Attention deficit hyperactivity disorder (ADHD) in children and adolescents

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Estimates of the prevalence of attention deficit hyperactivity (ADHD) vary widely which has led to some controversy over the diagnosis. Nevertheless, it is recognised in DSM-5 and as hyperkinetic disorder in ICD-10. Here the authors compare diagnostic criteria of ADHD in DSM-5 and ICD-10 and review its management.

Attention deficit hyperactivity disorder (ADHD) is a common childhood mental health disorder. There seems to be wide range in the prevalence of the condition throughout the world. Epidemiology of ADHD across the lifespan is also variable and heterogeneous. In the UK, a survey of 10 438 children between the ages of five and 15 years found that 3.62% of boys and 0.85% of girls had ADHD.[1] This survey was founded on careful assessment and included impairment in the diagnosis.

The more restricted diagnosis of hyperkinetic disorder (HD) in ICD-10, representing a severe subgroup of DSM-IV-TR combined-type ADHD, is naturally less common; prevalence estimates are around 1.5% for boys in the primary school years.[2] In the international studies prevalence estimates of ADHD vary widely and the reasons for which remain poorly understood. In 2007 Polanczyk and colleagues[3] undertook a systemic review of prevalence studies from January 1978 to December 2005 and reviewed textbooks and reference lists of the studies selected. The ADHD/HD worldwide-pooled prevalence was 5.29%. This estimate was associated with significant variability. In the multivariate metaregression model, diagnostic criteria, source of information, requirement of impairment for diagnosis, and geographic origin of the studies were significantly associated with ADHD/HD prevalence rates. Geographic location was associated with significant variability only between estimates from North America and both Africa and the Middle East. No significant differences were found between Europe and North America. The authors also commented that the source of information and assessment of clinical impairment could influence the prevalence rates. They concluded that population characteristics, methodology features, ethnic and cultural differences and diagnostic criteria involved in studies affect the prevalence of ADHD.

Another systemic review by Galanakis *et al.* in 2007 found wide variation in the prevalence of ADHD among different studies, ranging from 2.2 to 17.8%.[4] The BELLA study group's estimated prevalence rates for the diagnoses of ADHD according to DSM-IV criteria were 5.0% and the rate for HD according to ICD-10 criteria was 1.0%.[5] Higher prevalence rates were found in boys and in younger children. The lifetime administrative prevalence rate was 6.5%.

In a study to determine prevalence of ADHD in Colombian Paisa children and adolescents the prevalence rates were estimated to be 19.8% and 12.3% for boys and girls, respectively.[6]

Estimated prevalence of undiagnosed ADHD within substance use disorder inpatients in South London was around 12%. Those individuals with substance use disorders and ADHD had significantly higher self-rated impairments across several domains of daily life; and higher rates of substance abuse and alcohol consumption, suicide attempts, and depression recorded in their case records. It is also evident that the disorder persists into adulthood in two-thirds of cases. The best available estimate of ADHD prevalence is 4.4% in adulthood.[7]

Diagnosis

Attention Deficit Hyperactivity Disorder (ADHD) and hyperkinetic disorder (HD) are terms used by DSM-5[8] and ICD 10,[9] respectively. DSM-5 uses the same 18 symptoms that are used in DSM-IV, divided into two symptom domains (inattention and hyperactivity /impulsivity), of which at least six symptoms in one domain are required for diagnosis. However, several changes have been made in DSM-5:

– Examples have been added to the criterion items to facilitate application across the life span

– The cross-situational requirement has been strengthened to 'several' symptoms in each setting

– The onset criterion has been changed from

'symptoms that caused impairment were present before age seven years' to 'several inattentive or hyperactive-impulsive symptoms were present prior to age 12'.
– Subtypes have been replaced with presentation specifiers that map directly to the prior subtypes.
– A comorbid diagnosis with autism spectrum disorder is now allowed, and
– A symptom threshold change has been made for adults, to reflect their substantial evidence of clinically significant ADHD impairment, with the cut-off for ADHD of five symptoms, instead of six required for younger persons, both for inattention and for hyperactivity and impulsivity.

ADHD was placed in the neurodevelopmental disorders chapter to reflect brain developmental correlates with ADHD and the DSM-5 decision to eliminate the DSM-IV chapter that includes all diagnoses usually first made in infancy, childhood or adolescence.

