comprehensive clinical diagnostic assessment. Parents reported their own stress levels as well as the severity of their children's ADHD symptoms, aggression, emotional lability, and executive functioning difficulties. Results indicated that the severity of children's hyperactivity/impulsivity symptoms but not their inattention related to parenting stress. Multiple mediational analyses indicated that the association between hyperactivity/impulsivity and parenting stress was explained by children's perceived comorbid aggression levels, emotional lability, and executive functioning difficulties. No significant differences in the strength of the mediators were found. The current study provides initial data showing that the perceived impairments in children's self-regulation across emotional, cognitive, and behavioral domains are what parents report as stressful, not simply the severity of ADHD symptoms. Due to the cross-sectional nature of this study and shared variance from relying solely on parent report, it will be critical for future research to replicate our findings using longitudinal and multi-informant data such as teacher reports and standardized assessments.

Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2011 Oct;39:1047-57.

THE RELATION BETWEEN MATERNAL ADHD SYMPTOMS & IMPROVEMENT IN CHILD BEHAVIOR FOLLOWING BRIEF BEHAVIORAL PARENT TRAINING IS MEDIATED BY CHANGE IN NEGATIVE PARENTING.

Chronis-Tuscano A, O'Brien KA, Johnston C, et al.

This study examined the extent to which maternal attention-deficit/hyperactivity disorder (ADHD) symptoms predict improvement in child behavior following brief behavioral parent training. Change in parenting was examined as a potential mediator of the negative relationship between maternal ADHD symptoms and improvement in child behavior. Seventy mothers of 6–10 year old children with ADHD underwent a comprehensive assessment of adult ADHD prior to participating in an abbreviated parent training program. Before and after treatment, parenting was assessed via maternal reports and observations and child disruptive behavior was measured via maternal report. Controlling for pre-treatment levels, maternal ADHD symptomatology predicted post-treatment child disruptive behavior problems. The relation between maternal ADHD symptomatology and improvement in child behavior was mediated by change in observed maternal negative parenting. This study replicated findings linking maternal ADHD symptoms with attenuated child improvement following parent training, and is the first to demonstrate that negative parenting at least partially explains this relationship. Innovative approaches combining evidence-based treatment for adult ADHD with parent training may therefore be necessary for families in which both the mother and child have ADHD. Larger-scale studies using a full evidence-based parent training program are needed to replicate these findings.

Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2011 Oct;39:1035-45.

FRIENDSHIP AS PROTECTION FROM PEER VICTIMIZATION FOR GIRLS WITH AND WITHOUT ADHD.

Cardoos SL, Hinshaw SP.

The goal of this study was to examine the ability of friendship to moderate the association between behavioral risk and peer victimization for girls with attention-deficit/hyperactivity disorder (ADHD; $n = 140$) and comparison girls ($n = 88$) in a 5-week naturalistic summer camp setting. Participants were an ethnically

and socioeconomically diverse group of girls ages 6–12. Parents and teachers reported on pre-summer internalizing behavior, externalizing behavior, and social competence. Participants reported on friendships and peer victimization through a peer report measure at the summer camps; friendship was scored via mutual nominations. Pre-summer externalizing behavior, internalizing behavior, and low social competence predicted peer victimization at the summer camps. Friendship moderated the association between behavioral risk and victimization for the entire sample, such that the presence of at least one friend reduced the risk of victimization. Additional analyses suggested that girls with ADHD were no more or less protected by the presence of a friendship than were comparison girls. Finally, preliminary analyses suggested that girls having only friends with ADHD were not significantly less protected than girls with at least one comparison friend. Future directions and implications for intervention are discussed.

.....

Journal of Attention Disorders. 2011 Aug;15:499-505.

AN ASYMMETRIC STROOP/REVERSE-STROOP INTERFERENCE PHENOMENON IN ADHD.

Song Y, Hakoda Y.

Objective: To examine whether participants with ADHD showed a deficit in Stroop/reverse-Stroop interference by comparing them to non-ADHD participants.

Method: A group with ADHD, primarily inattentive type (n = 15), and a paired non-ADHD group (n = 15) completed the group version of the Stroop/reverse-Stroop test.

Results: Asymmetric interference was observed between the Stroop test and the reverse-Stroop test in ADHD participants, presenting evidence contrary to Barkley's behavioral inhibition model of ADHD in which response inhibition deficits pertained only to the ADHD-C subtype.

Conclusion: Participants with ADHD showed a control deficit in reverse-Stroop interference but not in Stroop interference.

.....

Journal of Attention Disorders. 2011 Aug;15:461-72.

WORKING MEMORY DEFICITS IN ADHD: THE CONTRIBUTION OF AGE, LEARNING/LANGUAGE DIFFICULTIES, AND TASK PARAMETERS.

Sowerby P, Seal S, Tripp G.

Objective: To further define the nature of working memory (WM) impairments in children with combined-type ADHD.

Method: A total of 40 Children with ADHD and an age and gender-matched control group (n = 40) completed two measures of visuo-spatial WM and two measures of verbal WM. The effects of age and learning/language difficulties on performance were evaluated.

Results: Children with ADHD obtained significantly lower scores than controls on measures of both visuo-spatial and verbal WM. The impairments in verbal WM were age related.

Conclusion: Children with ADHD exhibit impaired visuo-spatial WM performance. Younger (less than 8 years), but not older, children with ADHD demonstrate impairments in verbal WM. This latter result may explain the previously reported inconsistent performance of children with ADHD on verbal WM tasks. The importance of taking a developmental perspective in WM research is stressed.

.....

Journal of Attention Disorders. 2011 Aug;15:491-98.

EFFECT OF LISDEXAMFETAMINE DIMESYLATE ON SLEEP IN CHILDREN WITH ADHD.

Giblin JM, Strobel AL.

Objective: This study evaluated the potential effects of short-term treatment with lisdexamfetamine dimesylate (LDX) on both subjective and objective sleep characteristics in children aged 6 to 12 years (n = 24) with ADHD.

Method: Polysomnography (PSG) and actigraph measures as well as assessments of subjective sleep parameters were examined in children before and after treatment with either LDX or placebo in a randomized, double-blind, single-center, parallel-group study.

Results: There was no statistically significant increase in the primary endpoint of latency to persistent sleep (LPS) for the LDX-treated group compared to the placebo group. Secondary PSG or actigraph results generally supported primary endpoint results. Subjective sleep measure results indicated the possibility that responses are influenced by sleep hygiene counseling before and throughout the study.

Conclusions: In this pilot sleep study in children with ADHD, LDX did not appear to contribute to any sleep disturbances as measured by both objective and subjective sleep parameters. The sample used in this study was small, and the multifarious nature of findings in this study warranted that the study conclusions be interpreted cautiously and that further study is required focusing on the influence of LDX on sleep in larger samples of ADHD children.

Journal of Attention Disorders. 2011 Aug;15:516-24.

PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AND ASSOCIATED FEATURES AMONG CHILDREN IN FRANCE.

Lecendreux M, Konofal E, Faraone SV.

Background: Earlier studies point to the prevalence of attention deficit hyperactivity disorder (ADHD) to be similar around the world. There is, however, a wide variety in estimates. The prevalence of ADHD in youth has never been examined in France.

Method: Starting with 18 million telephone numbers, 7,912 numbers are randomly selected. Among the 4,186 eligible families, 1,012 (24.2%) are successfully recruited. A telephone interview is administered to all families about a child in the 6 to 12 age range. It covered family living situation, school performance, symptoms of ADHD, conduct disorder (CD), and oppositional-defiant disorder (ODD), and other features of ADHD.

Results: The prevalence of ADHD in France is between 3.5% and 5.6%. The population prevalence of treatment for ADHD is 3.5%. ADHD youth are more likely to be men than women, and, compared to non-ADHD children, ADHD children are more likely to have CD and ODD. Having ADHD is associated with a family history of the disorder. The ADHD youth are more likely to have had learning difficulties, to have repeated a grade, and to be functioning academically below grade level.

Conclusions: The epidemiology of ADHD in French children is similar to the epidemiology of ADHD in other countries. The disorder occurs in between 3.5% to 5.6% of youth and is more common among boys than among girls. The authors replicate the well-known association of ADHD with CD, ODD, and indices of school failure. The impact of ADHD symptoms on school performance highlights the importance of screening for such symptoms in schools.

Journal of Attention Disorders. 2011 Aug;15:473-84.

INFLUENCE OF ANXIETY ON THE SOCIAL FUNCTIONING OF CHILDREN WITH AND WITHOUT ADHD.

Mikami AY, Ransone ML, Calhoun CD.

Objective: This investigation examined the contribution of anxiety to the social functioning of children with and without ADHD.

Method: Participants were 62 children with ADHD (ages 6-10 years and 68% boys) and 62 age- and sex-matched comparison children. Children's social functioning was measured through parent and teacher reports, observations of social behaviors during a lab-based playgroup with previously unacquainted peers, and peer nominations during that lab-based playgroup.

Results: Anxiety symptoms incrementally predicted adult-informant reports of poorer social functioning after controlling for demographic covariates, ADHD status, and oppositional-defiant disorder (ODD) status. However, anxiety was not associated with peer nominations received at the playgroup. There were some indications that anxiety may have greater influence on the functioning of comparison children relative to

children with ADHD or ODD. Conclusion: Anxiety may contribute to the peer problems of children both with and without ADHD.

.....

Journal of Attention Disorders. 2011 Aug;15:485-90.

CO-OCCURRENCE OF ADHD AND HIGH IQ: A CASE SERIES EMPIRICAL STUDY.

Cordeiro ML, Farias AC, Cunha A, et al.

Objective: The validity of a diagnosis of ADHD in children with a high intelligence quotient (IQ) remains controversial. Using a multidisciplinary approach, rigorous diagnostic criteria, and worldwide-validated psychometric instruments, we identified a group of children attending public schools in southern Brazil for co-occurrence of high IQ and ADHD.

Method: Students attending public schools, in the first to fifth grades, were referred to our Research Center for behavioral and/ or learning difficulties. These children completed clinical, psychiatric, psychological, and pedagogical evaluations for assessment of IQ, ADHD, learning, and other emotional or behavioral disorders.

Results: Fifteen of the participants were identified to have a full-scale IQ = 120. Data show that 10 of these high-IQ children met the DSM-IV criteria diagnosis for ADHD combined type, 5 met criteria for current oppositional-defiant disorder, 2 had current major depression, and 2 had a learning disorder. Here we present the results as a case series.

Conclusion: Our data support the hypothesis that ADHD is a valid diagnosis in children with high IQs.

.....

Journal of Attention Disorders. 2011 Aug;15:506-15.

COEXISTING DISORDERS AND ACADEMIC ACHIEVEMENT AMONG CHILDREN WITH ADHD.

Barnard-Brak L, Sulak TN, Fearon DD.

Objective: ADHD is a commonly diagnosed neuropsychological disorder among school-aged children with reported high rates of coexisting or comorbid disorders. As ADHD has been associated with academic underachievement, the current study examines this association in view of the presence of coexisting disorders. The purpose of the current study is to examine the relationship between the presence of coexisting disorders and academic achievement among children with ADHD using a large, nationally representative, and community-based sample.

Method: To achieve this purpose, the presence of coexisting disorders with ADHD and academic achievement are examined across time utilizing latent growth models.

Results: Our results indicate an inverse relationship between the presence of coexisting disorders and academic achievement across time among children diagnosed with ADHD.

Conclusion: The authors conclude that practitioners must be concerned with the presence of coexisting disorders for children with ADHD with respect to academic achievement as well as other behavioral and psychological outcomes.

.....

Journal of Attention Disorders. 2011 Aug;15:439-51.

LONG-TERM TREATMENT OF ADHD WITH STIMULANTS: A LARGE OBSERVATIONAL STUDY OF REAL-LIFE PATIENTS.

Powell SG, Thomsen PH, Frydenberg M, et al.

Objective: To evaluate 410 real-life patients treated with stimulants and assessed systematically over several years.

Method: Naturalistic observational study. A database was compiled on the basis of a review of the medical charts of patients attending a specialized ADHD clinic.

Results: The diversity of ADHD patients was evident from the comorbidity, age at start, comedication, and treatment needs over time. Dosages corresponded to guidelines in most patients, but some needed higher

dosages or got along on lower dosages for long periods. Age at start and comorbidity influenced dosage, and dosage was associated to differential outcome groups.

Conclusion: The study findings underscored the diversity of ADHD patients and that individual factors should be taken into account when tailoring individual treatment schedules. Findings further showed that stimulant dosages are dynamic over time and depend on individual factors, that individual factors influence outcome, and that patients with ADHD should be individually monitored and stimulant dosages adjusted continuously.

J Child Neurol. 2011;26:1290-95.

DOWN SYNDROME AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Ekstein S, Glick B, Weill M, et al.

Clinicians might minimize the prevalence of behavioral disorders among mentally retarded people. Decreased attention, hyperactivity, and impulsivity are frequently reported in children with Down syndrome, yet the exact prevalence of attention-deficit/hyperactivity disorder (ADHD) has not been clearly estimated in this population. The objective of this study was to estimate the prevalence of ADHD in children with Down syndrome and to emphasize the possible relationship between ADHD symptoms and the level of mental retardation and common medical comorbidity. In this study, the prevalence of ADHD among Down syndrome children was very high, reaching 43.9%. No significant correlation was found between ADHD symptoms and the level of mental retardation, but significant correlation was found with ophthalmologic problems. We conclude that children with Down syndrome are at increased risk for ADHD. When evaluating children with Down syndrome for attention deficits, psychiatric comorbidity as well as medical problems should be carefully taken into consideration.

J Child Neurol. 2011;26:1296-302.

INCREASED REGIONAL FRACTIONAL ANISOTROPY IN HIGHLY SCREENED ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD).

Peterson DJ, Ryan M, Rimrodt SL, et al.

Diffusion tensor imaging data were collected at 3.0 Tesla from 16 children with attention-deficit hyperactivity disorder (ADHD) and 16 typically developing controls, ages 9 to 14 years. Fractional anisotropy images were calculated and normalized by linear transformation. Voxel-wise and atlas-based region-of-interest analyses were performed. Using voxel-wise analysis, fractional anisotropy was found to be significantly increased in the attention-deficit hyperactivity disorder group in the right superior frontal gyrus and posterior thalamic radiation, and left dorsal posterior cingulate gyrus, lingual gyrus, and parahippocampal gyrus. No regions showed significantly decreased fractional anisotropy in attention-deficit hyperactivity disorder. Region-of-interest analysis revealed increased fractional anisotropy in the left sagittal stratum, that is, white matter that connects the temporal lobe to distant cortical regions. Only fractional anisotropy in the left sagittal stratum was significantly associated with attention-deficit hyperactivity disorder symptom severity. Several recent studies have reported pathological increases in fractional anisotropy in other conditions, highlighting the relevance of diffusion tensor imaging in identifying atypical white matter structure associated with neurodevelopmental processes.

J Clin Exp Neuropsychol. 2011 Aug;33:805-19.

TRAUMATIC BRAIN INJURY AND SECONDARY ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS: THE EFFECT OF REWARD ON INHIBITORY CONTROL.

Sinopoli KJ, Schachar R, Dennis M.

Poor inhibitory control and abnormalities in responding to rewards are characteristic of the developmental or primary form of attention-deficit/hyperactivity disorder (P-ADHD). A secondary form of ADHD (S-ADHD)

may occur as a consequence of childhood traumatic brain injury (TBI), but the similarities and differences between these two forms of ADHD have not been well characterized. To address these issues, we studied two inhibitory control tasks under different reward conditions in four groups of children and adolescents: TBI who did not exhibit S-ADHD, TBI who did exhibit S-ADHD, P-ADHD, and healthy controls. Participants with TBI exhibited poor cancellation inhibition relative to controls. Although reward facilitated both cancellation and restraint inhibition similarly across groups, poor performance persisted in the P-ADHD group, and participants with S-ADHD exhibited a selective deficit in cancellation inhibition.

J Clin Exp Neuropsychol. 2011 Aug;33:753-64.

THE INFLUENCE OF WORKING MEMORY LOAD ON RESPONSE INHIBITION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER OR READING DISORDER.

Van De Voorde S, Roeyers H, Verté S, et al.

The aim of the present study was to examine the relationship between response inhibition and working memory in 8–12-year-old children with attention-deficit/hyperactivity disorder (ADHD; $n = 19$), reading disorder (RD; $n = 17$), ADHD + RD ($n = 21$), and control children ($n = 19$). For the first time a within-task methodology was used to study the combined effect of both executive functions on a common measure of task performance in two often comorbid childhood disorders, ADHD and RD. We found evidence of an interaction between both domains, suggesting that they rely on a common pool of resources. In addition, we found that children with ADHD or RD were not more seriously affected by the combined load of both executive functions than children without ADHD or RD.

Journal of Correctional Health Care. 2011 Jul;17:218-25.

STIMULANT USE UNDER A PRISON TREATMENT PROTOCOL FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Appelbaum KL.

Although stimulant medications are the mainstay of effective intervention for attention-deficit/hyperactivity disorder (ADHD), their use presents a daunting scenario for psychiatry, nursing, and custody staff in correctional settings, where reported prevalence rates range from 9% to 45%. The reported rates, however, may overestimate actual prevalence in general and need for treatment in particular. Under a monitored protocol that required documentation of history, diagnosis, lack of response to nonstimulant treatment, and significant functional impairment, less than 1% of male inmates in the Massachusetts state prison system met criteria for treatment with stimulants. Although this protocol did not attempt to determine overall ADHD prevalence rates, the relatively low number of inmates with compelling reasons for stimulant treatment may provide a more realistic idea of the likely consequences of allowing access to this intervention.

J Intellect Disabil Res. 2010;54:891.

NEUROPSYCHOLOGICAL ATTENTION SKILLS AND RELATED BEHAVIOURS IN ADULTS WITH TUBEROUS SCLEROSIS COMPLEX.

Tierney KM, McCartney DL, Serfontein JR, et al.

Background: Children with tuberous sclerosis complex (TSC) have significant deficits on neuropsychological attention tasks, particularly dual tasking and speed of processing measures. Very little is known about the attentional phenotype of adults with TSC. Here we investigate neuropsychological attentional skills and attention-related behaviours in daily life in adults with TSC.

Method: Adults with TSC who have global intelligence in the normal range and non-TSC control participants matched on age, gender and performance IQ were assessed using the Test of Everyday Attention for Children (TEA-Ch). Attention related behaviours in daily life were examined using the Attention-Deficit Scales for Adults (ADSA).

Results: No group differences were demonstrated on visual selective or auditory sustained attention tasks carried out alone. However, adults with TSC performed significantly worse when these tasks were combined in a cross-modal dual task condition. On the ADSA the TSC group had significantly elevated scores on the attention-focus/concentration, behaviour-disorganised activity, academic and emotive domains. Crossmodal dual task decrement scores were significantly correlated with these domains.

Conclusion: Normally intelligent adults with TSC have a significant ability correlated with a clear impact on attention-related behaviours in daily life. These findings, alongside findings from similar research with children, suggest that dual task deficits may be a consistent feature of the neuropsychological phenotype of TSC.

J Intellect Disabil Res. 2010;54:886.

PREVALENCE OF AUTISTIC SYMPTOMS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A CLINIC-BASED STUDY.

Mohiuddin S, Legrou R, Ghaziuddin M.

Background: Attention deficit hyperactivity disorder (ADHD), the most common child psychiatric disorder, is characterized by inattention, hyperactivity, and impulsivity. However, these symptoms are non-specific in nature and occur in a wide variety of disorders that can lead to diagnostic difficulties. One such disorder is autism. While studies have examined the occurrence of ADHD in children with autism, information is limited about the prevalence of autistic symptoms in children with ADHD. The purpose of this report is to examine this issue in a group of children referred to a specialist ADHD clinic.

Method: The study was conducted at a tertiary ADHD clinic for children and adolescents. Approval was obtained from the institutional review board for analyzing the collected data. Participants were referred by primary care doctors, school personnel, social agencies and parents. Each participant was examined by a PhD level Neuropsychologist, a Child and Adolescent Psychiatry Fellow, and a Board Certified Child Psychiatrist with over 20 years' experience. The following measures were used: Conner's Parent Rating Scale, Social Communication Questionnaire (SCQ) and Child Behavior Checklist (CBCL). A final diagnosis was made based on all the available information.

Results: Seventy-eight participants received a diagnosis of ADHD; nine (11.5%) of these received an additional diagnosis of an autistic spectrum disorder (ASD). None of these had previously been suspected of having an ASD or received a diagnosis of that disorder. The ADHD+ASD group was found to have a higher mean total score on the SCQ in contrast with the ADHD alone group (12.33 and 6.05 respectively; $p < .001$) and also scored higher on the CBCL social scores. Children with mixed ADHD+ASD had more ritualistic behaviours and social deficits than those with ADHD alone.

Conclusion: At least 10% of children referred to a specialist ADHD clinic had autistic symptoms. These children scored higher on the SCQ and on the social subscale of the CBCL. In addition, they had a history of ritualistic behaviours. These findings suggest that children referred for an evaluation of ADHD should be routinely screened for autism.

J Isfahan Med Sch. 2011;29:965-76.

COMPARISON OF THE EFFECTIVENESS OF DIFFERENT TREATMENT METHODS IN CHILDREN'S ATTENTION DEFICIT-HYPERACTIVITY DISORDERS.

Meftagh SD, Mohammadi N, Ghanizadeh A, et al.

Background: This study was designed to evaluate and compare the effectiveness of three treating methods; namely mother's behavioral education, Verbal self-instruction to the children, and Pharmacotherapy in children's attention deficit hyperactivity disorder (ADHD).

Methods: In this semi-experimental study, 51 elementary students with ADHD were randomly divided to three treatment groups including mothers' behavioral education, verbal self-instruction to the children, and control group. Moreover, 22 students with ADHD were selected among the patients referring to Hafez hospital and were put in pharmacotherapy group. Data collection tool was Child Symptoms Inventory (CSI-

4). All of the subjects were evaluated by CSI-4 before and after the intervention and also 2 months later, i.e. in follow up period.

Findings: The results show significant differences between the groups in mother's evaluation of attention deficit ($P = 0.04$), the severity of hyperactivity-impulsivity ($P = 0.005$), and the general/total severity of the symptoms of disorder ($P = 0.03$).

Conclusion: The most effective treatment for the severity of attention deficit in children is verbal selfinstruction. The severity of hyperactivity-impulsivity is best treated using mother's behavioral education. Considering the result obtained in the case of general severity of symptoms in children's ADHD, mother's behavior education and pharmacotherapy were the most effective and useful treatment methods.

.....

J Mental Health Policy Econ. 2011;14:137-47.

ECONOMIC OUTCOMES IN ADULTHOOD AND THEIR ASSOCIATIONS WITH ANTISOCIAL CONDUCT, ATTENTION DEFICIT AND ANXIETY PROBLEMS IN CHILDHOOD.

Knapp M, King D, Healey A, et al.

Background: Conduct disorder (antisocial conduct), attention deficit problems and anxiety in childhood have negative effects on individuals during their childhood, on their families, and often into adulthood. Aims of the Study: To quantify the connections between childhood antisocial conduct, attention deficit and anxiety, and some adulthood economic consequences.

Methods: Data from a British birth cohort study were examined for links between behavioural and emotional problems in childhood, and occupational status and earnings in adulthood, after adjusting for individual and family covariates.

Results: The effects of antisocial conduct on adult labour market outcomes were complex. Results for males with antisocial conduct at age 10 showed a higher probability of being unemployed at age 30 (after adjustment for other factors). However, males with antisocial conduct at age 10 had higher earnings than those without such behaviour, again after adjusting for other factors. There were no such differences for females with antisocial conduct. Attention deficit problems at age 10 were associated with lower employment rates, worse jobs, lower earnings if employed, and lower expected earnings overall - for both males and females. Anxiety problems were associated with lower earnings. Other childhood factors associated with worse adulthood economic outcomes included cognitive attainment, living in a disadvantaged neighbourhood, mother's educational qualifications, family income and being looked after by a local authority.

.....

J Psychiatr Res. 2011;45:1463-70.

EFFECTS OF METHYLPHENIDATE ON OLFACTION AND FRONTAL AND TEMPORAL BRAIN OXYGENATION IN CHILDREN WITH ADHD.

Schecklmann M, Schaldecker M, Aucktor S, et al.

Objective: Olfaction and attention-deficit/hyperactivity disorder (ADHD) are mediated by dopamine metabolism and fronto-temporal functioning converging in recent findings of increased olfactory sensitivity in children with ADHD modulated by methylphenidate (MPH) and altered frontal and temporal oxygenation in adults with ADHD.

Method: We investigated olfactory sensitivity, discrimination, and identification (Sniffin' Sticks) in 27 children and adolescents with ADHD under chronic MPH medication and after a wash-out period of at least 14 half-lives in balanced order and 22 controls comparable for handedness, age, and intelligence. In addition, inferior frontal and temporal oxygenation was measured by means of functional near-infrared spectroscopy (fNIRS) during the presentation of 2-phenylethanol. Group differences in regard to sex distribution were statistically controlled for by analysis of covariance.

Results: Patients did not differ from controls in any olfactory domain under treatment with MPH. Cessation of medication led to a significant increase in olfactory discrimination. Controls displayed typical inferior frontal and temporal brain activity in response to passive olfactory stimulation, while brain oxygenation was

diminished in the patient group when assessed without medication. Under medication ADHD patients showed a trend for a normalisation of brain activity in the temporal cortex.

Conclusions: The here reported effects of MPH cessation on olfactory discrimination and frontal and temporal oxygenation along with previous findings of increased olfactory sensitivity in medication-naïve ADHD children and its normalisation under chronic MPH treatment lead to the conclusion that MPH exerts differential chronic effects vs. acute cessation effects on altered olfactory function in ADHD. These effects are most probably mediated by modulation of the dopaminergic system.

J Psychopathol Behav Assess. 2011;1-10.

COMPARING FOUR METHODS OF INTEGRATING PARENT AND TEACHER SYMPTOM RATINGS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Shemmassian SK, Lee SS.

Although parents and teachers are valid informants in the assessment of childhood attention-deficit/hyperactivity disorder (ADHD), there is relatively little systematic research on how these ratings should be optimally combined. We compared four methods of ADHD assessment to determine how well they identified impaired children: (1) parent only, (2) teacher only, (3) parent or teacher ('or rule'), and (4) parent and teacher ('and rule'). We obtained parent and teacher ratings of ADHD from the Disruptive Behavior Disorder Rating Scale on 232 5- to 10-year-old children (69% male; 47% Caucasian) with ($n = 121$) and without ($n = 111$) ADHD. We used receiver operating characteristic curves (ROC) and seemingly unrelated regression analyses (SUR) to evaluate how accurately each method identified categorically- and dimensionally-defined measures of functional impairment. Parent ratings of ADHD optimally identified globally impaired children based on categorical and dimensional measures. However, teacher ratings of ADHD most accurately identified children who were negatively regarded by peers using categorical, but not dimensional, measures. No ADHD assessment method effectively identified children with academic difficulties. Although multiple informants are valuable in the assessment of ADHD, no single method was consistently superior in identifying impaired children across domains. We consider alternative assessment strategies in ADHD as well as other potential factors that may contribute to modest agreement among informants.

Journal of the American Academy of Child & Adolescent Psychiatry. 2011 Aug;50:e1-837.

ABNORMAL AMYGDALAR ACTIVATION AND CONNECTIVITY IN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Posner J, Nagel BJ, Maia TV, et al.

Objective: Emotional reactivity is one of the most disabling symptoms associated with attention-deficit/hyperactivity disorder (ADHD). We aimed to identify neural substrates associated with emotional reactivity and to assess the effects of stimulants on those substrates.

Method: We used functional magnetic resonance imaging (fMRI) to assess neural activity in adolescents with ($n = 15$) and without ($n = 15$) ADHD while they performed a task involving the subliminal presentation of fearful faces. Using dynamic causal modeling, we also examined the effective connectivity of two regions associated with emotional reactivity, i.e., the amygdala and the lateral prefrontal cortex (LPFC). The participants with ADHD underwent scanning both on and off stimulant medication in a counterbalanced fashion.

Results: During the task, we found that activity in the right amygdala was greater in adolescents with ADHD than in control subjects. In addition, in adolescents with ADHD, greater connectivity was detected between the amygdala and LPFC. Stimulants had a normalizing effect on both the activity in the right amygdala and the connectivity between the amygdala and LPFC.

Conclusions: Our findings demonstrate that in adolescents with ADHD, a neural substrate of fear processing is atypical, as is the connectivity between the amygdala and LPFC. These findings suggest possible neural substrates for the emotional reactivity that is often present in youths with ADHD, and provide putative neural targets for the development of novel therapeutic interventions for this condition.

J Am Acad Child Adolesc Psychiatry. 2011.

PARENTAL ATTENTION-DEFICIT/HYPERACTIVITY DISORDER PREDICTS CHILD AND PARENT OUTCOMES OF PARENTAL FRIENDSHIP COACHING TREATMENT.

Griggs MS, Mikami AY.

Objective: This study investigated the impact of parental attention-deficit/hyperactivity disorder (ADHD) symptoms on the peer relationships and parent-child interaction outcomes of children with ADHD among families completing a randomized controlled trial of parental friendship coaching (PFC) relative to control families.

Method: Participants were 62 children with ADHD (42 boys and 20 girls, 6 through 10 years old) and their parents. Approximately half of the families received PFC (a 3-month parent training intervention targeting the peer relationships of children with ADHD), and the remainder represented a no-treatment control group.

Results: Parental inattention predicted equivalent declines in children's peer acceptance in both treatment and control families. However, treatment amplified differences between parents with high versus low ADHD symptoms for some outcomes: Control families declined in functioning regardless of parents' symptom levels. However, high parental inattention predicted increased child peer rejection and high parental inattention and impulsivity predicted decreased parental facilitation among treated families (indicating reduced treatment response). Low parental symptoms among treated families were associated with improved functioning in these areas. For other outcomes, treatment attenuated differences between parents with high versus low ADHD symptoms: Among control parents, high parental impulsivity was associated with increasing criticism over time, whereas all treated parents showed reduced criticism regardless of symptom levels. Follow-up analyses indicated that the parents experiencing poor treatment response are likely those with clinical levels of ADHD symptoms.

Conclusions: Results underscore the need to consider parental ADHD in parent training treatments for children with ADHD.

J Tokyo Med Univ. 2011;69:374-81.

CLINICAL EFFECTS OF EXTENDED-RELEASE METHYLPHENIDATE IN 109 CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Ishida Y, Miyajima T, Morichi S, et al.

Background and aims: The basic methods of treatment for patients with attention-deficit/hyperactivity disorder (ADHD) include psychosocial and medical therapy-methylphenidate (MPH). The efficacy of immediate-release MPH (IR-MPH; Ritalin(registered trademark)) has been proved; however, this drug was banned in Japan since December 2007, because its abuse among adults became a social issue. Since then, the osmotic controlled-release oral system MPH (OROS-MPH ; Concerta(registered trademark)) was put on the market. We aimed to assess changes in ADHD clinical manifestations and frequency of OROS-MPH-induced side effects.

Methods: OROS-MPH was given to 109 ADHD children (96 boys, 13 girls, aged 7-16 years). To elucidate the effects of this drug, we calculated changes in scores on the ADHD Diagnostic and Statistical Manual of Mental disorders (DSM-IV) rating scale for children who continued intake of OROS-MPH for over 4 months and calculated the frequency of adverse reaction-abdominal discomfort, appetite suppression, and neurological symptoms. We compared the drug efficacy and frequency of adverse reaction between an isolated group consisting of only ADHD children (30 subjects) and a merged group consisting of children with ADHD and autistic symptoms (79 subjects), including pervasive developmental disorder (PDD) and Asperger syndrome.

Results and Conclusions: OROS-MPH improved ADHD symptoms in children (regardless of the presence or absence of accompanying autism) without having any severe adverse reaction.

.....

J Urol. 2011;186:2027-32.

ASSOCIATION OF ATTENTION DEFICIT AND ELIMINATION DISORDERS AT SCHOOL ENTRY: A POPULATION BASED STUDY.

Von Gontard A, Moritz AM, Thome-Granz S, et al.

Purpose: Attention deficit/hyperactivity disorder is a common comorbid disorder in children with nocturnal enuresis, daytime urinary incontinence and fecal incontinence. We assessed the specific association of these conditions in a population based sample. We hypothesized that children with elimination disorders have a higher rate of attention deficit/hyperactivity disorder, and that children with daytime urinary incontinence are more strongly affected than those with nocturnal enuresis.

Materials and Methods: All children in a defined geographic area (Saarpfalz Kreis) were examined at school entry. Mean age was 6.22 years in 734 boys and 6.18 years in 645 girls. A questionnaire regarding elimination problems and the attention problems scale of the Child Behavior Checklist were administered as an interview to parents. Participation rate was 99.1% (1,379 parents).

Results: Of the children 71 (5.1%) had attention deficit/hyperactivity disorder problems of clinical relevance (7.1% of boys and 2.9% of girls). A total of 185 children (13.4%) were wet (nocturnal enuresis in 9.1% and daytime urinary incontinence in 4.4%) and 19 (1.4%) had fecal incontinence. Attention deficit/hyperactivity disorder symptoms were more common in children with urinary incontinence than nonwetting children (16.8% vs 3.4%). When controlled for confounding variables, only children with daytime urinary incontinence (but not nocturnal enuresis) had a significantly higher risk of attention deficit/hyperactivity disorder symptoms (OR 4.4).

Conclusions: Attention deficit/hyperactivity disorder symptoms were increased in children with urinary incontinence in this population based sample. Children with daytime urinary incontinence were at greater risk for attention deficit/hyperactivity disorder than those with nocturnal enuresis. Screening and referral for specialized treatment of both disorders are recommended.

.....

Neurochem Res. 2011;1-5.

ALTERED BIOCHEMICAL PARAMETERS IN SALIVA OF PEDIATRIC ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Archana E, Pai P, Prabhu BK, et al.

Oxidative stress is one of the common causes in etiopathogenesis of attention deficit hyperactivity disorder (ADHD). Hence, the salivary levels of protein thiols, ceruloplasmin, magnesium and pseudocholinesterase were estimated in children with ADHD. The symptoms of ADHD were identified using Conner's rating and DSM IV criteria. Saliva was collected and assessed for the levels of protein thiols, ceruloplasmin, magnesium and pseudocholinesterase, spectrophotometrically. It was also checked for pH and the flow rate was noted down. There was a significant increase ($P < 0.001$) in the salivary protein thiols and pseudocholinesterase levels in ADHD children when compared to controls. Ceruloplasmin levels did not show any significant change. Magnesium levels were significantly decreased ($P < 0.001$) in cases when compared to controls. Further, a receiver operating characteristic curve for validity of the biochemical parameters in saliva of ADHD children indicated a sensitivity and specificity above 90% for protein thiols and magnesium values. Our study shows that protein thiols, magnesium, and pseudocholinesterase might have a role in the pathogenesis of ADHD and saliva can be effectively used as a non-invasive tool for evaluation of such children.

.....

NeuroImage. 2011.

BIRTH WEIGHT AND GESTATION INFLUENCE STRIATAL MORPHOLOGY AND MOTOR RESPONSE IN NORMAL SIX-YEAR-OLD BOYS.

Qiu A, Rifkin-Graboi A, Zhong J, et al.

The relation between fetal growth and attention deficit hyperactivity disorder (ADHD) cuts across the normal range of birth weights suggesting that subtle variations in fetal development may influence brain and cognitive function. We investigated the relation of ADHD-related endophenotypes, such as the striatum morphology, motor response and inhibition, with birth weight and gestational age in healthy children. 157 Six-year-old boys born at term (37 to 41 weeks) within the normal range for birth weight (2500 to 4630 g) underwent magnetic resonance imaging (MRI) and performed the stop signal task. Linear regression was used to examine effects of birth weight, gestational age, and their interaction on striatal volumes and shapes as well as motor response and inhibition. Interactive effects of birth weight and gestational age, even within the normal range, predicted caudate volumes and shapes. Boys with relatively low birth weight and shorter gestation had smaller caudate volumes, reflected by shape contraction in the middle body, and in addition performed worst in motor response, reflected by mean reaction time and its variability. Our results supported the idea that prenatal influences on neurocognitive and brain development are not limited to the extreme range, but occur across the entire population. Variations in brain structure and cognitive endophenotypes associated with childhood ADHD psychopathology are sensitive to subtle prenatal influences, which provides guidance for intervention research to improve mental health of children.

.....

Neuropsychiatr Dis Treat. 2011;7:267-73.

PHYSICIAN PERCEPTION OF CLINICAL IMPROVEMENT IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A POST HOC COMPARISON OF LISDEXAMFETAMINE DIMESYLATE AND MIXED AMPHETAMINE SALTS EXTENDED RELEASE IN A CROSSOVER ANALOG CLASSROOM STUDY.

Lopez FA, Scheckner B, Childress AC.

Objective: To assess effects of lisdexamfetamine dimesylate (LDX) and mixed amphetamine salts extended release (MAS XR) on symptom improvement in children with attention-deficit/ hyperactivity disorder (ADHD).

Methods: Post hoc analysis of a randomized, double-blind, placebo-controlled, crossover analog-classroom environment was conducted. The primary efficacy outcome was the deportment subscale of the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP-D) rating scale. The secondary efficacy outcome was the investigator-rated Clinical Global Impressions-Improvement (CGI-I), a 7-point scale ranging from 1 (very much improved) to 7 (very much worse), which assesses improvement over time from baseline. McNemar test was used to compare participants' responses to LDX and MAS XR on CGI-I scores dichotomized into 1 (very much improved) vs all other response scores (2 to 7) in a 2 null 2 table.

Results: Fifty-two children (aged 6 to 12 years) were enrolled, titrated, and randomized; 50 completed the study. Investigators rated 74% of LDX participants as either very much improved or much improved on the CGI-I scale relative to 72% of MAS XR participants and 18% of placebo participants. Of the 50 children who completed the study, 32% of LDX participants were very much improved vs 16% of MAS XR, and 2% of placebo participants relative to baseline. McNemar test indicated that 10 participants were very much improved with LDX, but not MAS XR; 2 participants were very much improved with MAS XR, but not LDX; 6 participants were very much improved with both, while 32 were not very much improved with either. Analysis showed that LDX had a significantly higher number of children with a very much improved score on the CGI-I than MAS XR ($P = 0.0386$).

Conclusion: Treatment of children with LDX resulted in a higher number of participants with a very much improved score on the CGI-I than treatment with MAS XR or placebo.

.....

No To Hattatsu. 2011;43:367-71.

CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND PERVASIVE DEVELOPMENTAL DISORDER: ATTENTION AND RESPONSE INHIBITION ON THE KIDDIE CONTINUOUS PERFORMANCE TEST.

Tsushima Y, Sanada S, Yanagihara M, et al.

Continuous Performance Test (CPT) is widely used to assess the attention function and response inhibition in both children and adults. This study attempts to examine the performances of boys with attention deficit/hyperactivity disorder (AD/HD) and pervasive developmental disorder (PDD) with and without comorbid AD/HD using a CPT. Among the various versions of the CPT available, we used the Kiddie CPT (K-CPT) modified for younger children. The K-CPT was administered to children with AD/HD (n=22), those with PDD (n=19), and typically developing children (n=41) from 7 to 12 years of age. All children were drug free at the time of examination. The performances were examined in 6 measures: total number of omission errors (OE), total number of commission errors (CE), mean hit reaction time (HRT), hit reaction time standard error (HRTSE), perceptual sensitivity (d'), and response style ((beta)). Significantly lower scores in d' and a tendency to more errors in CE were found in the AD/HD group compared with the control group. Significantly lower scores in d' and significantly more errors in CE were also found in the PDD group with AD/HD symptoms compared with the control group. Moreover the AD/HD group showed significantly more errors in OE and higher scores in HRTSE compared with the control group. There were no significant group differences between the PDD group without AD/HD symptoms and the control group on all measures. Less favorable scores in AD/HD suggest inadequate selective attention, sustained attention and/or response inhibition. Results of the PDD group with comorbid AD/HD may reflect a basis of AD/HD impairment. Our findings may provide an understanding of neuropsychological characteristics underlying developmental disorders.

.....

Paediatr Croat. 2011;55:61-67.

ATTENTION DEFICIT DISORDER/HYPERKINETIC DISORDER IN CHILDREN AND ADOLESCENTS.

Juretic Z, Petkovic ZB, Ercegovic N.

Attention deficit/hyperactivity disorder (ADHD) is a neurobiological disorder characterized with three core symptoms: hyperkinesia, attention deficit and impulsivity and secondary symptoms like learning disorders, behavioural disturbances and low self esteem. Soft neurological signs are very often present. The aetiology of the disorder is not yet well known and there are probably more neurobiological and psychosocial aetiological factors. The prevalence is 3-10% of school-age children. There is a greater incidence in boys than in girls with the ratio 9:1 in clinical, and 4:1 in epidemiological samples. Comorbidity is a major problem among children with ADHD, and two thirds of them have at least one more diagnosed psychiatric disorder, most often a conduct disorder, oppositional defiant disorder and learning disorder, but also disorders of speech and communication, anxiety disorders, mood disorders, tic disorders such as Sy Tourette s. Comorbidity is very important because it makes the diagnostic process more complicated, and has implications for the course, prognosis and treatment. Treatment of ADHD is multidimensional and combines psychosocial and pharmacological interventions, and it should start as early as possible. Today, cognitive behavioural treatment and drug treatment are most important in therapy.

.....

Patient. 2011;4:247-57.

ESTIMATION OF UTILITIES IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER FOR ECONOMIC EVALUATIONS .

Lloyd A, Hodgkins P, Sasane R, et al.

Background: Attempts to estimate the cost effectiveness of attention-deficit hyperactivity disorder (ADHD) treatments in the past have relied on classifying ADHD patients as responders or non-responders to treatment. Responder status has been associated with a small gain in health-related quality of life (HR-QOL) [or utility, as measured using the generic QOL measure EQ- 5D] of 0.06 (on a scale from 0 being dead to 1.0 being full health).

Objectives: The goal of the present study was to develop and validate several ADHD-related health states, and to estimate utility values measured amongst the general public for those states and to re-estimate utility values associated with responder status.

Methods: Detailed qualitative interview data were collected from 20 young ADHD patients to characterize their HR-QOL. In addition, item-by-item clinical and HR-QOL data from a clinical trial were used to define and describe four health states (normal; borderline to mildly ill; moderately to markedly ill; and severely ill). ADHD experts assessed the content validity of the descriptions. The states were rated by 100 members of the UK general public using the time trade-off (TTO) interview and visual analog scale. Statistical mapping was also undertaken to estimate Clinical Global Impression-Improvement (CGI-I) utilities (i.e. response status) from Clinical Global Impression-Severity (CGI-S) defined states. The mapping work estimated changes in utilities from study baseline to last visit for patients with a CGI-I score of (less-than or equal to)2 or (less-than or equal to)3.

Results: The validity of the four health states developed in this study was supported by in-depth interviews with ADHD experts and patients, and clinical trial data. TTO-derived utilities for the four health states ranged from 0.839 (CGI-S state 'normal') to 0.444 (CGI-S state 'severely ill'). From the mapping work, the change in utility for treatment responders was 0.19 for patients with a CGI-I score of (less-than or equal to)2 and 0.15 for patients with a CGI-I score of (less-than or equal to)3.

Conclusions: The present study provides utilities for different severity levels of ADHD estimated in a TTO study. This approach provides a more granular assessment of the impact of ADHD on HR-QOL than binary approaches employed in previous economic analyses. Change in utility for responders and nonresponders at different levels of CGI-I was estimated, and thus these utilities may be used to compare health gains of different ADHD interventions.

Pediatr Blood Cancer. 2011;57:1191-96.

SYMPTOMS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN LONG-TERM SURVIVORS OF CHILDHOOD LEUKEMIA.

Krull KR, Khan RB, Ness KK, et al.

Background: Survivors of childhood acute lymphoblastic leukemia (ALL) sometimes have clinical features that suggest attention-deficit/hyperactivity disorder (ADHD), though few studies have examined specific symptoms in survivors.

Procedure: Long-term survivors of childhood ALL (n=161) received a neurological examination, while parents completed rating scales to establish formal criteria for ADHD. Symptom profiles were generated and compared across demographic and treatment characteristics, as well as medical tests associated with brain pathology.

Results: Prevalence rates of ADHD were similar in survivors (10.5%) compared to those reported in the general population (7-10%). However, 25.5% of survivors reported symptoms that impair functioning in multiple settings, with attention problems being most common. These symptoms were associated with cranial radiation therapy (CRT) (mean inattentive symptoms [SD]=3.6 [3.19] for group treated with CRT vs. 1.6 [2.40] for non-CRT group, P=0.0006), and survivors who demonstrated impaired anti-saccades during the neurologic exam (mean inattentive symptoms [SD]=3.4 [3.29] for those with impaired anti-saccades vs. 1.4 [2.41] for those with normal anti-saccades; P=0.0004).

Conclusions: The presence of a neurologically-based phenotype of attention problems in survivors of leukemia that is not fully captured by the syndrome of ADHD suggests that treatments specific to childhood ALL should be explored.

Pediatr Pulmonol. 2011;46:408.

TWO LIFELONG DIAGNOSES: GROWING UP WITH CYSTIC FIBROSIS AND ADHD.

Havermans T.

Background: Patients with cystic fibrosis (CF) are, like healthy children, at risk for developmental problems. Attention Deficit Hyperactive Disorder (ADHD) is a psychiatric diagnosis and symptoms

(inattentive, hyperactive, impulsive) are prone to interfere with CF treatment. The aim of this paper is to evaluate the ADHD diagnostic process, its treatment and family experiences of living with two lifelong diagnoses.

Method: Retrospective review of medical and psychological charts.

Results: Twenty-one patients had suspicion of ADHD (Table). Parents reported disruptive behavioral problems at home and school. This behavior was also reported during out-patient clinics. The subsequent diagnostic process included 1) a detailed behavioral history; 2) observation and testing of the child; and 3) reports from the pediatrician, school, home physiotherapist and other caregivers involved. Results were discussed with the CF team, the parents and child. When there was strong suspicion of ADHD, a referral to an ADHD specialist was made. The remaining patients were counselled and/or referred appropriately. Mean age at ADHD diagnosis was 6.75 (range 4-9). All 10 patients initially started ADHD medication, with good result for 8. By reaching adulthood, 3 patients had stopped ADHD medical treatment because they experienced no benefit.

Follow-up of the pediatric patients included: three-monthly outpatient CF clinics and an annual follow-up with the ADHD specialist. The CF psychologist regularly contacted the family in between. Annual multidisciplinary meetings were organized for two children, because of additional problems (conduct disorder and learning difficulties). Follow-up for the adult patients included three-monthly CF follow-up, with support for ADHD when wanted. The combination of CF and ADHD was described as stressful and worrying. Parents noted that ADHD behavior strongly interfered with CF treatment. The ADHD medication was however frequently portrayed by both parents and physiotherapists as a relief: it helped to reduce disruptive behavior during CF treatment, e.g. problematic eating, incorrect use of the nebulizer or careless physiotherapy. The main concern with medical ADHD treatment was the potential impact on appetite and the extra burden of even more medication.

Conclusion: In case of ADHD, CF treatment is often disrupted causing additional stress within families. The results show the importance of a multidisciplinary diagnostic process and the regular follow-up of both medical and psycho-social problems. Help has to be tailored to patients' needs and with consideration of the interaction between the 2 treatment modules. (Table presented).

Pediatr Pulmonol. 2011;46:163.

COGNITIVE BEHAVIORAL THERAPY TO PROMOTE ADHERENCE IN ADHD AND MEDICAL ILLNESS.

Masek BJ.

Nonadherence with medical treatment regimens is prevalent in an estimated one out of two children with chronic medical illness. The model of adherence risks described by Ickovics and Meisler (1) provides a useful framework for the development of interventions to improve adherence to medical therapy in children with chronic illness. In this model five factors are considered, which include: 1) child's developmental stage; 2) disease symptoms; 3) complexity of treatment regimen; 4) child-parent relationship; and 5) clinical setting. Behaviorally-based interventions that address one or more of these factors are generally effective for increasing treatment regimen adherence for childhood illnesses (2). The CF patient with ADHD may present a special challenge to health care providers in terms of nonadherence due to behavioral noncompliance, which is so often a feature of the disorder. CBT approaches focused on skills-based interventions to treat ADHD symptoms in adults have recently gained empirical support (3). The aim of this talk will be to describe CBT interventions to promote medical adherence in children and adult CF patients with ADHD that can be delivered by a member of the multi-disciplinary health care team.

Pediatr Int. 2011;53:715-17.

ABLATION OF SUPRAVENTRICULAR TACHYCARDIA ALLOWS MORE LIBERAL THERAPY IN SOME CHILDREN WITH ATTENTION-DEFICIT-HYPERACTIVITY DISORDER.

Shetty I, Silver ES, Hordof AJ, et al.

Background: First-line therapy for children with attention-deficit- hyperactivity disorder (ADHD) is stimulant medication, which may have potential cardiovascular side-effects. In patients with supraventricular

tachycardia or Wolf-Parkinson-White syndrome (WPW), therapy for ADHD could become challenging. The purpose of the present study was to review the authors' experience of performing electrophysiologic study (EPS) with or without ablation to determine how it affected ADHD therapy.

Methods: Retrospective chart review of patients who underwent EPS between 2002 and 2009 was carried out. All patients under 21 years of age who had prior diagnosis of ADHD were included.

Results: Twenty patients met the inclusion criteria. The mean age was 12.1 (plus or minus) 2.7 years (range: 5.6-16.8 years). The patients were diagnosed with ADHD on average 3.9 (plus or minus) 2.7 years (range: 6 months-9 years) prior to the EPS. All patients had a structurally normal heart. Sixteen patients had cardiac symptoms. Seventeen patients underwent ablation of the arrhythmia substrate (16/17, 94% successful). Three patients with asymptomatic WPW were at low risk for life-threatening arrhythmias and did not have ablation. After the EPS, two patients had increased doses of their ADHD medications, and two patients whose health-care providers stopped the stimulant medication prior to EPS because of recurrent tachycardia were restarted on medications. All other patients on ADHD medications continued therapy.

Conclusions: EPS for risk stratification and ablation of arrhythmia substrate is safe and effective, allowing more liberal therapy in patients with ADHD and supraventricular tachycardia or WPW.

PM R. 2011;3:836-45.

CAREGIVER RATINGS OF LONG-TERM EXECUTIVE DYSFUNCTION AND ATTENTION PROBLEMS AFTER EARLY CHILDHOOD TRAUMATIC BRAIN INJURY: FAMILY FUNCTIONING IS IMPORTANT.

Kurowski BG, Taylor HG, Yeates KO, et al.

Objective: To evaluate the relationship of family and parenting factors to long-term executive dysfunction and attention problems after early childhood traumatic brain injury (TBI). We hypothesized that the magnitude of executive dysfunction and attention problems would be moderated by family and parenting factors.

Design: A multicenter, prospective cohort study that included an orthopedic injury (OI) reference group.

Setting: Three tertiary academic children's hospital medical centers and one general medical center.

Participants: Children, ages 3-7 years, hospitalized for OI, moderate TBI, or severe TBI. Methods and

Outcome Measurements: Parental ratings of family functioning and parenting styles were obtained 18 months after the injury occurred. The main outcome measurements, which were parental ratings of children's executive function and attention, were performed at least 24 months after the injury occurred (mean, 39 months; range, 25-63 months).

Analysis: Group comparisons were conducted with use of t-tests, (chi)² analysis, analysis of variance, and Pearson and Spearman correlations. Regression analysis was used to examine associations of the outcomes with family functioning and parenting styles and to test moderating effects of these factors on group differences.

Results: Participants with severe TBI demonstrated increased executive dysfunction and attention problems compared with those who sustained moderate TBI or OI. Lower levels of family dysfunction were associated with better executive function and attention across groups but did not moderate group differences. However, attention deficits after severe TBI were exacerbated under conditions of more permissive parenting relative to attention deficits after OIs.

Conclusions: Executive function and attention problems persisted on a long-term basis (>24 months) after early childhood TBI, and positive global family functioning and nonpermissive parenting were associated with better outcomes. Better characterization of the optimal family environment for recovery from early childhood TBI could help target future interventions.

Psychiatr. 2011;35:380-83.

ASSESSMENTS FOR ATTENTION-DEFICIT HYPERACTIVITY DISORDER: USE OF OBJECTIVE MEASUREMENTS.

Vogt C, Shameli A.

Aims and method: To appraise the value of additional information from objective measurements (QbTest system) in the clinical assessment of children and adolescents with attention-deficit hyperactivity disorder

(ADHD). Two groups of ADHD assessments were compared. In the first group, assessments were undertaken without objective measures, whereas in the second group objective measures were added to the assessment. Practice outcomes were followed up over 1 year.

Results: Objective measures improve differentiating between ADHD and other conditions whose symptoms are known to overlap with ADHD. Objective measurements reduce the risk of unidentified ADHD ($P < 0.0035$) as measured by subsequent rates of revised diagnosis over a 12-month period.

Clinical implications: Introducing objective measurements into the clinical assessment of ADHD provides an increased robustness of the clinical diagnosis strengthening clinical decisions for treatment interventions.

Declaration of interest: None.

Psychiatr Invest. 2011;8:227-33.