People with ADHD show a persistent pattern of inattention and / or hyperactivity-impulsivity that interferes with functioning or development:

Inattention: patients are required to show six or more symptoms of inattention (below) for children up to age 16 years, or five or more for adolescents 17 years and older and adults; symptoms of inattention have been present for at least six months, and they are inappropriate for developmental level:
i. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or with other activities.
ii. Often has trouble holding attention on tasks or play activities.
iii. Often does not seem to listen when spoken to directly.
iv. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (eg loses focus, side-tracked).
v. Often has trouble organising tasks and activities.
vi. Often avoids, dislikes, or is reluctant to do tasks that require mental effort over a long period of time (such as schoolwork or homework).
vii. Often loses things necessary for tasks and

ICD-10	DSM-5
Arise in first 5 years of life Excessive restlessness in the context of what is expected in comparison to other similar children Symptoms present in more than one situation Prematurely breaks off from tasks and leaves activities unfinished Changes frequently between activities Loses interest in tasks secondary to being diverted to another Disinhibition in social relationships Recklessness in dangerous situations Impulsive flouting of social rules Prematurely answering questions Difficulty waiting in turn	Several symptoms must have been present before age 12 Inattention and/or hyperactivity-impulsivity more severe than observed in individuals at comparable level of development Several (6) symptoms must be shown in two or more settings Failure to follow through on requests or instructions and fails to complete schoolwork, chores, duties Frequently shifts from one uncompleted activity to another Fidgeting, not remaining seated, excessive running/climbing, difficulty engaging quietly in leisure activities, appearing 'on the go', talking excessively Clear evidence of interference with developmentally appropriate social, academic or occupational settings Difficulty in delaying responses / blurting out answers Difficulty waiting in turn Fails to give close attention to details, or makes careless mistakes in tasks Work often messy and performed carelessly without considered thought Often appears as if mind is elsewhere or not listening/didn't hear what has just been said Tasks requiring sustained mental effort experienced as unpleasant and markedly aversive Disorganised work habits, materials required for task often scattered, lost, carelessly handled and/or damaged Easily distracted by irrelevant stimuli easily ignored by others Forgetful in daily activities Difficulty organising tasks and activities Difficulty sustaining attention in tasks of play activities, finds it hard to persist in tasks to completion Symptoms do not occur only during course of a psychotic disorder

Table 1. Comparison of diagnostic criteria for hyperkinetic disorder in ICD-10 with ADHD in DSM-5

activities (eg school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).
viii. Is often easily distracted
ix. Is often forgetful in daily activities.

Hyperactivity and impulsivity: patients are required to show six or more symptoms of hyperactivity-impulsivity (below) for children up to age 16 years, or five or more for adolescents 17 years and older and adults, and symptoms of hyperactivity-impulsivity need to have been present for at least six months to an extent that is disruptive and inappropriate for the person's developmental level:
i. Often fidgets with or taps hands or feet, or squirms in seat.
ii. Often leaves seat in situations when remaining seated is expected.
iii. Often runs about or climbs in situations where it is not appropriate (adolescents or adults may be limited to feeling restless).
iv. Often unable to play or take part in leisure activities quietly.
v. Is often 'on the go' acting as if 'driven by a motor'.
vi. Often talks excessively.
vii. Often blurts out an answer before a question has been completed.
viii. Often has trouble waiting his/her turn.
ix. Often interrupts or intrudes on others (eg butts into conversations or games).

In addition, the following conditions must be met:
– Several inattentive or hyperactive-impulsive symptoms were present before age 12 years.
– Several symptoms are present in two or more settings (eg at home, school or work, with friends or relatives or in other activities).
– Clear evidence that the symptoms interfere with, or reduce the quality of, social, school, or work functioning.
– Symptoms do not happen only during the course of schizophrenia or another psychotic disorder. The symptoms are not better explained by another mental disorder.

Based on the types of symptoms, three kinds (presentations) of ADHD can occur:
Combined presentation: if enough symptoms of both criteria inattention and hyperactivity-impulsivity were present for the past six months.
Predominantly inattentive presentation: if enough symptoms of inattention, but not hyperactivity-impulsivity, were present for the past six months.
Predominantly hyperactive-impulsive presentation: if enough symptoms of hyperactivity-impulsivity but not inattention were present for the past six months.

In this review, we will be using DSM-IV[10] for diagnostic criteria which are still widely used across Europe and North America.