DIFFERENCES IN PERFORMANCE OF ADHD CHILDREN ON A VISUAL AND AUDITORY CONTINUOUS PERFORMANCE TEST ACCORDING TO IQ.

Park MH, Kweon YS, Lee SJ, et al.

Objective Continuous performance tests (CPTs) are frequently used in clinical practice to assess the attentiveness of ADHD children. Although most CPTs do not categorize T scores by intelligence, there is great diversity of opinion regarding the interrelation between intelligence and CPT performance. This study aimed to determine if ADHD children with superior IQs would perform better than ADHD children with average IQs. Additionally, we aimed to examine the need for CPTs' to categorize according to IQ.

Methods Participants were 326 outpatients, aged 5-15 years, diagnosed with ADHD. All participants completed the Wechsler Intelligence Scale for Children-Revised and a CPT. After excluding those who meet exclusion criteria, we had 266 patients for our analysis.

Results The "Highly Intelligent Group" (HIG), patients with IQs 120 and above, performed superiorly to the "Normally Intelligent Group" (NIG) patients, with IQs between 70 and 120, with regard to omission and commission errors on the visual-auditory CPT, even after controlling for age and gender. The HIG had higher ratios of subjects with T scores <65 on the visual and auditory CPT variables than the NIG did.

Conclusion The results of this study suggest this CPT is not sensitive for discerning ADHD in children with superior IQs; thus, there is a need to standardize the variables based on IQ, as well as on age and gender. Moreover, clinicians need to pay attention to the effect of IQ in interpreting CPT scores; that is, a "normal" score does not rule out a diagnosis of ADHD.

Psychopharmacology. 2011;1-10.

MANIPULATION OF NICOTINIC ACETYLCHOLINE RECEPTORS DIFFERENTIALLY AFFECTS BEHAVIORAL INHIBITION IN HUMAN SUBJECTS WITH AND WITHOUT DISORDERED BASELINE IMPULSIVITY.

Potter AS, Bucci DJ, Newhouse PA.

Rationale: Evidence for a relationship between cigarette smoking and attention-deficit/hyperactivity disorder (ADHD) has prompted investigations into nicotinic treatments for this disorder. Impulsivity is a hallmark of ADHD and is measured in the laboratory as behavioral inhibition (BI) using the stop signal task (SST). Acute nicotine improves SST performance in adolescents and young adults who have both ADHD and impaired baseline SST performance, raising questions about the role of nicotinic acetylcholine receptor function in BI. The specificity of this effect to those with ADHD, the component processes of the SST affected by nicotine, and the effects of nicotinic antagonism are yet unknown.

Objectives: This study investigated the effects of both a nicotinic receptor agonist and antagonist on the SST and choice reaction time task (CRT) in highly impulsive (HI) and control (CTRL) subjects.

Methods: This was a within-subjects, double-blind study of: 7 mg transdermal nicotine, 20 mg oral mecamylamine, and placebo. Subjects were recruited into HI ($n = 11$) and CTRL ($n = 14$) groups based on both SST and clinical criteria.

Results: BI was significantly improved by nicotine compared with placebo in the HI group and impaired by mecamylamine in the CTRL group. Go signal reaction time on the SST was improved by nicotine compared with placebo in the CTRL group and was unchanged in both groups on the CRT.

Conclusions: These findings demonstrate nicotinic modulation of BI in subjects with both normal and disordered baseline performance. The effects on BI are consistent with cholinergic enhancement of signal detection processes and/or modulation of noradrenaline by nicotine.

Res Dev Disabil. 2011;32:2797-804.

AN EXAMINATION OF THE EFFECTS OF STIMULANT MEDICATION ON RESPONSE INHIBITION: A COMPARISON BETWEEN CHILDREN WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Brackenridge R, McKenzie K, Murray GC, et al .

This study investigated whether methylphenidate is effective in improving response inhibition in children with Attention Deficit Hyperactivity Disorder (ADHD). Children with ADHD were compared with normally developing children on measures of response inhibition. Participants with ADHD were compared across two conditions - medicated and unmedicated. There was no significant difference between the inhibitory control of children with and without ADHD. Children with ADHD showed significant improvements in inhibitory control following methylphenidate. The findings of the present study contrast with previous studies which document reduced inhibitory control in ADHD, compared with normally developing children. Reports of methylphenidate improving functioning in children with ADHD are supported. Limitation and implications of the study are discussed.

Res Dev Disabil. 2011;32:2927-34.

HANDWRITING CAPACITY IN CHILDREN NEWLY DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Brossard-Racine M, Majnemer A, Shevell M, et al.

Preliminary evidence suggests that children with Attention Deficit Hyperactivity Disorder (ADHD) may exhibit handwriting difficulties. However, the exact nature of these difficulties and the extent to which they may relate to motor or behavioural difficulties remains unclear. The aim of this study was to describe handwriting capacity in children newly diagnosed with ADHD and identify predictors of performance. Forty medication-naïve children with ADHD (mean age 8.1 years) were evaluated with the Evaluation Tool of Children's Handwriting-Manuscript, the Movement Assessment Battery for Children (M-ABC), the Developmental Test of Visual Motor Integration (VMI) and the Conner Global Index. An important subset (85.0%) exhibited manual dexterity difficulties. Handwriting performance was extremely variable in terms of speed and legibility. VMI was the most important predictor of legibility. Upper extremity coordination, as measured by the M-ABC ball skills subtest, was also a good predictor of word legibility. Conclusion: Poor handwriting legibility and slow writing speed were common in children newly diagnosed with ADHD and were associated with motor abilities. Future studies are needed to determine whether interventions, including stimulant medications, can improve handwriting performance and related motor functioning.

Res Dev Disabil. 2011;32:2608-13.

USING A VIRTUAL CLASSROOM ENVIRONMENT TO DESCRIBE THE ATTENTION DEFICITS PROFILE OF CHILDREN WITH NEUROFIBROMATOSIS TYPE 1.

Gilboa Y, Rosenblum S, Fattal-Valevski A, et al.

The objectives of this study were to describe the nature of the attention deficits in children with Neurofibromatosis type 1 (NF1) in comparison with typically developing (TD) children, using the Virtual Classroom (VC), and to assess the utility of this instrument for detecting attention deficits. Twenty-nine NF1 children and 25 age-and gender-matched controls, aged 8-16, were assessed in a VC. Parents' ratings on the Conners' Parent Rating Scales-Revised: Long (CPRS-R:L) questionnaire were used to screen for

Attention Deficit-Hyperactivity Disorder (ADHD). Significant differences were found between the NF1 and the control groups on the number of targets correctly identified (omission errors) and the number of commissions (commission errors) in the VC, with poorer performance by the NF1 children ($p < 0.005$). Significant correlations were obtained between the number of targets correctly identified, the number of commission errors, and the reaction time. Significant correlations were also found between the total correct hits and the cognitive problems/inattention scale, as well as two other indexes of the CPRS-R:L: the DSM-IV Symptoms Subscale and the ADHD Index. The VC results support the hypothesis that NF1 is marked by inattention and impulsivity and that participants with NF1 are more inattentive (omission errors) and impulsive (commission errors) than normal controls. The VC appears to be a sensitive and ecologically valid assessment tool for use in the diagnosis of attention deficits among children with NF1.

Res Dev Disabil. 2011;32:2805-09.

ADHD AND OTHER ASSOCIATED DEVELOPMENTAL PROBLEMS IN CHILDREN WITH MILD MENTAL RETARDATION. THE USE OF THE "FIVE-TO-FIFTEEN" QUESTIONNAIRE IN A POPULATION-BASED SAMPLE.

Lindblad I, Gillberg C, Fernell E.

The aim was to examine the rates and types of parent reported neuropsychiatric problems in children and adolescents with mild mental retardation (MMR) (mild intellectual disability/UK) using the Five-To-Fifteen questionnaire (FTF). The target group comprised all pupils with clinically diagnosed MMR, aged between 7 and 15 years, attending the special schools for children with MMR in two municipalities in a region in the South-West of Sweden. The FTF is a 181-item parent questionnaire with age and gender specific Swedish norms covering eight domains, including the phenomenology of early symptomatic syndromes eliciting neurodevelopmental examinations (ESSENCE), including ADHD, autism, tic syndromes, and various kinds of language, memory, and learning problems. Parents of 63% (39/62) of the eligible target group completed the FTF. After scrutiny of the medical records, 6 of the 39 children were found not to meet criteria for MR. Scores exceeding the 90th centile of the norm group were considered indicative of neuropsychiatric problems. Such high scores are strongly associated with clinically valid ESSENCE/neuropsychiatric disorders. All the examined children with validated MR were reported by their parents to have learning problems. There were very high rates of problems reported in all the other seven FTF domains: perception (88%), language (79%), social skills/autism (76%), memory (67%), emotional problems (58%), motor skills (55%) and executive functions/ADHD (55%). School age children with MMR are all in need of a comprehensive work-up covering not only general cognitive abilities, but also many other areas, including motor skills, executive function/attention, social and emotional/behavioural symptoms/functioning. Such broad assessment (including child screening by parent report with the FTF) will enable a better basis for understanding their special needs of support through life.

Res Dev Disabil. 2011 Sep;32:1988-97.

LATENT FACTOR STRUCTURE OF THE DAS-NAGLIERI COGNITIVE ASSESSMENT SYSTEM: A CONFIRMATORY FACTOR ANALYSIS IN A CHINESE SETTING.

Deng Cp, Liu M, Wei W, et al.

This study aims to measure the psychometric properties of the Das-Naglieri Cognitive Assessment System (D-N CAS) and to determine its clinical utility in a Chinese context. Confirmatory factor analysis (CFA) was conducted to examine the construct validity of the Chinese version of the D-N CAS among a group of 567, normally developed children. Test-retest reliability was examined in a random subsample of 30 children at a five-week interval. The clinical discrimination of the D-N CAS was also examined by comparing children with and without ADHD (18 children in each group) and by comparing children with and without Chinese reading disabilities (18 children in each group). The current Chinese sample demonstrated a four-factor solution for cognitive performance among children with normal development: Planning, Attention, Simultaneous processing and Successive processing ($\chi^2(48)=91.90$, $p = .000$; $\chi^2/df=1.92$, RMSEA=.050, GFI=.966, CFI=.954). Moreover, all subtests of the battery demonstrated acceptable test-retest reliability ($r = .72-.90$, $p < .01$) at a five-week interval among the subjects of the small subsample. Children with ADHD

performed significantly worse than normal children on the Attention factor ($p < .001$) and the Planning factor ($p < .05$) of the D-N CAS, and children with Chinese reading disabilities performed significantly worse than normal children on the Simultaneous processing factor ($p < .01$), the Successive processing factor ($p < .001$) and the Planning factor ($p < .05$) of the D-N CAS. These findings suggested that the current four-factor structure of the D-N CAS was similar to the original factor structure of the test. The latent factor of the D-N CAS was fairly stable across the cultures. Moreover, the D-N CAS can distinguish between children with ADHD or Chinese reading disabilities and normally developed children.

.....

Rev Paul Pediatr. 2011;29:437-42.

SLEEP/WAKE CYCLE AND THE ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Anacleto TS, Louzada FM, Pereira EF.

Objective: To analyze the relationship between the wake/ sleep cycle and the attention deficit/hyperactivity disorder.

Data Source: The articles were found in the SciELO and Pub Med databases, using "sleep", "attention deficit/ hyperactivity disorder", "motor activity" and "children" as search key-words.

Data Synthesis: The results of individual studies are inconclusive and frequently contradictory, not allowing the establishment of a clear relationship between sleep and the attention deficit/hyperactivity disorder. However, sleep patterns of children diagnosed with this disorder are different than those of healthy children. Thus, the possible role of sleep alterations in attention deficit/hyperactivity disorder etiology cannot be ruled out.

Conclusions: The lack of biological markers and knowledge about the etiology of the attention deficit/hyperactivity disorder results in some difficulties in determining its real prevalence. Moreover, this restricts our understanding of the attention deficit/hyperactivity disorder and the search for new forms of treatment and prevention. Although sleeping difficulties have been frequently mentioned in clinical practice studies and are already being used as one of the diagnostic criteria for the attention deficit/hyperactivity disorder, little is known about the possible participation of sleep deprivation in the etiology of the disorder.

.....

Sleep Med. 2011.

MANAGING SLEEP PROBLEMS IN SCHOOL AGED CHILDREN WITH ADHD: A PILOT RANDOMISED CONTROLLED TRIAL.

Sciberras E, Fulton M, Efron D, et al.

Objective: To evaluate the feasibility and helpfulness of a behavioral sleep program for children with ADHD, and explore the impact of different program dosages on child and family outcomes.

Methods: Randomised trial comparing a brief (1 session, $n = 13$) and extended (2-3 sessions, $n = 14$) sleep program in children with ADHD (aged 5-14 years) and at least one behavioral sleep disorder (American Academy of Sleep Medicine Criteria). Outcomes included helpfulness and use of interventions, child sleep (parent-reported sleep problem; Child Sleep Habits Questionnaire), ADHD symptoms (ADHD IV Rating Scale), daily functioning (Daily Parent Rating of Evening and Morning Behavior), quality of life (Pediatric Quality of Life Inventory), and caregiver mental health (Depression Anxiety Stress Scales).

Results: Twenty-seven families (63% of those eligible) took part. Most parents would recommend the program to others (95%) and found the strategies helpful. Five months post-randomisation, 67% of parents in both groups reported that their child's sleep problems had resolved. Child quality of life, daily functioning, and parental anxiety also improved in the extended group only (Cohen's d : 0.39, 0.47 and 0.50, respectively). There was minimal change in ADHD symptom scores from baseline to 5 months in either group.

Conclusions: A behavioral sleep intervention in children with ADHD is feasible to deliver and improves child sleep by parent report. The extended program resulted in greater improvements in child and caregiver outcomes.

.....

Sleep Med Rev. 2011.

SLEEP IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADULTS: PAST, PRESENT, AND FUTURE.
Yoon SYR, Jain U, Shapiro C.

The understanding that sleep can give rise to, or exacerbate symptoms of attention-deficit/hyperactivity disorder (ADHD), and that good sleep hygiene improves attention and concentration tasks has sparked interest in the investigation of possible etiological relationships between sleep disorders and ADHD. Studies indicate that 30% of children and 60-80% of adults with ADHD have symptoms of sleep disorders such as daytime sleepiness, insomnia, delayed sleep phase syndrome, fractured sleep, restless legs syndrome, and sleep disordered breathing. The range and diversity of findings by different researchers have posed challenges in establishing whether sleep disturbances are intrinsic to ADHD or whether disturbances occur due to co-morbid sleep disorders. As a result, understanding of the nature of the relationship between sleep disturbances/disorders and ADHD remains unclear. In this review, we present a comprehensive and critical account of the research that has been carried out to investigate the association between sleep and ADHD, as well as discuss mechanisms that have been proposed to account for the elusive relationship between sleep disturbances, sleep disorders, and ADHD.

Turk J Pediatr. 2011;53:397-403.

SLEEP HABITS, PARASOMNIAS AND ASSOCIATED BEHAVIORS IN SCHOOL CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Rodopman-Arman A, Perdahli-Fis N, Ekinci O, et al.

Considerable clinical data support an association between sleep problems and Attention Deficit Hyperactivity Disorder (ADHD). We aimed to investigate the sleep habits, associated parasomnias and behavioral symptoms in primary school children with ADHD. Forty primary school children with a clinical diagnosis of ADHD and 40 age-sex-matched healthy community controls were recruited. The Children's Sleep Habits Questionnaire providing information regarding sleep habits and nighttime and daytime symptoms was used. About 22% of children with ADHD (versus 2.9% of the controls) needed their parents to accompany them while going to sleep ($p: 0.008$). Transitional objects were needed by 8.1% of ADHD children in contrast to 2.9% of controls. Nightmares, overactivity during sleep, habitual snoring, and bed-wetting were significantly higher in the ADHD group. ADHD children needed significantly more time to go to sleep on school days ($p<0.02$). Children undergoing evaluation for ADHD should be routinely screened for sleep disturbances.

Turk J of Rheumatol. 2011;26:187-92.

BENIGN JOINT HYPERMOBILITY SYNDROME IN PATIENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDERS.

Dogan SK, Taner Y, Evcik D.

Objectives: In this study, we determined whether attention deficit/hyperactivity disorder (ADHD) is accompanied by benign joint hypermobility syndrome (BJHS) and evaluated the incidence of BJHS in patients with ADHD.

Patients and methods: This study was performed in the Ufuk University Faculty of Medicine, Departments of Physical Medicine and Rehabilitation and Psychiatry between November 2007 and February 2008. A total of 54 patients (45 males, 9 females; mean age 9.7 (plus or minus) 2.2 years; range 7 to 12 years) with ADHD and 36 healthy controls (19 males, 17 females; mean age 9.8 (plus or minus) 2.3 years; range 7 to 12 years) were included in the study. The sociodemographic and clinical characteristics of the individuals and the joint pain severity in the last month were recorded. Pain severity was assessed with the Faces Pain Scale-Revised (FPS-R) and the Likert Pain Scale. The joint hypermobility was evaluated by using Beighton scores.

Results: Benign joint hypermobility syndrome was found in 31.5% of the patients with ADHD and 13.9% of the individuals in the control group, and the difference was statistically significant ($p=0.05$). There were no statistically significant differences between the groups in FPS-R or Likert Pain Scale scores ($p>0.05$). A

statistically significant increase was observed in the Beighton total score in ADHD patients compared with the control group ($p=0.004$).

Conclusion: The results of this study support that joint hypermobility may be associated with ADHD, and this condition should be taken into consideration in assessing the complaints of patients with ADHD-related musculoskeletal symptoms.

World Psychiatry. 2010;9:111-17.

THE EFFECTIVENESS OF CHILD AND ADOLESCENT PSYCHIATRIC TREATMENTS IN A NATURALISTIC OUTPATIENT SETTING.

Bachmann M, Bachmann CJ, John K, et al.

Data concerning the effectiveness of naturalistic treatments (treatment-as-usual) in child and adolescent psychiatric (CAP) services are scarce. The purpose of this prospective observational study was to examine the effectiveness of CAP treatments in a naturalistic outpatient setting. Three hundred six patients (attention-deficit/hyperactivity disorder, ADHD, $n=94$; conduct disorder, CD, $n=57$; anxiety disorder, AD, $n=53$; depressive disorder, DD, $n=38$; other diagnostic categories, $n=64$), from nine child and adolescent psychiatric practices in Germany, were evaluated. Treatment effects were compared between patients who received frequent treatment and patients who only participated in diagnostics and short interventions. Since randomization was not feasible, propensity score analysis methods were used. Regarding the total sample, no significant treatment effects were found. However, a subgroup analysis of the four most frequent disorders (ADHD, CD, AD, DD) showed small to moderate treatment effects in patients with ADHD and AD. In CD and DD subgroups, no significant treatment effects could be found. "Real-world" CAP outpatient treatment seems to produce significant effects for ADHD and AD, but not for CD and DD. Compared to efficacy studies, our results show that naturalistic treatment might be better than expected.

Zeitschrift für Kinder- und Jugendpsychiatrie und Psychotherapie. 2011 Jul;39:277-85.

TRAINING SOZIALER FERTIGKEITEN FÜR KINDER MIT ADHS—ERGEBNISSE EINER PILOTSTUDIE.

Pothmann MSg, Petermann U, Petermann F, et al.

Objective: Insufficient social competence belongs to the most frequent concomitants of ADHD. This is the first therapeutic concept for the training of social skills adapted to the specific deficits of children with ADHD and developed in the German-speaking region.

Method: In a two-group, pre-posttest design with untreated waiting control group, 40 children between 7 and 13 years with the diagnoses F90.0, F90.1, and F98.8 were examined; 15% were female, 85% male. In groups of three they took part in the newly developed 10-h training TEAM. The record sheet of social skills for parents (ESF-E) was used to measure social competence. In addition, we recorded attention performances (FBB ADHS) and concomitant psychic factors.

Results: Significant effects of the training were demonstrated for almost all social skills (MANOVA/GLM). The outcomes on the different components of attention and the psychosocial concomitant factors are without uniformity. The strongest effects appeared in the areas of conflict management, regulation of emotions, and the capacity for empathy.

Conclusions: Training of social skills is a sensible and effective supplement in the therapy of ADHD. An examination of long-term effects still needs to be done.

Zeitschrift für Kinder- und Jugendpsychiatrie und Psychotherapie. 2011 Jul;39:265-76.

KOGNITIVE UND EMOTIONALE EMPATHIE BEI KINDERN UND JUGENDLICHEN MIT ADHS UND STÖRUNG DES SOZIALVERHALTENS .

Schwenck C, Schmitt D, Sievers S, et al.

Objectives: This study assesses the cognitive and emotional empathic competence in groups of children and adolescents with psychiatric disorders compared to a nonclinical control group. Subjective and objective diagnostic measures were employed.

Methods: A total of 96 boys were tested: 20 with attention-deficit/hyperactivity disorder (ADHD) predominantly inattentive subtype (ADHD-I); 20 with ADHD combined subtype (ADHD-C); 20 with conduct disorder (CD); 36 healthy boys (control group; CG). Mean age was 12.0 years (SD = 2.36). As aspects of cognitive and emotional empathy emotional reactivity, we tested emotion recognition and perspective taking with subjective questionnaires and objective tasks, using as subjective questionnaires the Interpersonal Reactivity Index (IRI; Davis, 1983) and the Index of Empathy for Children and Adolescents (IECA; Bryant, 1982). As objective tasks, we adopted the Empathy Response Task (ERT; Ricard & Kamberk-Kilicci, 1995) and a task measuring emotion recognition according to Buitelaar et al. (1999).

Results: The CG outperformed participants with ADHD-C and CD in objective tasks assessing perspective taking, particularly when complex tasks were applied as stimuli. Children with ADHD-I showed significantly more emotional empathy than boys with ADHD-C when presented with simple tasks. No group differences were found for emotion recognition and subjective questionnaires.

Discussion: Deficits in perspective taking and emotional empathy were found for children with ADHD-C and CD, largely in accordance with the literature. Similar to the processing of cognitive information, the processing of emotional information seems to differ in ADHD subtypes. Objective tasks and tasks with a high ecological validity seem suitable for the measurement of empathy.

American Academy
of Pediatrics



DEDICATED TO THE HEALTH OF ALL CHILDREN™

FROM THE AMERICAN ACADEMY OF PEDIATRICS

Guidance for the Clinician in
Rendering Pediatric Care

CLINICAL PRACTICE GUIDELINE

ADHD: Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents

SUBCOMMITTEE ON ATTENTION-DEFICIT/HYPERACTIVITY
DISORDER, STEERING COMMITTEE ON QUALITY
IMPROVEMENT AND MANAGEMENT

KEY WORDS

attention-deficit/hyperactivity disorder, children, adolescents,
preschool, behavioral therapy, medication

ABBREVIATIONS

AAP—American Academy of Pediatrics

ADHD—attention-deficit/hyperactivity disorder

DSMPC—*Diagnostic and Statistical Manual for Primary Care*

CDC—Centers for Disease Control and Prevention

FDA—Food and Drug Administration

DSMIV—*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*

MTA—Multimodal Therapy of ADHD

This document is copyrighted and is property of the American Academy of Pediatrics and its Board of Directors. All authors have filed conflict of interest statements with the American Academy of Pediatrics. Any conflicts have been resolved through a process approved by the Board of Directors. The American Academy of Pediatrics has neither solicited nor accepted any commercial involvement in the development of the content of this publication.

The recommendations in this report do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

www.pediatrics.org/cgi/doi/10.1542/peds.2011-2654

doi:10.1542/peds.2011-2654

All clinical practice guidelines from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2011 by the American Academy of Pediatrics

abstract



Attention-deficit/hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood and can profoundly affect the academic achievement, well-being, and social interactions of children; the American Academy of Pediatrics first published clinical recommendations for the diagnosis and evaluation of ADHD in children in 2000; recommendations for treatment followed in 2001. *Pediatrics* 2011;128:000

Summary of key action statements:

1. The primary care clinician should initiate an evaluation for ADHD for any child 4 through 18 years of age who presents with academic or behavioral problems and symptoms of inattention, hyperactivity, or impulsivity (quality of evidence B/strong recommendation).
2. To make a diagnosis of ADHD, the primary care clinician should determine that *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria have been met (including documentation of impairment in more than 1 major setting); information should be obtained primarily from reports from parents or guardians, teachers, and other school and mental health clinicians involved in the child's care. The primary care clinician should also rule out any alternative cause (quality of evidence B/strong recommendation).
3. In the evaluation of a child for ADHD, the primary care clinician should include assessment for other conditions that might coexist with ADHD, including emotional or behavioral (eg, anxiety, depressive, oppositional defiant, and conduct disorders), developmental (eg, learning and language disorders or other neurodevelopmental disorders), and physical (eg, tics, sleep apnea) conditions (quality of evidence B/strong recommendation).
4. The primary care clinician should recognize ADHD as a chronic condition and, therefore, consider children and adolescents with ADHD as children and youth with special health care needs. Management of children and youth with special health care needs should follow the principles of the chronic care model and the medical home (quality of evidence B/strong recommendation).

5. Recommendations for treatment of children and youth with ADHD vary depending on the patient's age:

a. For *preschool-aged children (4–5 years of age)*, the primary care clinician should prescribe evidence-based parent- and/or teacher-administered behavior therapy as the first line of treatment (quality of evidence A/strong recommendation) and may prescribe methylphenidate if the behavior interventions do not provide significant improvement and there is moderate-to-severe continuing disturbance in the child's function. In areas where evidence-based behavioral treatments are not available, the clinician needs to weigh the risks of starting medication at an early age against the harm of delaying diagnosis and treatment (quality of evidence B/recommendation).

b. For *elementary school-aged children (6–11 years of age)*, the primary care clinician should prescribe US Food and Drug Administration–approved medications for ADHD (quality of evidence A/strong recommendation) and/or evidence-based parent- and/or teacher-administered behavior therapy as treatment for ADHD, preferably both (quality of evidence B/strong recommendation). The evidence is particularly strong for stimulant medications and sufficient but less strong for atomoxetine, extended-release guanfacine, and extended-release clonidine (in that order) (quality of evidence A/strong recommendation). The school environment, program, or placement is a part of any treatment plan.

c. For *adolescents (12–18 years of age)*, the primary care clinician should prescribe Food and Drug Administration–approved medications for ADHD with the assent of the adolescent (quality of evidence A/strong recommendation) and may prescribe behavior therapy as treatment for ADHD (quality of evidence C/recommendation), preferably both.

6. The primary care clinician should titrate doses of medication for ADHD to achieve maximum benefit with minimum adverse effects (quality of evidence B/strong recommendation).

INTRODUCTION

This document updates and replaces 2 previously published clinical guidelines from the American Academy of Pediatrics (AAP) on the diagnosis and treatment of attention-deficit/hyperactivity disorder (ADHD) in children: "Clinical Practice Guideline: Diagnosis and Evaluation of the Child With Attention-Deficit/Hyperactivity Disorder" (2000)¹ and "Clinical Practice Guideline: Treatment of the School-aged Child With Attention-Deficit/Hyperactivity Disorder" (2001).² Since these guidelines were published, new information and evidence regarding the diagnosis and treatment of ADHD has become available. Surveys conducted before and after the publication of the previous guidelines have also provided insight into pediatricians' attitudes and practices regarding ADHD. On the basis of an increased understanding regarding ADHD and the challenges it raises for children and families and as a source for clinicians seeking to diagnose and treat children, this guideline pays particular attention to a number of areas.

Expanded Age Range

The previous guidelines addressed diagnosis and treatment of ADHD in chil-

dren 6 through 12 years of age. There is now emerging evidence to expand the age range of the recommendations to include preschool-aged children and adolescents. This guideline addresses the diagnosis and treatment of ADHD in children 4 through 18 years of age, and attention is brought to special circumstances or concerns in particular age groups when appropriate.

Expanded Scope

Behavioral interventions might help families of children with hyperactive/impulsive behaviors that do not meet full diagnostic criteria for ADHD. Guidance regarding the diagnosis of problem-level concerns in children based on the *Diagnostic and Statistical Manual for Primary Care (DSM-PC)*, *Child and Adolescent Version*,³ as well as suggestions for treatment and care of children and families with problem-level concerns, are provided here. The current DSM-PC was published in 1996 and, therefore, is not consistent with intervening changes to *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*. Although this version of the DSM-PC should not be used as a definitive source for diagnostic codes related to ADHD and comorbid conditions, it certainly may continue to be used as a resource for enriching the understanding of ADHD manifestations. The DSM-PC will be revised when both the DSM-V and ICD-10 are available for use.

A Process of Care for Diagnosis and Treatment

This guideline and process-of-care algorithm (see Supplemental Fig 2 and Supplemental Appendix) recognizes evaluation, diagnosis, and treatment as a continuous process and provides recommendations for both the guideline and the algorithm in this single publication. In addition to the formal recommendations for assessment, diagnosis, and treatment, this guideline

FROM THE AMERICAN ACADEMY OF PEDIATRICS

provides a single algorithm to guide the clinical process.

Integration With the Task Force on Mental Health

This guideline fits into the broader mission of the AAP Task Force on Mental Health and its efforts to provide a base from which primary care providers can develop alliances with families, work to prevent mental health conditions and identify them early, and collaborate with mental health clinicians.

The diagnosis and management of ADHD in children and youth has been particularly challenging for primary care clinicians because of the limited payment provided for what requires more time than most of the other conditions they typically address. The procedures recommended in this guideline necessitate spending more time with patients and families, developing a system of contacts with school and other personnel, and providing continuous, coordinated care, all of which is time demanding. In addition, relegating mental health conditions exclusively to mental health clinicians also is not a viable solution for many clinicians, because in many areas access to mental health clinicians to whom they can refer patients is limited. Access in many areas is also limited to psychologists when further assessment of cognitive issues is required and not available through the education system because of restrictions from third-party payers in paying for the evaluations on the basis of them being educational and not health related.

Cultural differences in the diagnosis and treatment of ADHD are an important issue, as they are for all pediatric conditions. Because the diagnosis and treatment of ADHD depends to a great extent on family and teacher perceptions, these issues might be even more prominent an issue for ADHD. Specific cultural issues

are beyond the scope of this guideline but are important to consider.

METHODOLOGY

As with the 2 previously published clinical guidelines, the AAP collaborated with several organizations to develop a working subcommittee that represented a wide range of primary care and subspecialty groups. The subcommittee included primary care pediatricians, developmental-behavioral pediatricians, and representatives from the American Academy of Child and Adolescent Psychiatry, the Child Neurology Society, the Society for Pediatric Psychology, the National Association of School Psychologists, the Society for Developmental and Behavioral Pediatrics, the American Academy of Family Physicians, and Children and Adults With Attention-Deficit/Hyperactivity Disorder (CHADD), as well as an epidemiologist from the Centers for Disease Control and Prevention (CDC).

This group met over a 2-year period, during which it reviewed the changes in practice that have occurred and issues that have been identified since the previous guidelines were published. Delay in completing the process led to further conference calls and extended the years of literature reviewed in order to remain as current as possible. The AAP funded the development of this guideline; potential financial conflicts of the participants were identified and taken into consideration in the deliberations. The guideline will be reviewed and/or revised in 5 years unless new evidence emerges that warrants revision sooner.

The subcommittee developed a series of research questions to direct an extensive evidence-based review in partnership with the CDC and the University of Oklahoma Health Sciences Center. The diagnostic review was conducted by the CDC, and the evidence was evaluated in a combined effort of

the AAP, CDC, and University of Oklahoma Health Sciences Center staff. The treatment-related evidence relied on a recent evidence review by the Agency for Healthcare Research and Quality and was supplemented by evidence identified through the CDC review.

The diagnostic issues were focused on 5 areas:

1. ADHD prevalence—specifically: (a) What percentage of the general US population aged 21 years or younger has ADHD? (b) What percentage of patients presenting at pediatricians' or family physicians' offices in the United States meet diagnostic criteria for ADHD?
2. Co-occurring mental disorders—of people with ADHD, what percentage has 1 or more of the following co-occurring conditions: sleep disorders, learning disabilities, depression, anxiety, conduct disorder, and oppositional defiant disorder?
3. What are the functional impairments of children and youth diagnosed with ADHD? Specifically, in what domains and to what degree do youth with ADHD demonstrate impairments in functional domains, including peer relations, academic performance, adaptive skills, and family functioning?
4. Do behavior rating scales remain the standard of care in assessing the diagnostic criteria for ADHD?
5. What is the prevalence of abnormal findings on selected medical screening tests commonly recommended as standard components of an evaluation of a child with suspected ADHD? How accurate are these tests in the diagnosis of ADHD compared with a reference standard (ie, what are the psychometric properties of these tests)?

The treatment issues were focused on 3 areas:

1. What new information is available

regarding the long-term efficacy and safety of medications approved by the US Food and Drug Administration (FDA) for the treatment of ADHD (stimulants and nonstimulants), and specifically, what information is available about the efficacy and safety of these medications in preschool-aged and adolescent patients?

2. What evidence is available about the long-term efficacy and safety of psychosocial interventions (behavioral modification) for the treatment of ADHD for children, and specifically, what information is available about the efficacy and safety of these interventions in preschool-aged and adolescent patients?
3. Are there any additional therapies that reach the level of consideration as evidence based?

Evidence-Review Process for Diagnosis

A multilevel, systematic approach was taken to identify the literature that built the evidence base for both diagnosis and treatment. To increase the likelihood that relevant articles were included in the final evidence base, the reviewers first conducted a scoping review of the literature by systematically searching literature using relevant key words and then summarized the primary findings of articles that met standard inclusion criteria. The reviewers then created evidence tables that were reviewed by content-area experts who were best able to identify articles that might have been missed through the scoping review. Articles that were missed were reviewed carefully to determine where the abstraction methodology failed, and adjustments to the search strategy were made as required (see technical report to be published). Finally, although published literature reviews did not contribute directly to the evidence

base, the articles included in review articles were cross-referenced with the final evidence tables to ensure that all relevant articles were included in the final evidence tables.

For the scoping review, articles were abstracted in a stratified fashion from 3 article-retrieval systems that provided access to articles in the domains of medicine, psychology, and education: PubMed (www.ncbi.nlm.nih.gov/sites/entrez), PsycINFO (www.apa.org/pubs/databases/psycinfo/index.aspx), and ERIC (www.eric.ed.gov). English-language, peer-reviewed articles published between 1998 and 2009 were queried in the 3 search engines. Key words were selected with the intent of including all possible articles that might have been relevant to 1 or more of the questions of interest (see the technical report to be published). The primary abstraction included the following terms: "attention deficit hyperactivity disorder" or "attention deficit disorder" or "hyperkinesis" and "child." A second, independent abstraction was conducted to identify articles related to medical screening tests for ADHD. For this abstraction, the same search terms were used as in the previous procedure along with the additional condition term "behavioral problems" to allow for the inclusion of studies of youth that sought to diagnose ADHD by using medical screening tests. Abstractions were conducted in parallel fashion across each of the 3 databases; the results from each abstraction (complete reference, abstract, and key words) were exported and compiled into a common reference database using EndNote 10.0.⁴ References were subsequently and systematically deduplicated by using the software's deduplication procedure. References for books, chapters, and theses were also deleted from the library. Once a deduplicated library was developed, the semifinal

database of 8267 references was reviewed for inclusion on the basis of inclusion criteria listed in the technical report. Included articles were then pulled in their entirety, the inclusion criteria were reconfirmed, and then the study findings were summarized in evidence tables. The articles included in relevant review articles were revisited to ensure their inclusion in the final evidence base. The evidence tables were then presented to the committee for expert review.

Evidence-Review Process for Treatment

In addition to this systematic review, for treatment we used the review from the Agency for Healthcare Research and Quality (AHRQ) Effective Healthcare Program "Attention Deficit Hyperactivity Disorder: Effectiveness of Treatment in At-Risk Preschoolers; Long-term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment."⁵ This review addressed a number of key questions for the committee, including the efficacy of medications and behavioral interventions for preschoolers, children, and adolescents. Evidence identified through the systematic evidence review for diagnosis was also used as a secondary data source to supplement the evidence presented in the AHRQ report. The draft practice guidelines were developed by consensus of the committee regarding the evidence. It was decided to create 2 separate components. The guideline recommendations were based on clear characterization of the evidence. The second component is a practice-of-care algorithm (see Supplemental Fig 2) that provides considerably more detail about how to implement the guidelines but is, necessarily, based less on available evidence and more on consensus of the committee members. When data were lacking, particularly in the

FROM THE AMERICAN ACADEMY OF PEDIATRICS

Evidence Quality	Preponderance of Benefit or Harm	Balance of Benefit and Harm
A. Well-designed RCTs or diagnostic studies on relevant population	Strong recommendation	Option
B. RCTs or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies	Recommendation	
C. Observational studies (case-control and cohort design)	Option	No Rec
D. Expert opinion, case reports, reasoning from first principles	Strong recommendation	Option
X. Exceptional situations in which validating studies cannot be performed and there is a clear preponderance of benefit or harm	Recommendation	

FIGURE 1

Integrating evidence-quality appraisal with an assessment of the anticipated balance between benefits and harms if a policy is conducted leads to designation of a policy as a strong recommendation, recommendation, option, or no recommendation. The evidence is discussed in more detail in a technical report that will follow in a later publication. RCT indicates randomized controlled trial; Rec, recommendation.

process-of-care algorithmic portion of the guidelines, a combination of evidence and expert consensus was used. Action statements labeled “strong recommendation” or “recommendation” were based on high- to moderate-quality scientific evidence and a preponderance of benefit over harm.⁶ Option-level action statements were based on lesser-quality or limited data and expert consensus or high-quality evidence with a balance between benefits and harms. These clinical options are interventions that a reasonable health care provider might or might not wish to implement in his or her practice. The quality of evidence supporting each recommendation and the strength of each recommendation were assessed by the committee member most experienced in epidemiology and graded according to AAP policy (Fig 1).⁶

The guidelines and process-of-care algorithm underwent extensive peer review by committees, sections, councils, and task forces within the AAP; numerous outside organizations; and other individuals identified by the subcommittee. Liaisons to the subcommittee also were invited to distribute the draft to entities within their organizations. The re-

sulting comments were compiled and reviewed by the chairperson, and relevant changes were incorporated into the draft, which was then reviewed by the full committee.

ABOUT THIS GUIDELINE

Key Action Statements

In light of the concerns highlighted previously and informed by the available evidence, the AAP has developed 6 action statements for the evaluation, diagnosis, and treatment of ADHD in children. These action statements provide for consistent and quality care for children and families with concerns about or symptoms that suggest attention disorders or problems.

Context

This guideline is intended to be integrated with the broader algorithms developed as part of the mission of the AAP Task Force on Mental Health.⁷

Implementation: A Process-of-Care Algorithm

The AAP recognizes the challenge of instituting practice changes and adopting new recommendations for care. To address the need, a process-of-care algorithm has been devel-

oped and has been used in the revision of the AAP ADHD toolkit.

Implementation: Preparing the Practice

Full implementation of the action statements described in this guideline and the process-of-care algorithm might require changes in office procedures and/or preparatory efforts to identify community resources. The section titled “Preparing the Practice” in the process-of-care algorithm and further information can be found in the supplement to the Task Force on Mental Health report.⁷ It is important to document all aspects of the diagnostic and treatment procedures in the patients’ records. Use of rating scales for the diagnosis of ADHD and assessment for comorbid conditions and as a method for monitoring treatment as described in the process algorithm (see Supplemental Fig 2), as well as information provided to parents such as management plans, can help facilitate a clinician’s accurate documentation of his or her process.

Note

The AAP acknowledges that some primary care clinicians might not be confident of their ability to successfully diagnose and treat ADHD in a child because of the child’s age, co-existing conditions, or other concerns. At any point at which a clinician feels that he or she is not adequately trained or is uncertain about making a diagnosis or continuing with treatment, a referral to a pediatric or mental health subspecialist should be made. If a diagnosis of ADHD or other condition is made by a subspecialist, the primary care clinician should develop a management strategy with the subspecialist that ensures that the child will continue to receive appropriate care consistent with a medical home model wherein the pediatrician part-

ners with parents so that both health and mental health needs are integrated.

KEY ACTION STATEMENTS FOR THE EVALUATION, DIAGNOSIS, TREATMENT, AND MONITORING OF ADHD IN CHILDREN AND ADOLESCENTS

Action statement 1: The primary care clinician should initiate an evaluation for ADHD for any child 4 through 18 years of age who presents with academic or behavioral problems and symptoms of inattention, hyperactivity, or impulsivity (quality of evidence B/strong recommendation).

Evidence Profile

- **Aggregate evidence quality:** B.
- **Benefits:** In a considerable number of children, ADHD goes undiagnosed. Primary care clinicians' systematic identification of children with these problems will likely decrease the rate of undiagnosed and untreated ADHD in children.
- **Harms/risks/costs:** Children in whom ADHD is inappropriately diagnosed might be labeled inappropriately, or another condition might be missed, and they might receive treatments that will not benefit them.
- **Benefits-harms assessment:** The high prevalence of ADHD and limited mental health resources require primary care pediatricians to play a significant role in the care of their patients with ADHD so that children with this condition receive the appropriate diagnosis and treatment. Treatments available have shown good evidence of efficacy, and lack of treatment results in a risk for impaired outcomes.
- **Value judgments:** The committee considered the requirements for establishing the diagnosis, the prevalence of ADHD, and the efficacy and adverse effects of treatment as well as the long-term outcomes.

- **Role of patient preferences:** Success with treatment depends on patient and family preference, which has to be taken into account.

- **Exclusions:** None.

- **Intentional vagueness:** The limits between what can be handled by a primary care clinician and what should be referred to a subspecialist because of the varying degrees of skill among primary care clinicians.

- **Strength: strong recommendation.**

The basis for this recommendation is essentially unchanged from that in the previous guideline. ADHD is the most common neurobehavioral disorder in children and occurs in approximately 8% of children and youth⁸⁻¹⁰; the number of children with this condition is far greater than can be managed by the mental health system. There is now increased evidence that appropriate diagnosis can be provided for preschool-aged children¹¹ (4–5 years of age) and for adolescents.¹²

Action statement 2: To make a diagnosis of ADHD, the primary care clinician should determine that *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR)* criteria have been met (including documentation of impairment in more than 1 major setting), and information should be obtained primarily from reports from parents or guardians, teachers, and other school and mental health clinicians involved in the child's care. The primary care clinician should also rule out any alternative cause (quality of evidence B/strong recommendation).

Evidence Profile

- **Aggregate evidence quality:** B.
- **Benefits:** The use of DSM-IV criteria has led to more uniform categorization of the condition across professional disciplines.

- **Harms/risks/costs:** The DSM-IV system does not specifically provide for developmental-level differences and might lead to some misdiagnoses.

- **Benefits-harms assessment:** The benefits far outweigh the harm.

- **Value judgments:** The committee took into consideration the importance of coordination between pediatric and mental health services.

- **Role of patient preferences:** Although there is some stigma associated with mental disorder diagnoses resulting in some families preferring other diagnoses, the need for better clarity in diagnoses was felt to outweigh this preference.

- **Exclusions:** None.

- **Intentional vagueness:** None.

- **Strength: strong recommendation.**

As with the findings in the previous guideline, the DSM-IV criteria continue to be the criteria best supported by evidence and consensus. Developed through several iterations by the American Psychiatric Association, the DSM-IV criteria were created through use of consensus and an expanding research foundation.¹³ The DSM-IV system is used by professionals in psychiatry, psychology, health care systems, and primary care. Use of DSM-IV criteria, in addition to having the best evidence to date for criteria for ADHD, also affords the best method for communication across clinicians and is established with third-party payers. The criteria are under review for the development of the DSM-V, but these changes will not be available until at least 1 year after the publication of this current guideline. The diagnostic criteria have not changed since the previous guideline and are presented in Supplemental Table 2. An anticipated change in the DSM-V is increasing the age limit for when ADHD needs to have first presented from 7 to 12 years.¹⁴

FROM THE AMERICAN ACADEMY OF PEDIATRICS

Special Circumstances: Preschool-aged Children (4–5 Years Old)

There is evidence that the diagnostic criteria for ADHD can be applied to preschool-aged children; however, the subtypes detailed in the DSM-IV might not be valid for this population.^{15–21} A review of the literature, including the multisite study of the efficacy of methylphenidate in preschool-aged children, revealed that the criteria could appropriately identify children with the condition.¹¹ However, there are added challenges in determining the presence of key symptoms. Preschool-aged children are not likely to have a separate observer if they do not attend a preschool or child care program, and even if they do attend, staff in those programs might be less qualified than certified teachers to provide accurate observations. Here, too, focused checklists can help physicians in the diagnostic evaluation, although only the Conners Comprehensive Behavior Rating Scales and the ADHD Rating Scale IV are DSM-IV–based scales that have been validated in preschool-aged children.²²

When there are concerns about the availability or quality of nonparent observations of a child's behavior, physicians may recommend that parents complete a parent-training program before confirming an ADHD diagnosis for preschool-aged children and consider placement in a qualified preschool program if they have not done so already. Information can be obtained from parents and teachers through the use of validated DSM-IV–based ADHD rating scales. The parent-training program must include helping parents develop age-appropriate developmental expectations and specific management skills for problem behaviors. The clinician may obtain reports from the parenting class instructor about the parents' ability to manage their children, and if the children are

in programs in which they are directly observed, instructors can report information about the core symptoms and function of the child directly. Qualified preschool programs include programs such as Head Start or other public prekindergarten programs. Preschool-aged children who display significant emotional or behavioral concerns might also qualify for Early Childhood Special Education services through their local school districts, and the evaluators for these programs and/or Early Childhood Special Education teachers might be excellent reporters of core symptoms.

Special Circumstances: Adolescents

Obtaining teacher reports for adolescents might be more challenging, because many adolescents will have multiple teachers. Likewise, parents might have less opportunity to observe their adolescent's behaviors than they had when their children were younger. Adolescents' reports of their own behaviors often differ from those of other observers, because they tend to minimize their own problematic behaviors.^{23–25} Adolescents are less likely to exhibit overt hyperactive behavior. Despite the difficulties, clinicians need to try to obtain (with agreement from the adolescent) information from at least 2 teachers as well as information from other sources such as coaches, school guidance counselors, or leaders of community activities in which the adolescent participates. In addition, it is unusual for adolescents with behavioral/attention problems not to have been previously given a diagnosis of ADHD. Therefore, it is important to establish the younger manifestations of the condition that were missed and to strongly consider substance use, depression, and anxiety as alternative or co-occurring diagnoses. Adolescents with ADHD, especially when untreated, are at greater risk of substance abuse.²⁶ In addition, the risks of

mood and anxiety disorders and risky sexual behaviors increase during adolescence.¹²

Special Circumstances: Inattention or Hyperactivity/Impulsivity (Problem Level)

Teachers, parents, and child health professionals typically encounter children with behaviors relating to activity level, impulsivity, and inattention who might not fully meet DSM-IV criteria. The DSM-PC³ provides a guide to the more common behaviors seen in pediatrics. The manual describes common variations in behavior as well as more problematic behaviors at levels of less impairment than those specified in the DSM-IV.

The behavioral descriptions of the DSM-PC have not yet been tested in community studies to determine the prevalence or severity of developmental variations and problems in the areas of inattention, hyperactivity, or impulsivity. They do, however, provide guidance to clinicians regarding elements of treatment for children with problems with mild-to-moderate inattention, hyperactivity, or impulsivity. The DSM-PC also considers environmental influences on a child's behavior and provides information on differential diagnosis with a developmental perspective.

Action statement 3: In the evaluation of a child for ADHD, the primary care clinician should include assessment for other conditions that might coexist with ADHD, including emotional or behavioral (eg, anxiety, depressive, oppositional defiant, and conduct disorders), developmental (eg, learning and language disorders or other neurodevelopmental disorders), and physical (eg, tics, sleep apnea) conditions (quality of evidence B/strong recommendation).

Evidence Profile

- **Aggregate evidence quality:** B.
- **Benefits:** Identifying coexisting conditions is important for developing the most appropriate treatment plan.
- **Harms/risks/costs:** The major risk is misdiagnosing the conditions and providing inappropriate care.
- **Benefits-harms assessment:** There is a preponderance of benefit over harm.
- **Value judgments:** The committee members took into consideration the common occurrence of coexisting conditions and the importance of addressing them in making this recommendation.
- **Role of patient preferences:** None.
- **Exclusions:** None.
- **Intentional vagueness:** None.
- **Strength:** strong recommendation.

A variety of other behavioral, developmental, and physical conditions can coexist in children who are evaluated for ADHD. These conditions include, but are not limited to, learning problems, language disorder, disruptive behavior, anxiety, mood disorders, tic disorders, seizures, developmental coordination disorder, or sleep disorders.^{23,24,27–38} In some cases, the presence of a coexisting condition will alter the treatment of ADHD. The primary care clinician might benefit from additional support and guidance or might need to refer a child with ADHD and coexisting conditions, such as severe mood or anxiety disorders, to subspecialists for assessment and management. The subspecialists could include child psychiatrists, developmental-behavioral pediatricians, neurodevelopmental disability physicians, child neurologists, or child or school psychologists.

Given the likelihood that another condition exists, primary care clinicians should conduct assessments that determine or at least identify the risk of coexisting conditions. Through its Task Force on Mental

Health, the AAP has developed algorithms and a toolkit³⁹ for assessing and treating (or comanaging) the most common developmental disorders and mental health concerns in children. These resources might be useful in assessing children who are being evaluated for ADHD. Payment for evaluation and treatment must cover the fixed and variable costs of providing the services, as noted in the AAP policy statement “Scope of Health Care Benefits for Children From Birth Through Age 26.”⁴⁰

Special Circumstances: Adolescents

Clinicians should assess adolescent patients with newly diagnosed ADHD for symptoms and signs of substance abuse; when these signs and symptoms are found, evaluation and treatment for addiction should precede treatment for ADHD, if possible, or careful treatment for ADHD can begin if necessary.²⁵

Action statement 4: The primary care clinician should recognize ADHD as a chronic condition and, therefore, consider children and adolescents with ADHD as children and youth with special health care needs. Management of children and youth with special health care needs should follow the principles of the chronic care model and the medical home (quality of evidence B/strong recommendation).

Evidence Profile

- **Aggregate evidence quality:** B.
- **Benefits:** The recommendation describes the coordinated services most appropriate for managing the condition.
- **Harms/risks/costs:** Providing the services might be more costly.
- **Benefits-harms assessment:** There is a preponderance of benefit over harm.
- **Value judgments:** The committee members considered the value of medical

home services when deciding to make this recommendation.

- **Role of patient preferences:** Family preference in how these services are provided is an important consideration.
- **Exclusions:** None.
- **Intentional vagueness:** None.
- **Strength:** strong recommendation.

As in the previous guideline, this recommendation is based on the evidence that ADHD continues to cause symptoms and dysfunction in many children who have the condition over long periods of time, even into adulthood, and that the treatments available address symptoms and function but are usually not curative. Although the chronic illness model has not been specifically studied in children and youth with ADHD, it has been effective for other chronic conditions such as asthma,²³ and the medical home model has been accepted as the preferred standard of care.⁴¹ The management process is also helped by encouraging strong family-school partnerships.⁴²

Longitudinal studies have found that, frequently, treatments are not sustained despite the fact that long-term outcomes for children with ADHD indicate that they are at greater risk of significant problems if they discontinue treatment.⁴³ Because a number of parents of children with ADHD also have ADHD, extra support might be necessary to help those parents provide medication on a consistent basis and institute a consistent behavioral program. The medical home and chronic illness approach is provided in the process algorithm (Supplemental Fig 2). An important process in ongoing care is bidirectional communication with teachers and other school and mental health clinicians involved in the child's care as well as with parents and patients.

FROM THE AMERICAN ACADEMY OF PEDIATRICS

Special Circumstances: Inattention or Hyperactivity/Impulsivity (Problem Level)

Children with inattention or hyperactivity/impulsivity at the problem level (DSM-PC) and their families might also benefit from the same chronic illness and medical home principles.

Action statement 5: Recommendations for treatment of children and youth with ADHD vary depending on the patient's age.

Action statement 5a: For preschool-aged children (4–5 years of age), the primary care clinician should prescribe evidence-based parent- and/or teacher-administered behavior therapy as the first line of treatment (quality of evidence A/strong recommendation) and may prescribe methylphenidate if the behavior interventions do not provide significant improvement and there is moderate-to-severe continuing disturbance in the child's function. In areas in which evidence-based behavioral treatments are not available, the clinician needs to weigh the risks of starting medication at an early age against the harm of delaying diagnosis and treatment (quality of evidence B/recommendation).

Evidence Profile

- **Aggregate evidence quality:** A for behavior; B for methylphenidate.
- **Benefits:** Both behavior therapy and methylphenidate have been demonstrated to reduce behaviors associated with ADHD and improve function.
- **Harms/risks/costs:** Both therapies increase the cost of care, and behavior therapy requires a higher level of family involvement, whereas methylphenidate has some potential adverse effects.
- **Benefits-harms assessment:** Given the risks of untreated ADHD, the benefits outweigh the risks.
- **Value judgments:** The committee mem-

bers included the effects of untreated ADHD when deciding to make this recommendation.