ICD-10 uses a different nomenclature – hyperkinetic disorder, a subgroup of the DSM-IV-TR ADHD combined-type diagnosis. The criteria are more stringent and require that symptoms of hyperactivity, inattention and impulsivity should be all present for a diagnosis. In contrast to DSM-5, there is only the subtype of 'combined type ADHD' in the ICD-10 classification.

For a diagnosis of hyperkinetic disorder ICD-10 requires at least six symptoms of inattention, at least three symptoms from hyperactivity and at least a symptom from impulsivity for a diagnosis. And symptoms have to persist for at least six months, to a degree that is maladaptive and inconsistent with the developmental level of the child. The onset of the disorder is no later than the age of seven years. The criteria should be met in more than one situation. There needs to be evidence that inattentive and impulsivity symptoms cause clinically significant distress or impairment in social, academic or occupational functioning.

Hyperkinetic disorder is further divided into hyperkinetic disorder with and without conduct disorder.

In children the criteria are usually applied on the basis of parent and teacher reports of behaviour, rather than subjective reports of mental state. Older children and adults are usually able to provide detailed descriptions of their subjective experiences of inattention, hyperactivity and impulsivity.

ADHD behaviours and symptoms result from genetic, physical environmental or social environmental causes.

In common with most mental health conditions there is no definitive biological test for ADHD; diagnosis depends on the observation of clusters of symptoms in three main behavioural domains according to the DSM-5 and ICD-10 criteria.

The diagnosis of ADHD has been the subject of considerable controversy and debate and the diagnosis itself has varied across time and place as diagnostic systems have evolved.[11]

The controversies were mainly due to the wide variation in prevalence rates reported for ADHD and the possible reasons for these differences, and the nature of the aetiological factors that increase the risk for ADHD. The considerable increase in diagnosis and treatment of the condition sparked a surge of conspiracy theories in electronic media questioning the validity of the diagnosis.

Although there are no gold standards in ADHD diagnosis that can be reliably applied when data capture tools such as standardised clinical interviews used

Drug, brand name, formulation, strength	Dosage	Common side effects	Onset and duration of action	Monitoring
Atomoxetine (noradrenaline re-uptake inhibitor) Strattera Capsule 10, 18, 25, 40, 80mg	Can be given as a single dose or in 2 divided doses, but last dose no later than early evening Children ≥6 years (body weight up to 70kg): initially 500mcg/kg daily for 7 days, increase according to response. Usual maintenance 1.2mg/kg daily BNFc: may be increased to 1.8mg/kg daily (unlicensed) (max 120mg daily) under the direction of a specialist Children ≥6 years (body weight >70kg): initially 40mg daily for 7 days, increase according to response, usual maintenance dose 80mg daily BNFc: may be increased to max 120mg daily (unlicensed) under the direction of a specialist	Anorexia, nausea and vomiting, increased alertness, insomnia, dizziness	Takes 4-6 weeks for the onset of action	Pulse, BP, height, weight
Dexamfetamine sulfate Dexamfetamine Tablet, scored 5mg	Child 6–18 years: initially 2.5mg 2–3 times daily, increase if necessary at weekly intervals by 5mg. Usual max 1mg/kg (max 20mg daily; occasionally 40mg) daily; maintenance dose given in 2–4 divided doses		Onset 20–60 min Duration 3–6 hours	Pulse, BP, weight, height
Methylphenidate hydrochloride immediate release Ritalin Tablet, scored 10mg Medikinet Tablet 5, 10, 20mg	Child 4–6 years: 2.5mg twice daily increased if necessary at weekly intervals by 2.5mg daily to max 1.4mg/kg daily in divided doses Discontinue if no response after 1 month Child over 6 years: initially 5mg 1–2 times daily, increased if necessary at weekly intervals by 5–10mg daily: licensed max 60mg daily in 2-3 divided doses BNFc: may be increased to 2.1mg/kg daily (unlicensed) in 2–3 divided doses (max 90mg daily) under the direct supervision of specialist Discontinue if no response in 1 month.	Headache, anorexia, nausea and vomiting, nervousness, nasopharyngitis, aggression, dizziness, insomnia	Onset 20-60min Duration 2-4 hours	BP, pulse, weight, height

Table 2. ADHD medication (source: British National Formulary for children (evidence.nhs.uk/formulary/bnfc/current; British National Formulary (evidence.nhs.uk/formulary/bnf/current); emc+ (medicines.org.uk/emc)

Drug, brand name, formulation, strength	Dosage	Common side effects	Onset and duration of action	Monitoring
Methylphenidate hydrochloride Concerta XL Tablet, modified release (22% immediate release, 78% modified release) 18, 27, 36, 54mg	Child 6–18 years: initially 18mg once daily in the morning, increased if necessary at weekly intervals by 18mg according to response, licensed max 54mg once daily BNFc: may be increased to 2.1mg/kg daily (unlicensed) (max 108mg daily) under the direct supervision of a specialist Discontinue if no response in 1 month	Headache, anorexia, nausea and vomiting, nervousness, nasopharyngitis, Aggression, dizziness, insomnia	Onset 30 min – 2 hours Duration 12 hours	BP, pulse, weight, height
Methylphenidate hydrochloride Equasym XL Capsule, modified release (30% immediate release, 70% modified release) 10, 20, 30mg	Child 6–18 years: initially 10mg once daily in the morning before breakfast, increased gradually at weekly intervals if necessary. Licensed max 60mg daily BNFc: may be increased to 2.1mg/kg daily (unlicensed) in 2–3 divided doses (max 90mg daily) under the direct supervision of specialist Discontinue if no response in 1 month.	Headache, anorexia, nausea and vomiting, nervousness, nasopharyngitis, aggression, dizziness, insomnia	Onset 20-60min Duration – 8 hours	BP, pulse, weight, height
Methylphenidate hydrochloride Medikinet XL Capsule, modified release (50% immediate release, 50% modified release) 5, 10, 20, 30, 40mg	Child 6–18 years: initially 10mg once daily in the morning before breakfast, increased gradually at weekly intervals if necessary. Licensed max 60mg daily BNFc: may be increased to 2.1mg/kg daily (unlicensed) in 2–3 divided doses (max 90mg daily) under the direct supervision of specialist Discontinue if no response in 1 month.	Headache, anorexia, nausea and vomiting, nervousness, nasopharyngitis, aggression, dizziness, insomnia	Onset 20-60min Duration – up to 8 hours	BP, pulse, weight, height
Lisdexamfetamine mesilate Elvanse Capsule 30, 50, 70mg	Child aged over 6 years refractory to methylphenidate; Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural disorders: initially 30mg once daily in the morning, increased if necessary at weekly intervals by 20mg; max. 70mg daily Discontinue if response insufficient after 1 month	Nausea, decreased appetite, vomiting, diarrhoea, dry mouth, abdominal cramps, dyspnoea, sleep disturbances, tics, aggression, headache, dizziness, drowsiness, mydriasis, labile mood, weight loss, pyrexia, malaise, growth restriction in children	It has a smooth onset of action, exerts its action for up to 13 hours and may have fewer rebound symptoms	Pulse, BP, weight, height

Table 2. ADHD medication (source: British National Formulary for children (evidence.nhs.uk/formulary/bnfc/current; British National Formulary (evidence.nhs.uk/formulary/bnf/current); emc+ (medicines.org.uk/emc) (cont.)

by trained individuals and operational diagnostic criteria are employed.[12-16]

Management

There are numerous considerations to bear in mind in the management of ADHD.[17] Whilst drugs are a mainstay of treatment,[2] changes in psychological and other domains of functioning are essential if patients are to capitalise on the improvements in the core symptoms of ADHD with treatment. Care should be tailored to individuals following assessment.[18]

Pre-school children

Drug treatments are not recommended in this age group due to the unknown long term effects on brain development.[2,19-20] They take longer to clear the drug from their body, and have higher rates of adverse effects.[17]

Referral to a parent training programme for behavioural management should be the first treatment, [2,19] ideally with specially trained facilitators.[20] Group-based parent training for conduct disorder should be available whether a child has a diagnosis of conduct disorder or not. Parents should have access to eight to 12 sessions.[19]

With consent, nursery or pre-school carers should be informed about ADHD and any special requirements.[19-20]

School children

For those with moderate impairment, parent education either alone, or with group CBT for the child, should be considered. Those who continue to suffer significant impairment despite intervention should be offered pharmacological intervention.[2,19] Those diagnosed with severe ADHD should be offered stimulants as a first-line treatment, though not if there is a history or family history of cardiac problems.[20] Teachers trained regarding ADHD should help to provide interventions in school[19] as improvement in behaviour at home does not correlate with an improvement in behaviour at school.[20]

Adults

In the UK, continuation of pharmacotherapy in ADHD into adulthood is licensed. However, initiation of treatment in adulthood is not[18-19,21] and requires off-label prescribing.