- **Role of patient preferences:** Family preference is essential in determining the treatment plan.
- **Exclusions:** None.
- **Intentional vagueness:** None.
- **Strength:** strong recommendation.

Action statement 5b: For elementary school-aged children (6–11 years of age), the primary care clinician should prescribe FDA-approved medications for ADHD (quality of evidence A/strong recommendation) and/or evidence-based parent- and/or teacher-administered behavior therapy as treatment for ADHD, preferably both (quality of evidence B/strong recommendation). The evidence is particularly strong for stimulant medications and sufficient but less strong for atomoxetine, extended-release guanfacine, and extended-release clonidine (in that order) (quality of evidence A/strong recommendation). The school environment, program, or placement is a part of any treatment plan.

Evidence Profile

- **Aggregate evidence quality:** A for treatment with FDA-approved medications; B for behavior therapy.
- **Benefits:** Both behavior therapy and FDA-approved medications have been demonstrated to reduce behaviors associated with ADHD and improve function.
- **Harms/risks/costs:** Both therapies increase the cost of care, and behavior therapy requires a higher level of family involvement, whereas FDA-approved medications have some potential adverse effects.
- **Benefits-harms assessment:** Given the risks of untreated ADHD, the benefits outweigh the risks.
- **Value judgments:** The committee members included the effects of untreated

ADHD when deciding to make this recommendation.

- **Role of patient preferences:** Family preference, including patient preference, is essential in determining the treatment plan.
- **Exclusions:** None.
- **Intentional vagueness:** None.
- **Strength:** strong recommendation.

Action statement 5c: For adolescents (12–18 years of age), the primary care clinician should prescribe FDA-approved medications for ADHD with the assent of the adolescent (quality of evidence A/strong recommendation) and may prescribe behavior therapy as treatment for ADHD (quality of evidence C/recommendation), preferably both.

Evidence Profile

- **Aggregate evidence quality:** A for medications; C for behavior therapy.
- **Benefits:** Both behavior therapy and FDA-approved medications have been demonstrated to reduce behaviors associated with ADHD and improve function.
- **Harms/risks/costs:** Both therapies increase the cost of care, and behavior therapy requires a higher level of family involvement, whereas FDA-approved medications have some potential adverse effects.
- **Benefits-harms assessment:** Given the risks of untreated ADHD, the benefits outweigh the risks.
- **Value judgments:** The committee members included the effects of untreated ADHD when deciding to make this recommendation.
- **Role of patient preferences:** Family preference, including patient preference, is essential in determining the treatment plan.
- **Exclusions:** None.
- **Intentional vagueness:** None.
- **Strength:** strong recommendation/recommendation.

Medication

Similar to the recommendations from the previous guideline, stimulant medications are highly effective for most children in reducing core symptoms of ADHD.⁴⁴ One selective norepinephrine-reuptake inhibitor (atomoxetine^{45,46}) and 2 selective α_2 -adrenergic agonists (extended-release guanfacine^{47,48} and extended-release clonidine⁴⁹) have also demonstrated efficacy in reducing core symptoms. Because norepinephrine-reuptake inhibitors and α_2 -adrenergic agonists are newer, the evidence base that supports them—although adequate for FDA approval—is considerably smaller than that for stimulants. None of them have been approved for use in preschool-aged children. Compared with stimulant medications that have an effect size [effect size = (treatment mean – control mean)/control SD] of approximately 1.0,⁵⁰ the effects of the nonstimulants are slightly weaker; atomoxetine has an effect size of approximately 0.7, and extended-release guanfacine and extended-release clonidine also have effect sizes of approximately 0.7.

The accompanying process-of-care algorithm provides a list of the currently available FDA-approved medications for ADHD (Supplemental Table 3). Characteristics of each medication are provided to help guide the clinician's choice in prescribing medication.

As was identified in the previous guideline, the most common stimulant adverse effects are appetite loss, abdominal pain, headaches, and sleep disturbance. The results of the Multimodal Therapy of ADHD (MTA) study revealed a more persistent effect of stimulants on decreasing growth velocity than have most previous studies, particularly when children were on higher and more consistently administered doses. The effects diminished by the third year of treatment, but no com-

pensatory rebound effects were found.⁵¹ However, diminished growth was in the range of 1 to 2 cm. An uncommon additional significant adverse effect of stimulants is the occurrence of hallucinations and other psychotic symptoms.⁵² Although concerns have been raised about the rare occurrence of sudden cardiac death among children using stimulant medications,⁵³ sudden death in children on stimulant medication is extremely rare, and evidence is conflicting as to whether stimulant medications increase the risk of sudden death.^{54–58} It is important to expand the history to include specific cardiac symptoms, Wolf-Parkinson-White syndrome, sudden death in the family, hypertrophic cardiomyopathy, and long QT syndrome. Preschool-aged children might experience increased mood lability and dysphoria.⁵⁹ For the nonstimulant atomoxetine, the adverse effects include initial somnolence and gastrointestinal tract symptoms, particularly if the dosage is increased too rapidly; decrease in appetite; increase in suicidal thoughts (less common); and hepatitis (rare). For the nonstimulant α_2 -adrenergic agonists extended-release guanfacine and extended-release clonidine, adverse effects include somnolence and dry mouth.

Only 2 medications have evidence to support their use as adjunctive therapy with stimulant medications sufficient to achieve FDA approval: extended-release guanfacine²⁶ and extended-release clonidine. Other medications have been used in combination off-label, but there is currently only anecdotal evidence for their safety or efficacy, so their use cannot be recommended at this time.

Special Circumstances: Preschool-aged Children

A number of special circumstances support the recommendation to initi-

ate ADHD treatment in preschool-aged children (ages 4–5 years) with behavioral therapy alone first.⁵⁷ These circumstances include:

- The multisite study of methylphenidate⁵⁷ was limited to preschool-aged children who had moderate-to-severe dysfunction.
- The study also found that many children (ages 4–5 years) experience improvements in symptoms with behavior therapy alone, and the overall evidence for behavior therapy in preschool-aged children is strong.
- Behavioral programs for children 4 to 5 years of age typically run in the form of group parent-training programs and, although not always compensated by health insurance, have a lower cost. The process algorithm (see Supplemental pages s15–16) contains criteria for the clinician to use in assessing the quality of the behavioral therapy. In addition, programs such as Head Start and Children and Adults With Attention Deficit Hyperactivity Disorder (CHADD) (www.chadd.org) might provide some behavioral supports.

Many young children with ADHD might still require medication to achieve maximum improvement, and medication is not contraindicated for children 4 through 5 years of age. However, only 1 multisite study has carefully assessed medication use in preschool-aged children. Other considerations in the recommendation about treating children 4 to 5 years of age with stimulant medications include:

- The study was limited to preschool-aged children who had moderate-to-severe dysfunction.
- Research has found that a number of young children (4–5 years of age) experience improvements in symptoms with behavior therapy alone.
- There are concerns about the possi-

FROM THE AMERICAN ACADEMY OF PEDIATRICS

ble effects on growth during this rapid growth period of preschool-aged children.

- There has been limited information about and experience with the effects of stimulant medication in children between the ages of 4 and 5 years.

Here, the criteria for enrollment (and, therefore, medication use) included measures of severity that distinguished treated children from the larger group of preschool-aged children with ADHD. Thus, before initiating medications, the physician should assess the severity of the child's ADHD. Given current data, only those preschool-aged children with ADHD who have moderate-to-severe dysfunction should be considered for medication. Criteria for this level of severity, based on the multisite study results,⁵⁷ are (1) symptoms that have persisted for at least 9 months, (2) dysfunction that is manifested in both the home and other settings such as preschool or child care, and (3) dysfunction that has not responded adequately to behavior therapy. The decision to consider initiating medication at this age depends in part on the clinician's assessment of the estimated developmental impairment, safety risks, or consequences for school or social participation that could ensue if medications are not initiated. It is often helpful to consult with a mental health specialist who has had specific experience with preschool-aged children if possible. Dextroamphetamine is the only medication approved by the FDA for use in children younger than 6 years of age. This approval, however, was based on less stringent criteria in force when the medication was approved rather than on empirical evidence of its safety and efficacy in this age group. Most of the evidence for the safety and efficacy of treating preschool-aged children with stimulant medications has been

from methylphenidate.⁵⁷ Methylphenidate evidence consists of 1 multisite study of 165 children and 10 other smaller single-site studies that included from 11 to 59 children (total of 269 children); 7 of the 10 single-site studies found significant efficacy. It must be noted that although there is moderate evidence that methylphenidate is safe and efficacious in preschool-aged children, its use in this age group remains off-label. Although the use of dextroamphetamine is on-label, the insufficient evidence for its safety and efficacy in this age group does not make it possible to recommend at this time.

If children do not experience adequate symptom improvement with behavior therapy, medication can be prescribed, as described previously. Evidence suggests that the rate of metabolizing stimulant medication is slower in children 4 through 5 years of age, so they should be given a lower dose to start, and the dose can be increased in smaller increments. Maximum doses have not been adequately studied.⁵⁷

Special Circumstances: Adolescents

As noted previously, before beginning medication treatment for adolescents with newly diagnosed ADHD, clinicians should assess these patients for symptoms of substance abuse. When substance use is identified, assessment when off the abusive substances should precede treatment for ADHD (see the Task Force on Mental Health report⁷). Diversion of ADHD medication (use for other than its intended medical purposes) is also a special concern among adolescents⁵⁸; clinicians should monitor symptoms and prescription-refill requests for signs of misuse or diversion of ADHD medication and consider prescribing medications with no abuse potential, such as atomoxetine (Strattera [Eli Lilly Co, Indianapolis, IN]) and

extended-release guanfacine (Intuniv [Shire US Inc, Wayne, PA]) or extended-release clonidine (Kapvay [Shionogi Inc, Florham Park, NJ]) (which are not stimulants) or stimulant medications with less abuse potential, such as lisdexamfetamine (Vyvanse [Shire US Inc]), dermal methylphenidate (Daytrana [Noven Therapeutics, LLC, Miami, FL]), or OROS methylphenidate (Concerta [Janssen Pharmaceuticals, Inc, Titusville, NJ]). Because lisdexamfetamine is dextroamphetamine, which contains an additional lysine molecule, it is only activated after ingestion, when it is metabolized by erythrocyte cells to dexamphetamine. The other preparations make extraction of the stimulant medication more difficult.

Given the inherent risks of driving by adolescents with ADHD, special concern should be taken to provide medication coverage for symptom control while driving. Longer-acting or late-afternoon, short-acting medications might be helpful in this regard.⁵⁸

Special Circumstances: Inattention or Hyperactivity/Impulsivity (Problem Level)

Medication is not appropriate for children whose symptoms do not meet DSM-IV criteria for diagnosis of ADHD, although behavior therapy does not require a specific diagnosis, and many of the efficacy studies have included children without specific mental behavioral disorders.

Behavior Therapy

Behavior therapy represents a broad set of specific interventions that have a common goal of modifying the physical and social environment to alter or change behavior. Behavior therapy usually is implemented by training parents in specific techniques that improve their abilities to modify and

TABLE 1 Evidence-Based Behavioral Treatments for ADHD

Intervention Type	Description	Typical Outcome(s)	Median Effect Size ^a
Behavioral parent training (BPT)	Behavior-modification principles provided to parents for implementation in home settings	Improved compliance with parental commands; improved parental understanding of behavioral principles; high levels of parental satisfaction with treatment	0.55
Behavioral classroom management	Behavior-modification principles provided to teachers for implementation in classroom settings	Improved attention to instruction; improved compliance with classroom rules; decreased disruptive behavior; improved work productivity	0.61
Behavioral peer interventions (BPI) ^b	Interventions focused on peer interactions/relationships; these are often group-based interventions provided weekly and include clinic-based social-skills training used either alone or concurrently with behavioral parent training and/or medication	Office-based interventions have produced minimal effects; interventions have been of questionable social validity; some studies of BPI combined with clinic-based BPT found positive effects on parent ratings of ADHD symptoms; no differences on social functioning or parent ratings of social behavior have been revealed	

^a Effect size = (treatment median — control median)/control SD.

^b The effect size for behavioral peer interventions is not reported, because the effect sizes for these studies represent outcomes associated with combined interventions. A lower effect size means that they have less of an effect. The effect sizes found are considered moderate.
Adapted from Pelham W, Fabiano GA. *J Clin Child Adolesc Psychol*. 2008;37(1):184–214.

shape their child's behavior and to improve the child's ability to regulate his or her own behavior. The training involves techniques to more effectively provide rewards when their child demonstrates the desired behavior (eg, positive reinforcement), learn what behaviors can be reduced or eliminated by using planned ignoring as an active strategy (or using praising and ignoring in combination), or provide appropriate consequences or punishments when their child fails to meet the goals (eg, punishment). There is a need to consistently apply rewards and consequences as tasks are achieved and then to gradually increase the expectations for each task as they are mastered to shape behaviors. Although behavior therapy shares a set of principles, individual programs introduce different techniques and strategies to achieve the same ends.

Table 1 lists the major behavioral intervention approaches that have been demonstrated to be evidence based for the management of ADHD in 3 different types of settings. The table is based on 22 studies, each completed between 1997 and 2006.

Evidence for the effectiveness of behavior therapy in children with ADHD is

derived from a variety of studies^{60–62} and an Agency for Healthcare Research and Quality review.⁶ The diversity of interventions and outcome measures makes meta-analysis of the effects of behavior therapy alone or in association with medications challenging. The long-term positive effects of behavior therapy have yet to be determined. Ongoing adherence to a behavior program might be important; therefore, implementing a chronic care model for child health might contribute to the long-term effects.⁶³

Study results have indicated positive effects of behavior therapy when combined with medications. Most studies that compared behavior therapy to stimulants found a much stronger effect on ADHD core symptoms from stimulants than from behavior therapy. The MTA study found that combined treatment (behavior therapy and stimulant medication) was not significantly more efficacious than treatment with medication alone for the core symptoms of ADHD after correction for multiple tests in the primary analysis.⁶⁴ However, a secondary analysis of a combined measure of parent and teacher ratings of ADHD symptoms revealed a significant advantage

for the combination with a small effect size of $d = 0.26$.⁶⁵ However, the same study also found that the combined treatment compared with medication alone did offer greater improvements on academic and conduct measures when ADHD coexisted with anxiety and when children lived in low socioeconomic environments. In addition, parents and teachers of children who were receiving combined therapy were significantly more satisfied with the treatment plan. Finally, the combination of medication management and behavior therapy allowed for the use of lower dosages of stimulants, which possibly reduced the risk of adverse effects.⁶⁶

School Programming and Supports

Behavior therapy programs coordinating efforts at school as well as home might enhance the effects. School programs can provide classroom adaptations, such as preferred seating, modified work assignments, and test modifications (to the location at which it is administered and time allotted for taking the test), as well as behavior plans as part of a 504 Rehabilitation Act Plan or special education Individualized Education Program (IEP) under the "other health impairment" designation as part of the Individuals With

FROM THE AMERICAN ACADEMY OF PEDIATRICS

Disability Education Act (IDEA).⁶⁷ It is helpful for clinicians to be aware of the eligibility criteria in their state and school district to advise families of their options. Youths documented to have ADHD can also get permission to take college-readiness tests in an untimed manner by following appropriate documentation guidelines.⁶⁸

The effect of coexisting conditions on ADHD treatment is variable. In some cases, treatment of the ADHD resolves the coexisting condition. For example, treatment of ADHD might resolve oppositional defiant disorder or anxiety.⁶⁹ However, sometimes the co-occurring condition might require treatment that is in addition to the treatment for ADHD. Some coexisting conditions can be treated in the primary care setting, but others will require referral and co-management with a subspecialist.

Action statement 6: Primary care clinicians should titrate doses of medication for ADHD to achieve maximum benefit with minimum adverse effects (quality of evidence B/strong recommendation).

Evidence Profile

- **Aggregate evidence quality:** B.
- **Benefits:** The optimal dose of medication is required to reduce core symptoms to or as close to the levels of children without ADHD.
- **Harms/risks/costs:** Higher levels of medication increase the chances of adverse effects.
- **Benefits-harms assessment:** The importance of adequately treating ADHD outweighs the risk of adverse effects.
- **Value judgments:** The committee members included the effects of untreated ADHD when deciding to make this recommendation.
- **Role of patient preferences:** The families' preferences and comfort need to be taken into consideration in developing a titration plan.
- **Exclusions:** None.

- **Intentional vagueness:** None.
- **Strength:** strong recommendation.

The findings from the MTA study suggested that more than 70% of children and youth with ADHD respond to one of the stimulant medications at an optimal dose when a systematic trial is used.⁶⁵ Children in the MTA who were treated in the community with care as usual from whomever they chose or to whom they had access received lower doses of stimulants with less frequent monitoring and had less optimal results.⁶⁵ Because stimulants might produce positive but suboptimal effects at a low dose in some children and youth, titration to maximum doses that control symptoms without adverse effects is recommended instead of titration strictly on a milligram-per-kilogram basis.

Education of parents is an important component in the chronic illness model to ensure their cooperation in efforts to reach appropriate titration (remembering that the parents themselves might be challenged significantly by ADHD).^{69,70} The primary care clinician should alert parents and children that changing medication dose and occasionally changing a medication might be necessary for optimal medication management, that the process might require a few months to achieve optimal success, and that medication efficacy should be systematically monitored at regular intervals. Because stimulant medication effects are seen immediately, trials of different doses of stimulants can be accomplished in a relatively short time period. Stimulant medications can be effectively titrated on a 3- to 7-day basis.⁶⁵

It is important to note that by the 3-year follow-up of 14-month MTA interventions (optimal medications management, optimal behavioral management, the combination of the 2, or community treatment), all differences among the initial 4

groups were no longer present. After the initial 14-month intervention, the children no longer received the careful monthly monitoring provided by the study and went back to receiving care from their community providers. Their medications and doses varied, and a number of them were no longer taking medication. In children still on medication, the growth deceleration was only seen for the first 2 years and was in the range of 1 to 2 cm.

CONCLUSION

Evidence continues to be fairly clear with regard to the legitimacy of the diagnosis of ADHD and the appropriate diagnostic criteria and procedures required to establish a diagnosis, identify co-occurring conditions, and treat effectively with both behavioral and pharmacologic interventions. However, the steps required to sustain appropriate treatments and achieve successful long-term outcomes still remain a challenge. To provide more detailed information about how the recommendations of this guideline can be accomplished, a more detailed but less strongly evidence-based algorithm is provided as a companion article.

AREAS FOR FUTURE RESEARCH

Some specific research topics pertinent to the diagnosis and treatment of ADHD or developmental variations or problems in children and adolescents in primary care to be explored include:

- identification or development of reliable instruments suitable to use in primary care to assess the nature or degree of functional impairment in children/adolescents with ADHD and monitor improvement over time;
- study of medications and other therapies used clinically but not approved by the FDA for ADHD, such as

electroencephalographic biofeedback;

- determination of the optimal schedule for monitoring children/adolescents with ADHD, including factors for adjusting that schedule according to age, symptom severity, and progress reports;
- evaluation of the effectiveness of various school-based interventions;
- comparisons of medication use and effectiveness in different ages, including both harms and benefits;
- development of methods to involve parents and children/adolescents in their own care and improve adherence to both behavior and medication treatments;
- standardized and documented tools that will help primary care providers in identifying coexisting conditions;
- development and determination of effective electronic and Web-based systems to help gather information to diagnose and monitor children with ADHD;
- improved systems of communication with schools and mental health professionals, as well as other community agencies, to provide effective collaborative care;
- evidence for optimal monitoring by

some aspects of severity, disability, or impairment; and

- long-term outcomes of children first identified with ADHD as preschool-aged children.

SUBCOMMITTEE ON ATTENTION DEFICIT HYPERACTIVITY DISORDER (OVERSIGHT BY THE STEERING COMMITTEE ON QUALITY IMPROVEMENT AND MANAGEMENT, 2005–2011)

WRITING COMMITTEE

- Mark Wolraich, MD, Chair – (periodic consultant to Shire, Eli Lilly, Shinogi, and Next Wave Pharmaceuticals)
- Lawrence Brown, MD – (neurologist; AAP Section on Neurology; Child Neurology Society) (Safety Monitoring Board for Best Pharmaceuticals for Children Act for National Institutes of Health)
- Ronald T. Brown, PhD – (child psychologist; Society for Pediatric Psychology) (no conflicts)
- George DuPaul, PhD – (school psychologist; National Association of School Psychologists) (participated in clinical trial on Vyvanse effects on college students with ADHD, funded by Shire; published 2 books on ADHD and receives royalties)
- Marian Earls, MD – (general pediatrician with QI expertise, developmental and behavioral pediatrician) (no conflicts)
- Heidi M. Feldman, MD, PhD – (developmental and behavioral pediatrician; Society for Developmental and Behavioral Pediatrics) (no conflicts)

Theodore G. Ganiats, MD – (family physician; American Academy of Family Physicians) (no conflicts)

Beth Kaplanek, RN, BSN – (parent advocate, Children and Adults With Attention Deficit Hyperactivity Disorder [CHADD]) (no conflicts)

Bruce Meyer, MD – (general pediatrician) (no conflicts)

James Perrin, MD – (general pediatrician; AAP Mental Health Task Force; AAP Council on Children With Disabilities) (consultant to Pfizer not related to ADHD)

Karen Pierce, MD – (child psychiatrist; American Academy of Child and Adolescent Psychiatry) (no conflicts)

Michael Reiff, MD – (developmental and behavioral pediatrician; AAP Section on Developmental and Behavioral Pediatrics) (no conflicts)

Martin T. Stein, MD – (developmental and behavioral pediatrician; AAP Section on Developmental and Behavioral Pediatrics) (no conflicts)

Susanna Visser, MS – (epidemiologist) (no conflicts)

CONSULTANT

Melissa Capers, MA, MFA – (medical writer) (no conflicts)

STAFF

Caryn Davidson, MA

ACKNOWLEDGMENTS

This guideline was developed with support from the Partnership for Policy Implementation (PPI) initiative. Physicians trained in medical informatics were involved with formatting the algorithm and helping to keep the key action statements actionable, decidable, and executable.

REFERENCES

1. American Academy of Pediatrics, Committee on Quality Improvement and Subcommittee on Attention-Deficit/Hyperactivity Disorder. Clinical practice guideline: diagnosis and evaluation of the child with attention-deficit/hyperactivity disorder. *Pediatrics*. 2000;105(5):1158–1170.
2. American Academy of Pediatrics, Subcommittee on Attention-Deficit/Hyperactivity Disorder, Committee on Quality Improvement. Clinical practice guideline: treatment of the school-aged child with attention-deficit/hyperactivity disorder. *Pediatrics*. 2001;108(4):1035–1044.
3. Wolraich ML, Felice ME, Drotar DD. *The Classification of Child and Adolescent Mental Conditions in Primary Care: Diagnostic and Statistical Manual for Primary Care (DSM-PC), Child and Adolescent Version*. Elk Grove, IL: American Academy of Pediatrics; 1996.
4. EndNote [computer program]. 10th ed. Carlsbad, CA: Thompson Reuters; 2008.
5. Charach A, Dashti B, Carson P, et al. *Attention Deficit Hyperactivity Disorder: Effectiveness of Treatment in At-risk Preschoolers; Long-term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment*. Rockville, MD: Agency for Healthcare Research and Quality; 2011. Comparative Effectiveness Review. 2011; in press.
6. American Academy of Pediatrics, Steering Committee on Quality Improvement. Classifying recommendations for clinical practice guidelines. *Pediatrics*. 2004;114(3):874–877.
7. Foy JM; American Academy of Pediatrics Task Force on Mental Health. Enhancing pediatric mental health care: report from the American Academy of Pediatrics Task Force on Mental Health. Introduction. *Pediatrics*. 2010;125(suppl 3):S69–S174.
8. Visser SM, Leseane CA, Perou R. National estimates and factors associated with medication treatment for childhood attention-deficit/hyperactivity disorder. *Pediatrics*. 2007;119(suppl 1):S99–S106.
9. Centers for Disease Control and Prevention. Mental health in the United States: prevalence of diagnosis and medication treatment for attention-deficit/

FROM THE AMERICAN ACADEMY OF PEDIATRICS

- hyperactivity disorder—United States, 2003. *MMWR Morb Mortal Wkly Rep*. 2005; 54(34):842–847
10. Centers for Disease Control and Prevention. Increasing prevalence of parent-reported attention deficit/hyperactivity disorder among children: United States, 2003–2007. *MMWR Morb Mortal Wkly Rep*. 2010;59(44):1439–1443
 11. Egger HL, Kondo D, Angold A. The epidemiology and diagnostic issues in preschool attention-deficit/hyperactivity disorder. *Infant Young Child*. 2006;18(2):109–122
 12. Wolraich ML, Wimbrelman CJ, Brown TE, et al. Attention-deficit/hyperactivity disorder among adolescents: a review of the diagnosis, treatment, and clinical implications. *Pediatrics*. 2005;115(6):1734–1746
 13. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Text Revision (DSM-IV-TR)*. Washington, DC: American Psychiatric Association; 2000
 14. American Psychiatric Association. Diagnostic criteria for attention deficit/hyperactivity disorder. Available at: www.dsm5.org/ProposedRevisions/Pages/proposedrevision.aspx?rid=383. Accessed September 30, 2011
 15. Lahey BB, Pelham WE, Stein MA, et al. Validity of DSM-IV attention-deficit/hyperactivity disorder for younger children [published correction appears in *J Am Acad Child Adolesc Psychiatry*. 1999;38(2):222]. *J Am Acad Child Adolesc Psychiatry*. 1998;37(7):695–702
 16. Pavuluri MN, Luk SL, McGee R. Parent reported preschool attention deficit hyperactivity: measurement and validity. *Eur Child Adolesc Psychiatry*. 1999;8(2):128–133
 17. Harvey EA, Youngwirth SD, Thakar DA, Errazuriz PA. Predicting attention-deficit/hyperactivity disorder and oppositional defiant disorder from preschool diagnostic assessments. *J Consult Clin Psychol*. 2009; 77(2):348–354
 18. Keenan K, Wakschlag LS. More than the terrible twos: the nature and severity of behavior problems in clinic-referred preschool children. *J Abnorm Child Psychol*. 2000; 28(1):33–48
 19. Gadow KD, Nolan EE, Litcher L, et al. Comparison of attention-deficit/hyperactivity disorder symptoms subtypes in Ukrainian schoolchildren. *J Am Acad Child Adolesc Psychiatry*. 2000;39(12):1520–1527
 20. Sprafkin J, Volpe RJ, Gadow KD, Nolan EE, Kelly K. A DSM-IV-referenced screening instrument for preschool children: the Early Childhood Inventory-4. *J Am Acad Child Adolesc Psychiatry*. 2002;41(5):604–612
 21. Poblano A, Romero E. ECI-4 screening of attention deficit/hyperactivity disorder and co-morbidity in Mexican preschool children: preliminary results. *Arg Neuropsiquiatr*. 2006;84(4):932–938
 22. McGee KE, DuPaul GJ, Haley E, Shelton TL. Parent and teacher ratings of attention-deficit/hyperactivity disorder in preschool: the ADHD Rating Scale-IV Preschool Version. *J Psychopathol Behav Assess*. 2007;29(4):269–278
 23. Young J. Common comorbidities seen in adolescents with attention-deficit/hyperactivity disorder. *Adolesc Med State Art Rev*. 2008;19(2):216–228, vii
 24. Freeman R; Tourette Syndrome International Database Consortium. Tic disorders and ADHD: answers from a worldwide clinical dataset on Tourette syndrome [published correction appears in *Eur Child Adolesc Psychiatry*. 2007; 16(8):536]. *Eur Child Adolesc Psychiatry*. 2007;16(1 suppl):15–25
 25. Riggs P. Clinical approach to treatment of ADHD in adolescents with substance use disorders and conduct disorder. *J Am Acad Child Adolesc Psychiatry*. 1998;37(3):351–352
 26. Kratochvil CJ, Vaughan BS, Stoner JA, et al. A double-blind, placebo-controlled study of atomoxetine in young children with ADHD. *Pediatrics*. 2011;127(4). Available at: www.pediatrics.org/cgi/content/full/127/4/e862
 27. Rowland AS, Lesesne GA, Abramowitz AJ. The epidemiology of attention-deficit/hyperactivity disorder (ADHD): a public health view. *Ment Retard Dev Disabil Res Rev*. 2002;8(3):162–170
 28. Cuffie SP, Moore CG, McKeown RE. Prevalence and correlates of ADHD symptoms in the national health interview survey. *J Atten Disord*. 2005;9(2):392–401
 29. Pastor PN, Reuben CA. Diagnosed attention deficit hyperactivity disorder and learning disability: United States, 2004–2006. *Vital Health Stat 10*. 2008;(237):1–14
 30. Biederman J, Faraone SV, Wozniak J, Mick E, Kwon A, Aleardi M. Further evidence of unique developmental phenotypic correlates of pediatric bipolar disorder: findings from a large sample of clinically referred preadolescent children assessed over the last 7 years. *J Affect Disord*. 2004;82(suppl 1):S45–S58
 31. Biederman J, Kwon A, Aleardi M. Absence of gender effects on attention deficit hyperactivity disorder: findings in nonreferred subjects. *Am J Psychiatry*. 2005;162(6):1085–1089
 32. Biederman J, Ball SW, Monuteaux MC, et al. New insights into the comorbidity between ADHD and major depression in adolescent and young adult females. *J Am Acad Child Adolesc Psychiatry*. 2008; 47(4):426–434
 33. Biederman J, Melmed RD, Patel A, McBurnett K, Donahue J, Lyne A. Long-term, open-label extension study of guanfacine extended release in children and adolescents with ADHD. *CNS Spectr*. 2008;13(12):1047–1055
 34. Crabtree VM, Iwanenko A, Gozal D. Clinical and parental assessment of sleep in children with attention-deficit/hyperactivity disorder referred to a pediatric sleep medicine center. *Clin Pediatr (Phila)*. 2005;44(9):807–813
 35. LeBourgeois MK, Avis K, Mixon M, Olmi J, Harsh J. Snoring, sleep quality, and sleepiness across attention-deficit/hyperactivity disorder subtypes. *Sleep*. 2004;27(3):520–525
 36. Chan E, Zhan C, Homer CJ. Health care use and costs for children with attention-deficit/hyperactivity disorder: national estimates from the medical expenditure panel survey. *Arch Pediatr Adolesc Med*. 2002; 156(5):504–511
 37. Newcorn JH, Miller SR, Ivanova I, et al. Adolescent outcome of ADHD: impact of childhood conduct and anxiety disorders. *CNS Spectr*. 2004;9(9):668–678
 38. Sung V, Hiscock H, Sciberras E, Efron D. Sleep problems in children with attention-deficit/hyperactivity disorder: prevalence and the effect on the child and family. *Arch Pediatr Adolesc Med*. 2008; 162(4):336–342
 39. American Academy of Pediatrics, Task Force on Mental Health. *Addressing Mental Health Concerns in Primary Care: A Clinician's Toolkit* [CD-ROM]. Elk Grove Village, IL: American Academy of Pediatrics; 2010
 40. American Academy of Pediatrics, Committee on Child Health Financing. Scope of health care benefits for children from birth through age 26. *Pediatrics*. 2012; In press
 41. Brito A, Grant R, Overholt S, et al. The enhanced medical home: the pediatric standard of care for medically underserved children. *Adv Pediatr*. 2008;55:9–28
 42. Homer C, Klatka K, Romm D, et al. A review of the evidence for the medical home for children with special health care needs. *Pediatrics*. 2008;122(4). Available at: www.pediatrics.org/cgi/content/full/122/4/e922
 43. Ingram S, Hechtman L, Morgenstern G. Out-

- come issues in ADHD: adolescent and adult long-term outcome. *Ment Retard Dev Disabil Res Rev*. 1999;5(3):243–250
44. Barbaresi WJ, Katusic SK, Colligan RC, Weaver AL, Jacobsen SJ. Modifiers of long-term school outcomes for children with attention-deficit/hyperactivity disorder: does treatment with stimulant medication make a difference? Results from a population-based study. *J Dev Behav Pediatr*. 2007;28(4):274–287
 45. Cheng JY, Cheng RY, Ko JS, Ng EM. Efficacy and safety of atomoxetine for attention-deficit/hyperactivity disorder in children and adolescents: meta-analysis and meta-regression analysis. *Psychopharmacology*. 2007;194(2):197–209
 46. Michelson D, Allen AJ, Busner J, Casat C, Dunn D, Kratochvil CJ. Once daily atomoxetine treatment for children and adolescents with ADHD: a randomized, placebo-controlled study. *Am J Psychiatry*. 2002;159(11):1896–1901
 47. Biederman J, Melmed RD, Patel A, et al; SPDS03 Study Group. A randomized, double-blind, placebo-controlled study of guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder. *Pediatrics*. 2008;121(1). Available at: www.pediatrics.org/cgi/content/full/121/1/e73
 48. Sallee FR, Lyne A, Wigal T, McGough JJ. Long-term safety and efficacy of guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol*. 2009;19(3):215–226
 49. Jain R, Segal S, Kollins SH, Khayrallah M. Clonidine extended-release tablets for pediatric patients with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2011;50(2):171–179
 50. Newcorn J, Kratochvil CJ, Allen AJ, et al. Atomoxetine and osmotically released methylphenidate for the treatment of attention deficit hyperactivity disorder: acute comparison and differential response. *Am J Psychiatry*. 2006;163(8):721–730
 51. Swanson J, Elliott GR, Greenhill LL, et al. Effects of stimulant medication on growth rates across 3 years in the MTA follow-up. *J Am Acad Child Adolesc Psychiatry*. 2007;46(8):1015–1027
 52. Mosholder AD, Gelperin K, Hammad TA, Phelan K, Johann-Liang R. Hallucinations and other psychotic symptoms associated with the use of attention-deficit/hyperactivity disorder drugs in children. *Pediatrics*. 2009;123(2):611–618
 53. Avigan M. Review of AERS Data From Marketed Safety Experience During Stimulant Therapy: Death, Sudden Death, Cardiovascular SAEs (Including Stroke). Silver Spring, MD: Food and Drug Administration, Center for Drug Evaluation and Research; 2004. Report No. D030403
 54. Perrin JM, Friedman RA, Nilans TK, et al; American Academy of Pediatrics, Black Box Working Group, Section on Cardiology and Cardiac Surgery. Cardiovascular monitoring and stimulant drugs for attention-deficit/hyperactivity disorder. *Pediatrics*. 2008;122(2):451–453
 55. McCarthy S, Cranswick N, Potts L, Taylor E, Wong IC. Mortality associated with attention-deficit hyperactivity disorder (ADHD) drug treatment: a retrospective cohort study of children, adolescents and young adults using the general practice research database. *Drug Saf*. 2009;32(11):1089–1110
 56. Gould MS, Walsh BT, Munfakh JL, et al. Sudden death and use of stimulant medications in youths. *Am J Psychiatry*. 2008;165(9):992–1001
 57. Greenhill L, Kollins S, Abikoff H, McCracken J, Riddle M, Swanson J. Efficacy and safety of immediate-release methylphenidate treatment for preschoolers with ADHD. *J Am Acad Child Adolesc Psychiatry*. 2008;45(11):1284–1293
 58. Low K, Gendaszek AE. Illicit use of psychostimulants among college students: a preliminary study. *Psychol Health Med*. 2002;7(3):283–287
 59. Cox D, Merkel RL, Moore M, Thorndike F, Muller C, Kovatchev B. Relative benefits of stimulant therapy with OROS methylphenidate versus mixed amphetamine salts extended release in improving the driving performance of adolescent drivers with attention-deficit/hyperactivity disorder. *Pediatrics*. 2008;118(3). Available at: www.pediatrics.org/cgi/content/full/118/3/e704
 60. Pelham W, Wheeler T, Chronis A. Empirically supported psychological treatments for attention deficit hyperactivity disorder. *J Clin Child Psychol*. 1998;27(2):190–205
 61. Sonuga-Barke E, Daley D, Thompson M, Laver-Bradbury C, Weeks A. Parent-based therapies for preschool attention-deficit/hyperactivity disorder: a randomized, controlled trial with a community sample. *J Am Acad Child Adolesc Psychiatry*. 2001;40(4):402–408
 62. Pelham W, Fabiano GA. Evidence-based psychosocial treatments for attention-deficit/hyperactivity disorder. *J Clin Child Adolesc Psychol*. 2008;37(1):184–214
 63. Van Cleave J, Leslie LK. Approaching ADHD as a chronic condition: implications for long-term adherence. *J Psychosoc Nurs Ment Health Serv*. 2008;46(8):28–36
 64. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder: The MTA Cooperative Group. Multimodal Treatment Study of Children With ADHD. *Arch Gen Psychiatry*. 1999;56(12):1073–1086
 65. Jensen P, Hinshaw SP, Swanson JM, et al. Findings from the NIMH multimodal treatment study of ADHD (MTA): implications and applications for primary care providers. *J Dev Behav Pediatr*. 2001;22(1):80–73
 66. Pelham WE, Gnagy EM. Psychosocial and combined treatments for ADHD. *Ment Retard Dev Disabil Res Rev*. 1999;5(3):225–236
 67. Davila FR, Williams ML, MacDonald JT. Memorandum on clarification of policy to address the needs of children with attention deficit disorders within general and/or special education. In: Parker HC. *The ADD Hyperactivity Handbook for Schools*. Plantation, FL: Impact Publications Inc; 1991:261–268
 68. The College Board. Services for Students With Disabilities (SSD). Available at: www.collegeboard.com/ssd/student. Accessed July 8, 2011
 69. Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness. *JAMA* 2002;288:1775–1779
 70. Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness: the chronic care model, Part 2. *JAMA* 2002;288:1908–1914

Summary of Current Evidence

CADTH October 2011	Guidelines and Recommendations for ADHD in Children and Adolescents
------------------------------	--

This report is prepared by the Canadian Agency for Drugs and Technologies in Health (CADTH). This report contains a comprehensive review of existing public literature, studies, materials, and other information and documentation (collectively the “source documentation”) available to CADTH at the time it was prepared.

The information in this report is intended to help health care decision-makers, patients, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services.

The information in this report should not be used as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process, nor is it intended to replace professional medical advice. While CADTH has taken care in the preparation of the report to ensure that its contents are accurate, complete, and up-to-date, CADTH does not make any guarantee to that effect. CADTH is not responsible for any errors or omissions or injury, loss, or damage arising from or as a result of the use (or misuse) of any information contained in or implied by the information in this report.

CADTH takes sole responsibility for the final form and content of this report. The statements, conclusions, and views expressed herein do not necessarily represent the view of Health Canada or any provincial or territorial government.

Production of this report is made possible through a financial contribution from Health Canada and the governments of Alberta, British Columbia, Manitoba, New Brunswick, Newfoundland and Labrador, Northwest Territories, Nova Scotia, Nunavut, Prince Edward Island, Saskatchewan, and Yukon.

Copyright © 2011 CADTH. This report may be reproduced for non-commercial purposes only and provided appropriate credit is given to CADTH.

PREPARED BY:

Canadian Agency for Drugs and Technologies in Health

Tel: 1-866-898-8439

www.cadth.ca

EXECUTIVE SUMMARY

Issue

Medications to treat attention-deficit/hyperactivity disorder (ADHD) in children and adolescents are available in short- and long-acting formulations. Short-acting formulations of methylphenidate (e.g., Ritalin) and dextroamphetamine (e.g., Dexedrine) are generally given two to three times daily.¹ They have been shown to be effective in reducing ADHD symptoms and provide dosing flexibility.²⁻⁴ Compared with short-acting formulations, long-acting formulations are given less frequently, but are more expensive and are not covered in all insurance plans.⁵ Recommendations about the use of long- or short-acting formulations are largely derived from expert opinion of best practices. Discourse on the use of long-acting formulations have centred on the following issues: compliance, social stigma, in-school dosing, and drug diversion.^{6,7}

In 2010, publicly funded drug plans in Canada spent more than \$35 million on long-acting formulations, which represented 77% of total expenditures on ADHD medications. As expenditures on ADHD medications continue to rise, health care decision-makers require evidence-based information on the issue of selecting the most appropriate formulation for treating ADHD in children and adolescents.

Objectives

The objective of this report was to summarize the current clinical evidence and findings of guidelines and recommendations. The report was also designed to explore the current utilization patterns and costs associated with the use of long- and short-acting ADHD medications.

The information in this report is intended to help health care decision-makers, patients, health care professionals, health systems leaders, and policy-makers make informed decisions.

Methods

Information provided is based on a review of eight Canadian and major international guidelines addressing long-acting and short-acting medications for ADHD in children and adolescents. In addition, drug payment information (i.e., administrative claims data) was obtained from IMS Brogan Inc.

Conclusions

Evidence-based recommendations support the use of stimulants as first-line therapy and the consideration of symptom profile in the use of long- or short-acting formulations when treating children and adolescents with severe ADHD.

The drug payment information presented in this summary report reveals substantial use of health care budgets to reimburse long-acting formulations. In 2010, expenditures on long-acting medications had exceeded \$35 million (or 77% of total expenditures on ADHD medications) by public drug plans in Canada.

ABBREVIATIONS

AACAP	American Academy of Child & Adolescent Psychiatry
ADHD	attention-deficit/hyperactivity disorder
ADHD/HKD	attention-deficit and hyperkinetic disorders
AGREE	Appraisal of Guidelines for Research & Evaluation
AMP	amphetamines
CADDRA	Canadian ADHD Resource Alliance
CADTH	Canadian Agency for Drugs and Technologies in Health
CPP	clinical practice points
CPS	Canadian Paediatric Society
DEX	dextroamphetamine
DSM	Diagnostic and Statistical Manual of Mental Disorders
ER	extended release (also XR)
IR	immediate release
LA	long-acting
MPH	methylphenidate
MR	modified release
NCCMH	National Collaborating Centre for Mental Health
NHMRC	National Health and Medical Research Council
NICE	National Institute for Health and Clinical Excellence
NIHB	Non-Insured Health Benefits Program
RCT	randomized controlled trial
SA	short-acting
SIGN	Scottish Intercollegiate Guidelines Network
SR	sustained release
XR	extended release (also ER)

TABLE OF CONTENTS

EXECUTIVE SUMMARY	I
ABBREVIATIONS	II
1 INTRODUCTION.....	1
1.1 CONDITION	1
1.2 PHARMACOLOGICAL TREATMENTS.....	1
2 ISSUE	2
3 OBJECTIVES.....	3
4 METHODS.....	3
4.1 Guidelines and Recommendations	3
4.2 Economic Data.....	3
5 SUMMARY OF FINDINGS	4
5.1 Guidelines and Recommendations	4
5.2 Limitations	13
6 CONCLUSIONS AND IMPLICATIONS FOR DECISION- OR POLICY-MAKING.....	14
7 REFERENCES	15
APPENDIX 1: RECOMMENDATIONS FROM NATIONAL EVIDENCE-BASED GUIDELINES DEVELOPED USING RIGOROUS SCIENTIFIC METHODS.....	17
APPENDIX 2: SUMMARY OF EVIDENCE AND RECOMMENDATIONS FROM GUIDELINES ON ADHD	19

1 INTRODUCTION

1.1 CONDITION

Attention-deficit/hyperactivity disorder (ADHD) is a developmental disorder that affects approximately one in 20 children.⁸ Core symptoms include inattention, hyperactivity, and impulsivity. Some children with ADHD show symptoms of inattention and are not hyperactive or impulsive. Others show symptoms of hyperactivity-impulsivity only. In most cases, however, symptoms of both inattention and hyperactivity-impulsivity are present. The fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) identifies three subtypes of ADHD:

- ADHD, Combined Type
- ADHD, Predominantly Inattentive Type
- ADHD, Predominantly Hyperactive-Impulsive Type.

The core symptoms of ADHD will often persist throughout a person's lifetime, and approximately one-half to two-thirds of children with ADHD will continue to have significant problems as adults.⁹ Management of ADHD may involve a combination of pharmacological treatments, behaviour modifications, lifestyle changes, and counselling.

1.2 PHARMACOLOGICAL TREATMENTS

Stimulants, including methylphenidate (MPH) and amphetamines (AMP) such as dextroamphetamine (DEX), have been used for more than 50 years to treat symptoms of ADHD and are considered the pharmacological treatment of choice.¹⁰

Medications to treat ADHD are available in short-acting (SA) and long-acting (LA) formulations. SA formulations of MPH (e.g., Ritalin) and DEX (e.g., Dexedrine) are generally given two to three times daily.¹ They have been shown to be effective in reducing ADHD symptoms and provide dosing flexibility.²⁻⁴ Compared with SA formulations, LA formulations are given less frequently but are more expensive and are not covered in all insurance plans.⁵ Recommendations to use LA or SA formulations have not been developed based on evidence. Discourse on the use of LA formulations has centred on the following issues: compliance, social stigma, in-school dosing, and drug diversion.^{6,7}

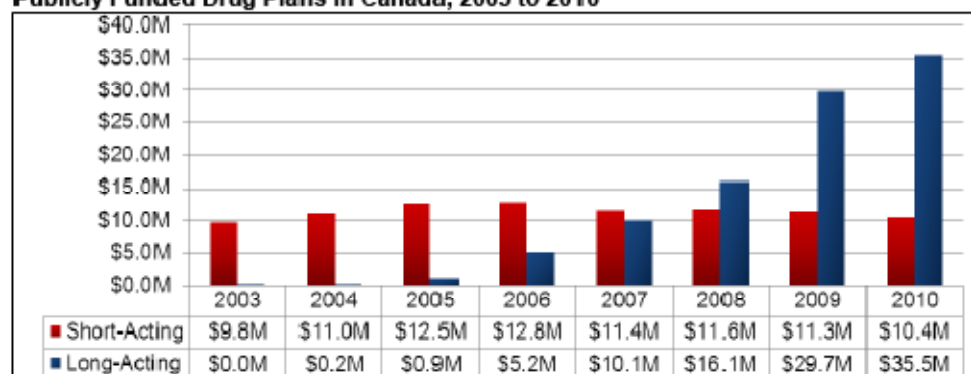
LA MPH stimulants include Concerta (extended-release MPH), generic extended-release MPH, and Biphentin (controlled-release MPH). LA AMP stimulants include Adderall XR (mixed salts AMP) and Vyvanse (lisdexamfetamine dimesylate). Strattera (atomoxetine) is a non-stimulant, LA medication indicated to treat ADHD. These medications are all indicated for the treatment of ADHD in patients aged six years and older.¹

In various publications,^{2-8,11} LA formulations are also referred to as extended release (ER or XR) or modified release (MR), while SA formulations are also referred to as immediate release (IR).

2 ISSUE

In 2010, publicly funded drug plans in Canada spent more than \$35 million on LA formulations (see Figure 1), which represented 77% of total expenditures on ADHD medications (see Figure 2). As expenditures on ADHD medications continue to rise, health care decision-makers require evidence-based information on the issue of selecting the most appropriate formulation for treating ADHD in children and adolescents.

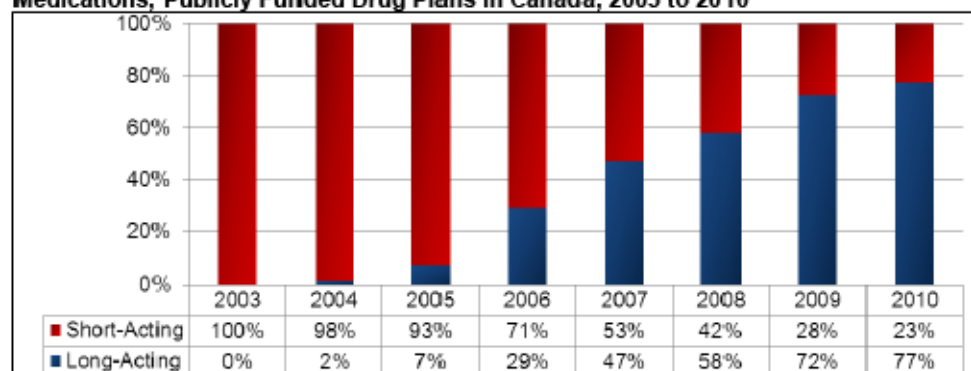
Figure 1: Expenditures (\$) for Short-Acting and Long-Acting ADHD Medications, Publicly Funded Drug Plans in Canada, 2003 to 2010



ADHD = attention-deficit/hyperactivity disorder; M = millions.

Figure 1 results were prepared using data from Brogan Inc., a unit of IMS, PharmaStat®, Public Drug Plan databases, 2003-2010, but the analyses, conclusions, opinions and statements expressed are those of CADTH and not of Brogan Inc., a unit of IMS.

Figure 2: Share of Expenditures (%) by Short-Acting versus Long-Acting ADHD Medications, Publicly Funded Drug Plans in Canada, 2003 to 2010



ADHD = attention-deficit/hyperactivity disorder.

Figure 2 results were prepared using data from Brogan Inc., a unit of IMS, PharmaStat®, Public Drug Plan databases, 2003-2010, but the analyses, conclusions, opinions and statements expressed are those of CADTH and not of Brogan Inc., a unit of IMS.

3 OBJECTIVES

The objective of this report is to summarize the current clinical evidence and findings of guidelines and recommendations. The report was also designed to explore the current utilization patterns and costs associated with the use of LA and SA ADHD medications.

The information in this report is intended to help health care decision-makers, patients, health care professionals, health systems leaders, and policy-makers make informed decisions.

4 METHODS

4.1 Guidelines and Recommendations

A limited literature search was conducted on key resources including PubMed, ECRI, and Canadian and major international guidelines, as well as a focused Internet search. Methodological filters were applied to limit retrieval to guidelines. The search was also limited to English language documents published between January 1, 2006 and May 19, 2011.

Guidelines were included in the review if they were major national ADHD guidelines or produced by a recognized national organization and systematically developed. Relevant to the local environment, two Canadian guidelines were included.^{5,8} The relevant population consisted of children and adolescents (aged ≤ 18 years). Guidelines were excluded if they were not systematically developed or were representative of a smaller jurisdiction (i.e., a US state), or a specific health care organization or health plan.

The Appraisal of Guidelines for Research & Evaluation (AGREE) instrument was used to evaluate the quality of the guidelines identified in the literature search.¹² Domains considered included scope and purpose, stakeholder involvement, rigour of development, clarity and presentation, applicability, and editorial independence. Numeric domain scores were not calculated. Instead, narrative assessment of each guideline is provided.

4.2 Economic Data

The following information refers to the economic data presented in Figures 1 and 2 of the Issues section of the report.

Aggregate-level data were obtained from IMS Brogan Inc. The IMS Brogan Inc. database is the largest source of drug payment information (i.e., administrative claims data) in Canada. IMS Brogan Inc. databases comply with federal and provincial privacy legislation.¹³

Aggregate-level data from public drug plans in Canada were available for nine of the 10 provinces (i.e., British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Québec, New Brunswick, Nova Scotia, and Newfoundland) and the Non-Insured Health Benefits (NIHB) Program. Aggregate-level data were not available for publicly funded programs in Prince Edward Island, Northwest Territories, Yukon Territory, and Nunavut Territory, because data from these programs are not provided to IMS Brogan Inc.

ADHD medications that were identified in the IMS Brogan Inc. database for publicly funded drug plans are presented in Table 1.

Table 1: Publicly Funded ADHD Medications in Canada (identified for the purpose of this report)

Brand Name		
	Available Strengths (mg)*	Average Cost (\$)†
Long-Acting Formulations		
Adderall XR (<i>amphetamine mixed salts</i>)	5, 10, 15, 20, 25, 30	82.52
Biphentin (<i>methylphenidate HCl</i>)	10, 15, 20, 30, 40, 50, 60, 80	48.18
Concerta (<i>methylphenidate HCl</i>)	18, 27, 36, 54	73.58
Strattera (<i>atomoxetine</i>)	10, 18, 25, 40, 60, 80, 100	93.17
Vyvanse (<i>lisdexamfetamine dimesylate</i>)	20, 30, 40, 50, 60	79.86
Short-Acting and Intermediate-Acting Formulations		
Adderall (<i>amphetamine mixed salts</i>)	20	N/A
Dexedrine (<i>dexamphetamine sulfate</i>)	5	50.44
Dexedrine Spansule (<i>dextroamphetamine sulphate</i>)	10, 15	46.08
Ritalin (<i>methylphenidate HCl</i>)	5, 10, 20	9.35
Ritalin SR (<i>methylphenidate HCl</i>)	20	14.54

Table 1 results were prepared using data from Brogan Inc., a unit of IMS, PharmaStat®, Public Drug Plan databases, 2003-2010, but the analyses, conclusions, opinions and statements expressed are those of CADTH and not of Brogan Inc., a unit of IMS.

* Strengths listed include available generic versions.

† Average cost (total cost divided by total claims) was calculated using 2010 data.

5 SUMMARY OF FINDINGS

5.1 Guidelines and Recommendations

Eight guidelines that addressed LA and SA medications for ADHD were identified. All guidelines were informed by evidence and include statements of consensus or best practice recommendations. The guidelines reviewed are found in Table 2.

Three national evidence-based guidelines were produced using rigorous scientific methods. These include guidelines by the Scottish Intercollegiate Guidelines Network (SIGN), the National Institute for Health and Clinical Excellence (NICE), and the Royal Australasian College of Physicians. Selected recommendations from these guidelines are found in Appendix 1.²⁻⁴

Table 2: Evidence-based Guidelines for ADHD

Organization	Year of Publication	Title of Publication
<i>Major National Guidelines</i>		
SIGN ²	2009	<i>Management of Attention Deficit and Hyperkinetic Disorders in Children and Young People: A National Clinical Guideline</i>
NICE ³	2009	<i>Attention Deficit Hyperactivity Disorder: Diagnosis and Management of ADHD in Children, Young People and Adults</i>
Royal Australasian College of Physicians ⁴	2009	<i>Australian Guidelines on Attention Deficit Hyperactivity Disorder</i>
<i>Additional Guidelines</i>		
CADDRA ⁵	2011	<i>Canadian ADHD Practice Guidelines (3rd Edition)</i>
CPS (Feldman et al) ⁶	2009	<i>Extended-release Medications for Children and Adolescents with Attention-Deficit Hyperactivity Disorder</i>
AACAP ¹¹	2007	<i>Practice Parameter for the Assessment and Treatment of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder</i>
AACAP (Gleason et al) ⁶	2007	<i>Psychopharmacological Treatment for Very Young Children: Contexts and Guidelines</i>
European Society of Child and Adolescent Psychiatry (Banaschewski et al) ⁷	2006	<i>Long-acting Medications for the Hyperkinetic Disorders: A Systematic Review and European Treatment Guideline</i>

AACAP = American Academy of Child & Adolescent Psychiatry; CADDRA = Canadian ADHD Resource Alliance; CPS = Canadian Paediatric Society; NICE = National Institute for Health and Clinical Excellence; SIGN = Scottish Intercollegiate Guidelines Network

SIGN (2009) National Clinical Guideline on ADHD

In 2009, SIGN published a national clinical guideline on the management of attention-deficit and hyperkinetic disorders (ADHD/HKD) in children and young people, which is an update of a 2001 guideline.² This clinical guideline was developed using a standard methodology based on a systematic review of the evidence. The complete guideline development methodology is found on the SIGN website.¹⁴

The overall aim of the guideline was to provide a framework for the evidence-based assessment and management of ADHD/HKD from which multidisciplinary and multi-agency approaches could be developed locally. The Guideline Development Group was multidisciplinary, including practising clinicians and patient or caregiver representatives. In addition, SIGN provided support for guideline development, literature review, and facilitation.

There was a clear link between recommendations and the supporting evidence. The recommendations were specific and easily identifiable, and levels of supporting evidence and grades of recommendations were stated. A number of independent expert referees reviewed the guideline. NHS Quality Improvement Scotland funded the guideline. All members of the guideline development group made declarations of interest.

*Summary of recommendations from SIGN**Evidence-based:*

- a) SIGN recommends treatment of children with severe ADHD using stimulants as the first choice of medications. (Grade A.)
- b) Atomoxetine is recommended in children where psychostimulant medication is not appropriate, not tolerated, or is ineffective. (Grade A.)

Grade A: at least one meta-analysis, systematic review, or good quality randomized controlled trial (RCT), and directly applicable to the target population

Consensus-based (good practice):

- a) LA medications should be considered if there is a likelihood of diversion.
- b) When selecting a formulation, clinicians should consider practical issues of convenience and applicability on an individual case basis.

Australian Guidelines on ADHD (2009)

Since November 2009, the Royal Australasian College of Physicians has provided access to draft Australian guidelines on ADHD.⁴ This is an extensive guideline that includes recommendations and a discussion of the supporting evidence for all aspects of the diagnosis and treatment of ADHD. The guidelines are available in draft because a formal conflict of interest investigation into a researcher has not been completed in the United States.

In May 2011, the conflict of interest allegations had not been resolved, so the National Health and Medical Research Council (NHMRC) decided to convene a working party to develop clinical practice points (CPPs) to ensure up-to-date clinical advice on ADHD. The website noted that “the final CPPs will be provided to the Minister for Mental Health and Ageing for his consideration and possible public consultation, by the end of September 2011.”¹⁵

In June 2011, the website stated, “while the work of this US-based researcher is referenced in the draft Guidelines, the researcher has not been involved in any way in the production of the Guidelines.”¹⁵ NHMRC guideline development processes were followed. The complete guideline development process was available as a separate appendix.¹⁶ Steps included a literature review, stakeholder consultation, public consultation, email, and face-to-face meetings. As a result, until an update to the guidelines is ready, NHMRC will continue to provide access to the 2009 draft guidelines as an information resource.¹⁵

The aim of these guidelines was to support and inform the care of individuals with ADHD by providing a series of recommendations to guide assessment, management, and care. The guidelines apply to the care of preschoolers, children, adolescents, and adults with ADHD. They are intended to provide a framework based on the best available evidence that can be adapted to local needs and resources, and individual circumstances. The guideline development group included experts from key professional disciplines, including pediatrics, child and adolescent psychiatry, adult psychiatry, psychology, general practice, and education, as well as consumers

and caregivers. These guidelines addressed social and economic considerations in the treatment of ADHD, including the economic burden of ADHD and the cost-effectiveness of treatment.

The method for formulating the recommendations was clearly described. In the document, the research question, summary evidence statements (with level of evidence), and resulting recommendations were provided, followed by the research evidence. For areas of practice not addressed by current research, recommendations were developed based on the consensus opinion of the clinicians, educators, and consumers from the reference group. Funding for these guidelines was provided by the Australian Government's Department of Health and Ageing. Conflicts of interest were recorded for each member of the development group.

Summary of recommendations from the Australian guidelines

Evidence-based:

- a) Where severe, impairing ADHD is present, treatment with stimulants (MPH or DEX) should be considered as a first-line pharmacological treatment. (Grade A.)
- b) The choice of IR-MPH or ER-MPH depends on the symptom profile, as well as individual child and parent or caregiver preferences. (Grade A for children, grade B for adolescents.)
- c) Atomoxetine should be considered for children and adolescents with severe ADHD who do not respond to or are intolerant of stimulant medication, or in whom stimulant medication is contraindicated. (Grade B.)

Grade A: Body of evidence can be trusted to guide practice.

Grade B: Body of evidence can be trusted to guide practice in most situations.

Consensus-based (best practice):

- a) Not all people with ADHD require pharmacological management. Medications should only be used when symptoms are pervasive across settings and cause significant impairment in academic, social, or behavioural function.
- b) IR forms should be the initial treatment, to titrate to the optimal dose, and they may be the preferred maintenance therapy for various reasons; for example, flexibility of dosing. If starting on IR stimulants, consideration should be given to changing to an ER form once the optimal dose has been established. This can help to avoid the stigma and inconvenience of taking medication at school.
- c) Atomoxetine may be considered as the first-line medication if there is comorbid substance abuse, severe tic disorder, or anxiety disorder.

NICE (2009) Clinical Guideline on ADHD

In 2009, NICE published a clinical practice guideline on the diagnosis and management of ADHD in children, young people, and adults.³ A technology appraisal on "methylphenidate, atomoxetine and dexamfetamine for the treatment of ADHD in children and adolescents" informed the recommendations on drug treatment.¹⁷ The clinical practice guideline is high quality and was developed based on methods outlined in the NICE Guideline Manual.¹⁸ Steps in developing this guideline included a literature review, stakeholder consultation, public consultation, and face-to-face meetings.

The aim of the NICE guideline was to advise on the treatment and management of ADHD. It is considered a patient-centred, evidence-based guideline and is relevant for children (older than three years), young people, and adults with ADHD. The guideline development group consisted of health care professionals, lay representatives, and technical experts. Consulted stakeholders included service users and caregivers, professional groups, and manufacturers. Health economic evidence was assessed and incorporated into the recommendations.

The guideline review process is available in a flow chart in the guideline (p. 47). The method for formulating the recommendations was clearly described. The guideline was developed over a series of meetings, in which clinical questions and clinical evidence were reviewed and assessed and recommendations formulated and reviewed. Recommendations were evidence based, where possible, and if evidence was not available, informal consensus methods were used. Recommendations were specific and easily identifiable and an extensive evidence review for each topic was provided. Various stakeholders reviewed the guideline extensively prior to publication. This guideline was commissioned by NICE and developed within the National Collaborating Centre for Mental Health (NCCMH). Conflicts of interest for each member of the Guideline Development Group were recorded.

An extensive review of the evidence for drug treatment of ADHD is provided. The quality of evidence for each drug or topic was rated. Following the evidence review is a summary and a list of recommendations. Individual recommendations were not assigned a level for the supporting evidence on which they were based or a strength of recommendation. Therefore, it is not clear to what extent each recommendation is based on evidence or expert opinion.

Summary of recommendations from NICE

- a) Drug treatment is not indicated as the first-line treatment for all school-aged children and young people with ADHD. It should be reserved for those with severe symptoms and impairment. Where drug treatment is considered appropriate, MPH, atomoxetine, and DEX are recommended.
- b) If there is a choice of more than one appropriate drug, the product with the lowest cost should be prescribed.
- c) To improve adherence to drug treatment, simple drug regimens (for example, once-daily MR doses) are recommended for people with ADHD.
- d) The decision regarding which product to use should be based on factors including:
 - specific issues regarding compliance; i.e., midday treatment dose at school
 - the potential for drug diversion and/or misuse
 - the preferences of the child or adolescent and/or his or her parent or guardian.
- e) When prescribing MPH for the treatment of children or young people, MR preparations should be considered for the following reasons:
 - convenience
 - improving adherence
 - reducing stigma (does not need to take medication at school)
 - reducing problems schools have in storing and administering controlled drugs
 - their pharmacokinetic profiles.
- f) Alternatively, IR preparations may be considered if more flexible dosing regimens are required, or during initial titration to determine correct dosing levels.

- g) Consider atomoxetine if MPH has been tried and has been ineffective at the maximum tolerated dose, or if intolerant to low or moderate doses of MPH.

Additional ADHD Guidelines

Five additional ADHD guidelines were identified that included recommendations on LA versus SA drugs in children and adolescents. These guidelines varied with regard to their methodological quality. Recommendations on the use of LA versus SA drugs, along with relevant statements of evidence from each guideline, are found in Appendix 2.

In 2011, the Canadian ADHD Resource Alliance (CADDRA) published the third edition of its Canadian ADHD Practice Guidelines.⁵ CADDRA is a national, independent, not-for-profit association with members from family practice, pediatrics, psychiatry, psychology, and other health professions. No objective or clinical question was specified for the guideline, but the authors included a list of core principles for the treatment of ADHD. The targeted users of the guideline are Canadian physicians who diagnose and treat ADHD, and the guideline applies to patients and their families living with ADHD.

Strengths of this guideline include the tools available for physicians and patients. Information, diagnostic instruments, forms, and scales that have been selected based on their validity, reliability and accessibility can be downloaded. These guidelines are considered an active document that will be revised online as new information comes available.

The major limitation is the lack of rigour used in the development of this guideline. For example, the methods used to search for evidence were not specified and no criteria were described for selecting the evidence. Specific recommendations were not identifiable and there was no link between recommendations and the supporting evidence. The authors state that evidence-based data were cited in the literature detailed in the reference section, and consensus-based statements were identified in the text. The introduction to the guideline states, "Consensus decisions have been made if there was no current evidence-based data available to deal with a specific clinical issue or where evidence-based data may have been impractical in the Canadian environment" (p. v).

CADDRA is an active advocacy group. Several statements were made in the document about the cost of many ER preparations, which are "beyond the reach" of many patients without extended health insurance: "CADDRA continues to advocate for a resolution of this problem at the government level" (p. 57). The Guidelines Committee "recommends that all medication approved for ADHD treatment should be accessible and covered by provincial drug plans" (p. 67). This advocacy, combined with a lack of supporting evidence for the group's recommendations, creates significant bias that threatens the validity of the recommendations.

Individual recommendations are not assigned a level for the supporting evidence on which they were based, or a strength of recommendation. Therefore, it is not clear to what extent each recommendation is based on evidence or expert opinion.

Recommendations

- a) LA preparations, including Adderall XR, Biphentin, Concerta, Strattera, and Vyvanse, are recommended as first-line treatment of ADHD.
- b) SA and intermediate-acting preparations are listed as second-line or adjunctive agents.

In 2009, the Canadian Paediatric Society published a statement on “extended-release medications for children and adolescents with attention-deficit disorder.”⁸ The objective of the statement was to critically appraise the evidence for the relative effectiveness of XR versus IR medications and to make recommendations for their appropriate use in the treatment of ADHD. The statement was targeted at physicians prescribing medication for ADHD.

Strengths included a clearly described scope and purpose. Stakeholder involvement included physicians but not patients or their families. Key recommendations were specific, unambiguous, and easily identifiable. The authors of the paper indicated that they had no conflicts of interest to declare. The major limitation is the lack of rigour of development. Clinical questions were not provided, and although the search strategy was detailed, the criteria for selecting the evidence and the methods for formulating the recommendations were not provided. The statement indicates that the quality of the studies was appraised, although the details of the appraisal of individual studies or systematic reviews were not provided. References were provided throughout the statement. There was no link between the recommendations and the supporting evidence and no levels of evidence were assigned. Therefore, it is not clear to what extent each recommendation is based on evidence or expert opinion.

This statement made the distinction between “efficacy” and “effectiveness,” defining efficacy as how well a treatment works under tightly controlled study conditions, and effectiveness as how well a treatment works in a natural, real-world setting. The statement identified that cost is the major barrier to accessing XR preparations, and recommended that industry, private health insurance companies, and government work together to make these medications more accessible to all children with ADHD. No specific solutions were provided.

Recommendations

- a) The authors acknowledge that the efficacy of IR and XR preparations are similar, as demonstrated through RCTs. Although not necessarily more efficacious than IR medication, the authors feel the XR preparations are more effective than IR and less likely to be diverted. Therefore, the authors recommend that XR preparations should be considered as first-line therapy.

In 2006, Banaschewski et al. published a supplement to European guidelines (2004) to provide recommendations about the use of LA medications for the hyperkinetic disorders.⁷ The guideline was developed by a panel of experts from several European countries, including academic clinicians and clinical researchers. The author meetings were funded by several companies and authors’ expenses were also paid. Potential conflicts of interests were declared.

The authors identified the clinical questions. The guideline states that a systematic review of published and unpublished trials was completed. Details of the search were not provided,

although it was stated that the authors used recent systematic reviews by NICE and SIGN to identify papers. They also referred to recent meta-analyses. In addition, the manufacturers were asked to submit information (published and unpublished). A “quantitative review of data” was also conducted, including the calculation of effect sizes using standard methodology. The criteria for selecting the evidence were not described. The methods for formulating the recommendations were not specified, although the method of guideline development was described as “iterative.” Drafts of the paper were exchanged and discussed iteratively and all authors subscribed to the final document (and recommendations). There was a method for resolving disagreements, but in the end, all conclusions were unanimous. The paper included a narrative summary of each conclusion and a scientific examination of the data.

Strengths include the description of the guideline process and the clear presentation of the recommendations. Limitations include the lack of patient input. For each recommendation, there is a discussion of the supporting evidence and levels of evidence are assigned to certain, but not all, statements within the discussion.

Evidence statements

- a) XR preparations are superior to placebo and some are equivalent to multiple doses of IR methylphenidate. (Grade A.)
- b) LA stimulants have similar effect sizes than IR stimulants (level 1a), while effect sizes for non-stimulants (atomoxetine) are somewhat smaller.
- c) SR medications may be less prone to abuse because they tend to have a slower rate of onset than IR. (Grade C.)
- d) Key advantages of IR: lower cost and flexibility of dosages. (Consensus.)
- e) Key advantages of LA: potential reduction of stigma at school, improved compliance, and possible reduced risk of misuse. (Consensus.)

Level 1a: the authors assigned a level of 1a; however, this does not match the grading systems described in the paper.

Grade A: at least one meta-analysis, systematic review, or good quality RCT, and directly applicable to the target population.

Grade C: well-conducted case control or cohort studies; directly applicable to target population.

Recommendations

- a) LA preparations should be available and used.
- b) They should not replace SA drugs (which will be the initial treatment for many children, for reasons of cost and flexibility of dosing). Individual clinical choice will determine the choice of formulation used.

The American Academy of Child & Adolescent Psychiatry (AACAP) published two guidelines on the treatment of ADHD. The *Practice Parameter for the Assessment and Treatment of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder* was published in July 2007 and *Psychopharmacological Treatment for Very Young Children: Contexts and Guidelines* was published in December 2007.^{6,11}

The objective of the practice parameter was to describe the assessment and treatment of children and adolescents with ADHD, based on the current scientific evidence and clinical consensus of experts in the field.¹¹ The Working Group consisted of academic clinicians and researchers. The parameter was targeted at clinicians who treat children and adolescents with ADHD. Clinical questions were not defined, although areas of discussion included clinical evaluation, comorbid conditions, research on the etiology, and interventions. The funding body for this Working Group and development of the practice parameter was not clear, although it was sponsored by the AACAP. Conflicts of interest for all members of the panel were recorded.

Details of the systematic literature search were provided, including databases searched from 1996 to 2006. In addition, bibliographies were reviewed and references were included from the previous version of the parameter. Articles were included if they “appeared to inform the field on the diagnosis and/or treatment of ADHD.” Priority was given to recent authoritative reviews of literature and recent treatment studies within the previous two to three years. Treatment recommendations were based on empirical evidence and clinical consensus and were graded according to the strength of the underlying empirical and/or clinical support. The methods for formulating the recommendations were not described. The overall recommendations on best treatment practices were stated with a strength of underlying evidence, followed by a discussion of the supporting evidence. Specific recommendation statements about the use of LA agents were found within the text, and referenced. Individual references were not assigned a level of evidence and therefore it not clear to what extent each recommendation is based on evidence or expert opinion. Additional limitations included the lack of patient or family involvement.

Evidence statements

- a) LA formulations are as efficacious as the IR forms and have been shown to be efficacious in adolescents as well as children (reference cited).
- b) Advantages of LA: greater convenience for patient and family; enhanced confidentiality at school (no dose given at school); greater compliance (no references cited).
- c) Disadvantages of LA: may have greater problematic effects on evening appetite and sleep (no references cited).
- d) LA MPH may improve driving performance in adolescents relative to SA MPH (reference cited; RCT).
- e) SA stimulants are often used as initial treatment in small children (< 16 kg) for whom there are no LA forms in sufficiently low dose (no references cited).

Although references were cited for some statements, the level of evidence was assigned for only one statement (see above statement (d)).

Recommendations (found within the body of the text)

- a) Stimulants are recommended first-line treatment for ADHD. No specific formulation is recommended; it is the sole choice of the family and the clinician as to which agent should be used; each patient’s treatment must be individualized.
- b) Atomoxetine may be considered as the first-line agent for ADHD in individuals with an active substance abuse problem, comorbid anxiety, or tics.

The aim of the AACAP Working Group on Medication Treatment in Very Young Children was to develop best-practice algorithms for the use of psychopharmacological agents in preschool

children, based upon literature review, clinical experience, and expert consensus.⁶ The Working Group included professionals with expertise in early childhood psychiatric disorders, psychopharmacology, pediatrics, psychology, and neurodevelopmental processes. The development of this algorithm was supported by a grant from the AACAP, which is the same organization that was responsible for editing and publishing the guideline. Conflicts of interest for all members of the panel were recorded. The target population of this guideline was preschool-aged children (three to six years). In Canada, ADHD medication is indicated in children aged six and older.

Systematic methods were used to search for evidence, and included a defined search period (1990 to 2007), a list of databases searched (limited to PubMed and PsycINFO), and defined search terms. Criteria for selecting the evidence were described as those publications that were “relevant,” including evidence in preschool-aged children as well as the highest level of evidence in older children. Although specific methods for developing the algorithm were not described, input included a systematic literature review, survey responses from practising clinicians, and the research and clinical expertise of the Working Group.

Steps in the algorithm were specific and clearly identifiable. Each step of the algorithm was labelled with the level of supporting evidence and included different options for treatment. There was a discussion of the available evidence within the text of the document. Limitations included the lack of patient and/or family involvement. Clinical questions were not described.

Statements about the evidence

- a) No data exist to support ER stimulants in preschoolers.
- b) Clinical experience highlights the challenges of dosing three times a day.

Recommendations for preschoolers (steps of the algorithm)

- a) First-line: MPH (level A); second-line: AMP (level C); third-line option: atomoxetine (level C); no formulations are specified.
- b) ER formulations can be used to address compliance considerations. ER formulations limit dosing flexibility in the lowest dose ranges and therefore may be contraindicated in children whose optimal tolerated dose is lower than the ER dose.

Level A: well-controlled, randomized trials, large meta-analysis, or overwhelming clinical consensus.

Level B: empirical evidence, open trials, case series, or strong clinical consensus.

Level C: single case reports or no published reports, recommendation based on clinical and research experiences.

5.2 Limitations

Three national evidence-based guidelines were identified that were produced using rigorous scientific methods.²⁻⁴ No major limitations were identified for the SIGN and Australia guidelines. Although the development process was rigorous in the NICE guideline, individual recommendations were not assigned a level for the supporting evidence on which it was based, or a strength of recommendation. Therefore, it is not clear to what extent each recommendation is based on evidence or expert opinion.

Five additional ADHD guidelines were identified that made recommendations for LA versus SA formulations.^{5-8,11} These guidelines varied in their methodological quality. In general, guidelines were lacking in their rigour of development. In many cases, there was no link between recommendations and the supporting evidence. As there was no level of supporting evidence or grade provided for recommendations, it was not clear if they were based on evidence or expert opinion.

Vyvanse (lisdexamfetamine dimesylate) has been available in Canada since 2009.¹⁹ It is not included in the guidelines reviewed, with the exception of the 2011 CADDRA guideline.

6 CONCLUSIONS AND IMPLICATIONS FOR DECISION- OR POLICY-MAKING

Three national evidence-based guidelines were identified that were produced using rigorous scientific methods.²⁻⁴ Five additional guidelines were identified that varied with regard to methodological quality.^{5-8,11} All guidelines reviewed were informed by evidence and developed by consensus.

Evidence-based recommendations support the use of stimulants as first-line therapy when treating children and adolescents with severe ADHD. Atomoxetine is an LA non-stimulant treatment alternative that is generally considered a third-line treatment alternative after methylphenidate and amphetamine stimulants, except in the presence of certain comorbidities.

Evidence-based recommendations support the consideration of symptom profile in the use of LA or SA formulations. Discussions of evidence within the guidelines reviewed also state that LA formulations are as efficacious as SA, but not superior. Other recommendations about the use of LA or SA formulations are largely derived from expert opinion of best practice. Advantages of one formulation over another cannot be determined and guideline developers acknowledge the need for more research comparing LA and SA medications.

The drug payment information presented in this summary report reveals substantial use of health care budgets to reimburse LA formulations. In 2010, expenditures on LA formulations had exceeded \$35 million (or 77% of total expenditures on ADHD medications) by public drug plans in Canada.

7 REFERENCES

1. e-CPS [Internet]. 2009. Ottawa: Canadian Pharmacists Association [cited 2010 Jun 2]. Available from: <https://www.e-therapeutics.ca> Subscription required.
2. Scottish Intercollegiate Guidelines Network. Management of attention deficit and hyperkinetic disorders in children and young people: a national clinical guideline [Internet]. Edinburgh: The Network; 2009 Oct. [cited 2011 Jun 1]. (112). Available from: <http://www.sign.ac.uk/pdf/sign112.pdf>
3. National Collaborating Centre for Mental Health. Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults [Internet]. London: British Psychological Society; 2009. [cited 2011 Jun 1]. (National clinical practice guideline 72). Available from: <http://www.nice.org.uk/nicemedia/live/12061/42060/42060.pdf>
4. Royal Australasian College of Physicians. Australian guidelines on attention deficit hyperactivity disorder (ADHD) [Internet]. Sydney: The College; 2009 Jun. [cited 2011 Jun 1]. Available from: http://www.nhmrc.gov.au/files/nhmrc/publications/attachments/ch54_draft_guidelines.pdf
5. Canadian attention deficit hyperactivity disorder resource alliance (CADDRA): Canadian ADHD practice guidelines [Internet]. 3rd ed. Toronto: CADDRA; 2011. [cited 2011 Jun 1]. Available from: <http://www.caddra.ca/cms4/pdfs/caddraGuidelines2011.pdf>
6. Gleason MM, Egger HL, Emslie GJ, Greenhill LL, Kowatch RA, Lieberman AF, et al. Psychopharmacological treatment for very young children: contexts and guidelines. *J Am Acad Child Adolesc Psychiatry*. 2007 Dec;46(12):1532-72.
7. Banaschewski T, Coghill D, Santosh P, Zuddas A, Asherson P, Buitelaar J, et al. Long-acting medications for the hyperkinetic disorders. A systematic review and European treatment guideline. *Eur Child Adolesc Psychiatry*. 2006 Dec;15(8):476-95.
8. Feldman M, Bélanger S. Extended-release medications for children and adolescents with attention-deficit hyperactivity disorder. *Paediatr Child Health [Internet]*. 2009 [cited 2011 Jun 1];14(9):593-7. Available from: <http://www.cps.ca/english/statements/CP/CP09-04.pdf>
9. Laksa J. Attention deficit hyperactivity disorder (ADHD/ADD): fact sheet. 1998 [cited 2011 Sep 7]. In: [Internet]. Wilmington (DE): Attention Deficit Disorder Association. Available from: http://www.add.org/?page=ADHD_Fact_Sheet.
10. Keen D, Hadjikhouni D. ADHD in children and adolescents. *Clin Evid [Internet]*. 2011 [cited 2011 Jun 17];02(312). Available from: <http://clinicalevidence.bmj.com/ceweb/conditions/chd/0312/0312-get.pdf>
11. Pliszka S, AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2007 Jul;46(7):894-921.
12. The AGREE Collaboration. Appraisal of guidelines for research and evaluation (AGREE) instrument [Internet]. London: St. George's Hospital Medical School; 2001 Sep. [cited 2011 Jun 16]. Available from: <http://www.agreecollaboration.org/pdf/agreeinstrumentfinal.pdf>
13. IMS Brogan [Internet]. Norwalk (CT): IMS Health Inc. 2011 [cited 2011 Sep 7]. Available from: http://www.imshealth.com/portal/site/imshealth?CURRENT_LOCALE=en_ca

14. Scottish Intercollegiate Guidelines Network [Internet]. Edinburgh: Scottish Intercollegiate Guidelines Network. 2011 [cited 2011 Jun 20]. Available from: <http://www.sign.ac.uk/>
15. National Health and Medical Research Council [Internet]. Canberra (ACT): National Health and Medical Research Council. Draft Australian Guidelines on ADHD; 2011 Jun 14 [cited 2011 Jun 17]. Available from: http://www.nhmrc.gov.au/publications/synopses/adhd_draft.htm
16. Royal Australasian College of Physicians. Australian guidelines on attention deficit hyperactivity disorder (ADHD):systematic review [Internet]. Sydney: The College; [cited 2011 Jun 17]. Available from: http://www.nhmrc.gov.au/files_nhmrc/publications/attachments/adhd_draft_literature_review.pdf
17. National Institute for Health and Clinical Excellence. Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents: review of technology appraisal 13 [Internet]. London: The Institute; 2006 Mar. [cited 2011 Jun 1]. (NICE technology appraisal 98). Available from: <http://www.nice.org.uk/nicemedia/live/11572/33222/33222.pdf>
18. National Institute for Health and Clinical Excellence. The guidelines manual 2006 [Internet]. London: The Institute; 2009 Jan 21. [cited 2011 Jun 22]. Available from: <http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/theguidelinesmanual2006/theguidelinesmanual2006.jsp>
19. Notice of compliance (NOC) database [Internet]. Ottawa: Health Canada; 2010 [cited 2011 Jun 22]. Available from: <http://www.hc-sc.gc.ca/dhp-mpps/prodpharma/notices-avis/noc-acc/index-eng.php>

APPENDIX 1: RECOMMENDATIONS FROM NATIONAL EVIDENCE-BASED GUIDELINES DEVELOPED USING RIGOROUS SCIENTIFIC METHODS

Organization	Recommendations
SIGN ² (2009)	<p>Overall recommendations (excerpts)</p> <ul style="list-style-type: none"> For school-aged children and young people with HKD (severe ADHD), medication is recommended (Grade A) Psychostimulants are recommended as the first choice of medication for the core symptoms of ADHD/HKD in children (Grade A). <p>IR versus ER</p> <ul style="list-style-type: none"> Use of MR formulations or ATX should be considered where there is likelihood of diversion (good practice point) Clinicians should familiarize themselves with the release patterns of the different MPH formulations. It may be necessary to combine IR and MR preparations to provide medications cover throughout the day (good practice point) When selecting a formulation, clinicians should consider practical issues of convenience and applicability on an individual case basis (good practice point). <p>Place in therapy: ATX</p> <ul style="list-style-type: none"> ATX is recommended as treatment for the core symptoms of ADHD/HKD in children where psychostimulant medication is not appropriate, not tolerated, or is ineffective (Grade A). <p>Grade A: at least one MA, SR, or good quality RCT, and directly applicable to the target population. Good practice point: recommended best practice based on the clinical experience of the guideline development group.</p>
NICE ² (2009)	<p>Overall recommendations (excerpts)</p> <ul style="list-style-type: none"> Drug treatment is not indicated as the first-line treatment for all school-aged children and young people with ADHD. It should be reserved for those with severe symptoms and impairment. Where drug treatment is considered appropriate, MPH, ATX, and DEX are recommended. If there is a choice of more than one appropriate drug, the product with the lowest cost should be prescribed. To improve adherence to drug treatment, simple drug regimens (e.g., once-daily MR doses) are recommended for people with ADHD. <p>IR versus ER</p> <ul style="list-style-type: none"> The decision regarding which product to use should be based on factors including: <ul style="list-style-type: none"> specific issues regarding compliance; i.e., midday treatment dose at school the potential for drug diversion and/or misuse the preferences of the child or adolescent and/or his or her parent or guardian. When prescribing MPH for the treatment of children or young people, MR preparations should be considered for the following reasons: <ul style="list-style-type: none"> convenience improving adherence reducing stigma (does not need to take medication at school) reducing problems schools have in storing and administering controlled drugs their pharmacokinetic profiles. Alternatively, IR preparations may be considered if more flexible dosing regimens are required, or during initial titration to determine correct dosing levels. <p>Place in therapy: ATX</p> <ul style="list-style-type: none"> Consider ATX if MPH has been tried and has been ineffective at the maximum tolerated dose, or if the child or young person is intolerant to low or moderate doses of MPH. <p>No grades were provided for each recommendation. No link between the recommendation and supporting evidence was provided.</p>

Organization	Recommendations
Royal Australasian College of Physicians ⁴ (2009)	<p>Overall recommendations (excerpts)</p> <ul style="list-style-type: none"> Not all people with ADHD require pharmacological management (recommended best practice). Medications should only be used when symptoms are pervasive across settings (e.g., school and home) and causing significant impairment in academic, social, or behavioural function, and after careful consideration of non-pharmacological approaches (recommended best practice). Where severe, impairing ADHD is present, treatment with MPH or DEX should be considered as a first-line pharmacological treatment (grade A). <p>IR versus ER</p> <ul style="list-style-type: none"> The choice of IR-MPH or ER-MPH depends on the symptom profile, as well as individual child and parent or caregiver preferences (grade A for children, grade B for adolescents). IR forms should be the initial treatment, to titrate to the optimal dose, and they may be the preferred maintenance therapy for various reasons; for example, flexibility of dosing (recommended best practice). If starting on IR stimulants, consideration should be given to changing to an ER form once the optimal dose has been established. This can help to avoid the stigma and inconvenience of taking medication at school (recommended best practice). In some cases, the combined use of IR and ER forms is required. This should only be considered if there is inadequate symptom control with the ER form (recommended best practice). ER forms of stimulants should not be routinely used in preschool-aged children (recommended best practice). <p>Place in therapy: ATX</p> <ul style="list-style-type: none"> ATX should be considered for children and adolescents with severe ADHD who do not respond to or are intolerant of stimulant medication, or in whom stimulant medication is contraindicated (grade B). ATX may be considered as the first-line medication if there is comorbid substance abuse, severe tic disorder, or anxiety disorder (recommended best practice). <p>Grade A: Body of evidence can be trusted to guide practice. Grade B: Body of evidence can be trusted to guide practice in most situations. Best practice points: Recommended best practice based on clinical experience and expert opinion.</p>

ADHD = attention-deficit/hyperactivity disorder; ATX = atomoxetine; DEX = dextroamphetamine / dexamphetamine; ER = extended release; HKD = hyperkinetic disorder; IR = immediate release; MA = meta-analysis; MPH = methylphenidate; MR = modified release; NICE = National Institute for Health and Clinical Excellence; RCT = randomized controlled trial; SIGN = Scottish Intercollegiate Guidelines Network; SR = systematic review.

APPENDIX 2: SUMMARY OF EVIDENCE AND RECOMMENDATIONS FROM GUIDELINES ON ADHD

Guideline	Relevant Statements about the Available Evidence	Relevant Recommendations on Long-acting versus Short-acting Drugs	Major Strengths/Limitations of Guideline
CADDRA ⁹ (2011)	<ul style="list-style-type: none"> The evidence for treating ADHD is not discussed. The evidence comparing LA and SA agents is not discussed. Central philosophy: treat each patient as a unique being; 13 principles for medication selection in the treatment of ADHD are provided (p. 55). 	<p>Medical treatment for uncomplicated ADHD for children and adolescents:</p> <ul style="list-style-type: none"> LA preparation, including Adderall XR, Biphentin, Concerta, Strattera, and Vyvanse are recommended as first line SA and intermediate-acting preparations are listed as second-line/adjunctive agents 	<p>Major limitation: rigour of development.</p> <p>No discussion of evidence supporting its practice guideline; no levels of evidence provided or strength of recommendations.</p>
CP3: Statement ⁸ (2009)	<ul style="list-style-type: none"> The authors acknowledge that the efficacy of IR and XR preparations are similar, as demonstrated through RCTs. Although not necessarily more <i>efficacious</i> than IR medication, the authors feel the XR preparations are more <i>effective</i> than IR. 	<ul style="list-style-type: none"> When stimulant medications for ADHD are indicated, XR preparations should be considered as first-line therapy because these preparations are more <i>effective</i> and less likely to be diverted. XR medications are more likely than IR medications to be used by the children and teenagers with ADHD for whom they have been prescribed. 	<p>Strength: identified scope and purpose and stakeholder involvement.</p> <p>Major limitation: rigour of development.</p> <p>No link between the recommendation and supporting evidence; no levels of evidence provided or strength of recommendations.</p>
European: <i>Long-acting Medications for the Hyperkinetic Disorders</i> ⁷ (2006)	<ul style="list-style-type: none"> XR preparations are superior to placebo and some are equivalent to multiple doses of IR MPH (grade A). XR stimulants have similar effect sizes to IR stimulants (level 1a) while effect sizes for non-stimulants (ATX) are somewhat smaller. SR medications may be less prone to abuse because they tend to have a slower rate of onset than IR (grade C). Key advantages of IR: lower cost and flexibility of dosages (consensus). Key advantages of LA: potential reduction of stigma at school, improved compliance, and possible reduced risk of misuse (consensus). 	<ul style="list-style-type: none"> LA preparations should be available and used. They should not replace SA drugs (which will be the initial treatment for many children, for reasons of cost and flexibility of dosing). Individual clinical choice will determine the choice of formulation used. 	<p>Strength: clinical questions defined, as well as method of guideline development (iterative); link between supporting evidence and recommendation; levels of evidence are provided for some, but not all; statement of supporting evidence</p> <p>Limitations: recommendations are not assigned a level of evidence on which they are based.</p>

Guideline	Relevant Statements about the Available Evidence	Relevant Recommendations on Long-acting versus Short-acting Drugs	Major Strengths/Limitations of Guideline
AACAP: Practice Parameter ¹¹ (2007)	<ul style="list-style-type: none"> LA formulations are as efficacious as the IR forms and have been shown to be efficacious in adolescents as well as children (reference cited). Advantages of LA: greater convenience for patient and family; enhanced confidentiality at school (no dose given at school); greater compliance (no references cited). Disadvantages of LA: may have greater problematic effects on evening appetite and sleep (no references cited). LA MPH may improve driving performance in adolescents relative to SA MPH (reference cited; RCT). SA stimulants often used as initial treatment in small children (< 16 kg) for whom there are no LA forms in sufficiently low dose (no references cited). 	<ul style="list-style-type: none"> Overall recommendation for treatment: The initial psychopharmacological treatment of ADHD should be a trial with an agent approved by the FDA for the treatment of ADHD (minimal standard). Stimulants are recommended first line (references cited). No specific formulation is recommended; it is the sole choice of the family and the clinician as to which agent should be used; each patient's treatment must be individualized. <p>Place in therapy: ATX</p> <ul style="list-style-type: none"> May be considered as the first-line agent for ADHD in individuals with an active substance abuse problem, comorbid anxiety, or tics (references cited). Preferred if the patient experiences severe side effects of stimulants, such as mood lability, tics (references cited). 	<p>Strength: major recommendations are easily identifiable, followed by a discussion of the relevant evidence.</p> <p>Limitation: rigour of development — methods for formulating the recommendations are not described.</p>
AACAP: Treatment for the Very Young ⁶ (2007)	<ul style="list-style-type: none"> No data exist to support ER stimulants in preschoolers. Clinical experience highlights the challenges of dosing three times a day. 	<p>Steps of the algorithm:</p> <ul style="list-style-type: none"> First-line: MPH (level A) Second-line: AMP (level C) Third-line option: ATX (level C) <p>No formulations are specified.</p> <p>ER formulations can be used to address compliance considerations. ER formulations limit dosing flexibility in the lowest dose ranges and therefore may be contraindicated in children whose optimal tolerated dose is lower than the ER dose.</p> <p>Level A: Well-controlled, randomized trials, large meta-analysis, or overwhelming clinical consensus.</p> <p>Level B: Empirical evidence, open trials, case series, or strong clinical consensus.</p> <p>Level C: Single case reports or no published reports, recommendation based on clinical and research experiences.</p>	<p>Strength: identified scope and purpose and stakeholder involvement; levels of evidence assigned to each step of the algorithm.</p> <p>Limitation: specific criteria for selecting evidence were not described.</p>

AACAP = American Academy of Child and Adolescent Psychiatry; ADHD = attention-deficit/hyperactivity disorder; AMP = amphetamine; ATX = atomoxetine; CADDRA = Canadian ADHD Resource Alliance; DEX = dextroamphetamine / dexamphetamine; CPS = Canadian Paediatric Society; ER = extended release; FDA = Food and Drug Administration; IR = immediate release; LA = long-acting; MD = medical doctor; MPH = methylphenidate; RCT = randomized controlled trial; SA = short-acting; XR = extended release.

Quaderni acp 2011; 18(5): 226

ADHD e genetica Uno studio e molte reazioni

Silvia Zanini
Pediatra di famiglia, ACP Verona

Abstract

ADHD and genetic. A study and many reactions

The Lancet recently published a study suggesting that ADHD determinants are not only social but also genetic (deletion and duplication of chromosome 16). All this aroused a great debate in UK media and strong criticism, but it has been considered by Lancet has a contribute to a further comprehension of the problem.

Quaderni acp 2011; 18(5): 226

Key words ADHD. Copy Number Variations. Heredità

La pubblicazione di uno studio su Lancet che suggerisce che i determinanti dell'ADHD non sono solo sociali, ma anche genetici (delezioni e duplicazioni sul cromosoma 16), ha portato a un dibattito che si è esteso ai media in Gran Bretagna. L'articolo ha provocato forti critiche, ma è stato difeso da Lancet come contributo alla comprensione del problema.

Parole chiave ADHD. Copy Number Variations. Ereditarietà

"ADHD news" è la Newsletter prodotta dal Laboratorio per la Salute materno-infantile dell'Istituto "Mario Negri" di Milano con l'aggiornamento bibliografico mensile di tutto ciò che viene indicizzato nel mese precedente nelle banche dati (Medline, Embase, PsycINFO e PsycArticle) in tema di ADHD nel bambino e nell'adolescente [1].

Lo studio di Lancet e le reazioni

Nell'ottobre 2010 segnalava la pubblicazione su Lancet di uno studio i cui risultati suggeriscono che i determinanti dell'ADHD non sono solo sociali, ma anche genetici [2]. Sono riportate alterazioni osservate nel patrimonio genetico (delezioni e duplicazioni) simili a quanto descritto per l'autismo e la schizofrenia [3]. L'articolo, pubblicato online a fine settembre prima della versione cartacea, ha suscitato da subito un forte e vivace dibattito ripreso anche dai media britannici, di cui la Newsletter dà testimonianza e riferimenti.

Mail Online: ADHD is "in a child genes" as scientist provide hope to ending bad behaviour stigma. Jenny Hope – BBC Radio 4 Today. 30 settembre 2010. Intervista al dr. Tim Kendall – BBC. Thought for the Day. 1 October 2010. Abdal Hakim Murad. Lo studio pubblicato da Lancet, letto e commentato dal gruppo di lettura ACP di Verona*, è abbastanza complesso e ben condotto nel suo disegno, con risultati che trovano conferma in un lavoro parallelo condotto su una popolazione islandese.

L'obiettivo che si sono dati gli Autori era quello di evidenziare e quantificare la presenza di microalterazioni cromosomiche (variazioni rare di copie numeriche, intese come delezioni o duplicazioni di poche unità di basi nei singoli alleli) in pazienti con diagnosi di ADHD accertata.

Nell'analisi finale sono stati inseriti 366 bambini e 1047 controlli. L'età media dei bambini era 10,5 anni ed erano per la stragrande maggioranza maschi (316 vs 50 bambine).

Tutte le analisi effettuate hanno identificato 135 CNVs (Copy Number Variations) rare di dimensioni superiori a 500 kb (57 nei pazienti e 78 nei controlli). È stato perciò identificato un eccesso altamente significativo di rare e ampie CNVs nei pazienti con ADHD.

In particolare il numero medio di CNVs in un bambino con ADHD era 2,09 volte più alto che nei controlli. 50 bambini (14% del totale) avevano una CNV superiore a 500 kb, contro 75 (7%) nei controlli. Non ci sono differenze tra maschi e femmine. Nei bambini con disabilità intellettiva (QI<70) il numero medio di CNVs era 5,69 volte più alto: 12 (36% del totale dei bambini con disabilità) avevano una CNV superiore a 500 kb, contro 38 (11%) in chi non aveva disabilità.

In ogni caso la presenza di duplicazioni o delezioni è comunque maggiore anche in quei bambini che non presentano disabilità intellettiva (+ 1,68 volte).

Il significato dello studio

Per quanto riguarda la possibile ereditarietà di queste modificazioni genetiche, là dove era disponibile il genoma dei genitori, è stata condotta un'analisi che ha dimostrato che di 15 CNVs quattro erano mutazioni *de novo*. Sei CNVs sono state ereditate dalla mamma e cinque dal padre. Le anomalie genetiche sono inoltre risultate particolarmente presenti su un cromosoma coinvolto nella schizofrenia e nell'autismo (il cromosoma 16p13.11).

Come sottolineato da "ADHD news", lo studio è pressoché unico per dimensioni, accuratezza e originalità metodologica. Pur con ricadute pratiche (cliniche) attualmente nulle, i risultati contribuiscono all' ampliamento delle conoscenze della genetica clinica e della relazione tra genotipo e fenotipo [3]. La Newsletter riporta anche quanto scritto in tal senso su Lancet nell'Editoriale, nel Comment di P. Burbach e nella rubrica "Perspective" di S. Jones [4-5-6]. In particolare l'editoriale conclude che "Far from closing the book on ADHD, Williams and colleagues' results represent the first tentative steps on a journey toward new insights into the pathogenesis and neurobiology of a condition misunderstood for far too long". Una sorta di difesa degli Autori dopo le forti reazioni e critiche (the blogosphere is cracking with argument and counter-argument: are naughty children the victims of nature, or nurture?) seguite alla pubblicazione dell'articolo on line a fine settembre 2010. ♦

Bibliografia

- [1] <http://www.marionegri.it/mn/it/riservamedico/newsletterADHD/arcivio.html>.
- [2] Williams NM. Rare chromosomal deletions and duplications in attention-deficit hyperactivity disorder: a genome-wide analysis. Lancet 2010;376:1041-08.
- [3] Bonati M. ADHD news n° 35, ottobre 2010.
- [4] Reflections on ADHD. Editoriale. Lancet 2010; 376:1364.
- [5] Neuropsychiatric connections of ADHD genes. Lancet 2010;376:1367-8.
- [6] The art of medicine. Bad seeds, bad science, and fairly black cats? Lancet 2010;376:1384.

*Maddalena Agostini, Daniela Bennati, Paolo Brutti, Federica Carraro, Claudio Chiamenti, Paolo Fortunati, Maria Iuliano, Maria Stella Lonardi, Giancarlo Melotti, Donatella Merlin, Maddalena Nardi, Francesco Raimo, Mauro Previdi, Mara Tommasi, Silvia Zanini.

Per corrispondenza:
Silvia Zanini
e-mail: silviazanini@aliceposta.it

il punto su

Presidente del Corso e Segreteria Scientifica:

Prof. Giuseppe Chiarenza
 Primario di Neuropsichiatria Infantile
 Azienda Ospedaliera G. Salvini – Garbagnate Milanese
Giuseppe.Chiarenza@fastwebnet.it

Sede:

Auditorium - Collegio Padri Oblati
 Corso Europa, 228
 Rho (Milano)

**Segreteria Organizzativa e
Provider ECM (1293)**

 S.r.l.
 Via Nizza, 45 - 00198 Roma
 Tel: 06 85355590
 Fax: 06 85356060
 e-mail: Manuela.Morandini@ptsroma.it
www.ptsroma.it

Patrocini

Con il contributo non condizionato di



Con il Patrocinio di
 IOP (International Organization of Psychophysiology)
 SINPIA (Società Italiana di Neuropsichiatria
 dell'Infanzia e dell'Adolescenza)

Progetto Regionale: Condivisione di percorsi
 diagnostico-terapeutici per l'ADHD dei Centri di
 riferimento della Regione Lombardia

Evidence-based treatment of ADHD: Neuropsychological and psychophysiological endophenotypes



18 Novembre 2011
 Auditorium
 Collegio Padri Oblati
 Rho (Milano) - Italy

Modalità di iscrizione

Le iscrizioni saranno ammesse esclusivamente tramite email indirizzata alla Segreteria Organizzativa entro e non oltre il 10 Novembre. Nella mail ogni partecipante dovrà chiaramente riportare: nome e cognome / qualifica professionale / ente di appartenenza e città / recapito telefonico.

L'evento fa parte del Progetto Regionale "Condivisione di percorsi diagnostico-terapeutici per l'ADHD dei Centri di riferimento della Regione Lombardia". La partecipazione è gratuita per tutti i professionisti e gli specializzandi afferenti ai centri ADHD ed alle UONPIA della Lombardia (riferirsi alle categorie dichiarate in ECM), nonché per i Soci SINPIA della medesima Regione (nella email d'iscrizione gli interessati dovranno chiaramente specificare l'ente di appartenenza in forma di autocertificazione).

Quota di iscrizione per i partecipanti provenienti da altre regioni:

Soci SINPIA: € 50,00 + IVA 21% (ovvero € 60,50)

Specializzandi: € 50,00 + IVA 21% (ovvero € 60,50)

Non Soci SINPIA: € 100,00 + IVA 21% (ovvero € 121,00)

La quota di partecipazione dovrà essere saldata entro e non oltre il 10 Novembre a mezzo bonifico bancario: Beneficiario: PTS SRL / ADHD RHO
IBAN: IT27 P030 6903 2271 0000 000 2695
Specificare chiaramente nella motivazione: il nome dell'ordinante e "iscrizione Corso ADHD Rho 18 novembre"

Le iscrizioni "on-site" saranno possibili previa disponibilità di posti.

È prevista la traduzione simultanea dall'italiano all'inglese e viceversa

Crediti Formativi ECM:

All'evento sono stati assegnati 5 crediti formativi per le seguenti categorie professionali (massimo 150 partecipanti):

- ✓ Logopedista
- ✓ Medico chirurgo (Neuropsichiatria Infantile, Pediatria)
- ✓ Psicologo
- ✓ Terapista della neuro e psicomotricità dell'età evolutiva

Al fine di ottenere i crediti il partecipante dovrà:

- ✓ garantire il 100% della propria presenza in aula, presenza che verrà monitorata attraverso l'obbligo di firma
- ✓ ritirare presso la Segreteria la scheda nella quale dovranno essere riportati i dati anagrafici, la valutazione dell'evento e il questionario a risposta multipla
- ✓ riconsegnare i suddetti documenti, debitamente compilati, al termine dell'evento formativo (schede incomplete non verranno prese in considerazione ai fini dell'ottenimento dei crediti)

08:30 Registration

09:15 Welcome address and Introduction
Giuseppe Chiarenza (Rho, IT)

09:30 Differential diagnosis of ADHD
Charles Njokiktjen (Amsterdam, NL)

10:30 QEEG in childhood psychiatric disorders: subtyping and diagnostic utility
Leslie Prichep (New York, USA)

11:30 Reliability, sensitivity, and specificity in ADHD
Leo de Sonnevill (Amsterdam, NL)

12:30 Brunch

13:30 Neuroimaging correlates of task performance
Ilse Schuitema (Leiden, NL)

14:30 QEEG and source localization in subtyping ADHD
Leslie Prichep (New York, USA)

15:30 The ANT profiles of responders and non responders ADHD children chronically treated with Atomoxetine
Grazia Lo Torto (Rho, IT)

16:30 The qEEG characteristics following long-term treatment with Atomoxetine
Luciano Montaldi (Rho, IT)

17:30 Discussion and End of symposium
Giuseppe Chiarenza (Rho, IT)

P
R
O
G
R
A
M
M
A





UNIVERSITÀ
DEGLI STUDI
DI PADOVA

FACOLTÀ DI PSICOLOGIA

MASTER IN GENITORIALITÀ E SVILUPPO DEI FIGLI:

interventi preventivi e psicoterapeutici

Direttore: Prof.ssa G. Fava Vizziello



**Corso di
VALUTAZIONE DI SITUAZIONI CLINICHE
CON L'AIUTO DELL'AAI, DELL'LTP,
DELLO SPECCHIO E DELLE SCALE DI SVILUPPO**

18- 19- 20- 21 Gennaio 2012

Per sette laureati non iscritti al Master sarà possibile frequentare un primo breve corso di valutazione di situazioni cliniche con l'aiuto dell'AAI, dell'LTP, dello Specchio e delle Scale di sviluppo.

Il corso si propone di fornire per ciascuno strumento una breve presentazione teorica ed esemplificazioni di codifica clinica con l'ausilio di materiale audiovisivo.

Chi vorrà continuare la formazione avrà la possibilità di proseguire partecipando a supervisioni di casi clinici studiati con gli strumenti sopra citati. In queste supervisioni periodiche i partecipanti discuteranno i propri casi a cui sarà stato possibile applicare almeno uno degli strumenti.

Il corso si terrà presso le aule della Facoltà.

Il costo è di € 223,12 e per l'ammissione è richiesta una Laurea in Psicologia, Medicina o Servizio Sociale.

Al termine verrà rilasciato uno specifico attestato di partecipazione.

Informazioni sulle modalità di iscrizione sono reperibili al seguente link:

http://www.unipd.it/unipdWAR/page/unipd/studenti0/it_5_11_1_1_P61



Considerando il recente avvio del Registro regionale Lombardo per l'ADHD, il programmato avvio di altri registri regionali e di una nuova forma ridotta di registro Nazionale, la possibile autorizzazione all'immissione al commercio per alcune formulazioni a lento rilascio per il prossimo anno, e l'interesse suscitato dalle scorse edizioni, è in preparazione il

4° Workshop sull'ADHD

che si terrà a

Cagliari dall'8 al 10 Marzo 2012.

Quest'anno parteciperanno allo workshop anche alcuni colleghi europei che stimoleranno la discussione su argomenti controversi (p. es., comorbidità con Disturbi pervasivi dello sviluppo e/o ritardo mentale, neuro feedback come pratica terapeutica, efficacia degli interventi non farmacologici).

Come lo scorso anno lo workshop sarà articolato in Letture, Simposi, Dibattiti e Poster, cui si aggiungeranno i Seminari. I Seminari si svolgeranno in piccoli gruppi (25-30 partecipanti) e avranno due animatori (un italiano e uno straniero). I risultati di ciascun Seminario saranno riportati nella sessione plenaria per la discussione collettiva.

Alcuni dei temi saranno ulteriormente discussi nell'ambito della *EUNETHYDIS 2nd International ADHD Conference* che si terrà a Barcellona il 23-25 Maggio.

Per maggiori informazioni: <http://eunethydisconference.com/index.html>

Alessandro Zuddas, Maurizio Bonati, Antonella Costantino, Gabriele Masi, Pietro Panei

Per ricevere la newsletter iscriversi al seguente indirizzo:

<http://crc.marionegri.it/bonati/adhdnews/subscribe.html>

Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia
(in attuazione della D.G. sanità n. 3250 del 11/04/2011)
Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia"
"Condivisione dei percorsi diagnostico-terapeutici per l'ADHD in Lombardia".

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI
DIPARTIMENTO DI SALUTE PUBBLICA
Laboratorio per la Salute Materno Infantile
Via Giuseppe La Masa, 19 - 20156 Milano MI - Italia - www.marionegri.it
tel +39 02 39014.511 - fax +39 02 3550924 - mother_child@marionegri.it