Drug treatment with methylphenidate is the first-line choice, unless there is preference for a psychological approach.[2,19] If there is a poor response to this after an adequate trial over six weeks, atomoxetine or dexamfetamine are the next line of drug treatment.[19]

Drug treatments should form part of a comprehensive treatment programme addressing psychological, behavioural, educational and occupational needs.[2,19]

A psychological approach can be used if a patient refuses drug treatment, or has an inadequate response to drug therapy.[19]

Children with learning disability

IQ, neurodisability and co-morbidities are not a barrier to standard treatment. Small studies show that treatment with methylphenidate in children with learning disabilities is less effective and more likely to result in adverse effects when compared to a normal population.[20]

Psychological interventions

Families with children with ADHD are often dysfunctional in multiple domains. Co-existing problems may not improve with medication.[22]

The aim of psychological intervention is improvement in daily functioning through behaviour and relationships, whilst giving parents strategies to cope with difficult behaviour.[19]

Behavioural therapy uses rewards or reinforcements, to implement changes in motor, impulse or attention control.[19,23] Techniques involving negative consequences are less commonly implemented. 'Time out' involves removing the child from the attention of others.[19]

Parent training involves teaching behaviour therapy intervention to carers. This increases parental competence, confidence and improves the carer / child relationship.[19]

Self-instructional training comprises techniques to help children develop a reflective, systematic and goal-directed approach to tasks, identifying the impact of behaviour and emotions from maladaptive cognitions and replacing them.[23]

Social skills training helps those with ADHD develop behaviours to maintain constructive social relationships using CBT techniques.[23]

Pharmacotherapy

Medications used to treat ADHD act as agonists or reuptake inhibitors of dopamine or noradrenalin neurotransmitters. The role of these neurotransmitters in ADHD is not yet understood. Methylphenidate is commonly used first line, followed by atomoxetine, then dexamfetamine. Tertiary services may use alternatives such as clonidine, imipramine, bupropion and modafinil.[24] Atomoxetine is metabolised by CYP2D6, therefore poor metabolisers should be prescribed a lower dose.

Psychostimulants show an effect within hours of administration, whereas atomoxetine requires four to six weeks of administration to have an effect.[24] Some studies have shown that response rates and symptom improvement seen with atomoxetine are similar to those associated with psychostimulants,[20,25] though some show a lesser effect.[20]

Treatments should be titrated upwards according to individual needs until no further improvement is noted and side-effects are tolerable. Response to a test dose should be reviewed within a few weeks, with efficacy monitored using a rating scale.[17]

In children, height should be checked prior to initiation[17,19,20] and every six months thereafter,[19] weight checked at initiation,[17,19,20] at three months, six months, then every six months thereafter.[19] Heart rate and blood pressure should be checked prior to initiation and every three months thereafter.[19]

Managing side-effects

Methylphenidate and atomoxetine are generally well tolerated.[24]

Lack of weight gain and growth should lead to medication review. Reduced weight gain may be managed by providing higher calorie meals during breakfast and dinner whilst stimulant effect is low.[17]

Pharmacological treatments increase blood pressure and pulse to a small degree statistically, which can be problematic with antecedent cardiac disease, requiring review of the risk / benefit ratio of treatment.[18]

Rash and pruritis may warrant discontinuation if severe and do not settle.[24]

Patients are not always aware that psychiatric side-effects may be medication related.[18] Symptoms of psychosis, mania, panic attacks and violent behaviour should be reported urgently with a view to dose reduction or cessation. Tics, dysphoria and 'zombie-like' states may be resolved with dose reduction.[17]

Children starting atomoxetine and their carers should be advised to recognise severe hepatic disorders and suicidal thoughts and behaviours. Atomoxetine should be discontinued following any evidence of liver injury.[24]

Long-term outcome

ADHD is a chronic disorder, increasingly being recognised as a lifelong condition which starts in childhood but may continue in adolescence and into adulthood. It is globally recognised as a serious medical condition, as evidenced by a rise in published research into ADHD long-term outcomes signalling an increase in global interest and recognition of consequences and impairment associated with ADHD.[26]

The criteria for ADHD are well defined; the long-term outcomes in children, adolescents and adult will largely depend upon whether these groups receive treatment, as without treatment people with ADHD experience poor long-term outcomes in day-to-day functioning across all age groups.[27]

Children with ADHD are more likely than unaffected children to experience learning difficulties, miss school, become injured, experience troublesome relationships with family members and peers and exhibit mental and physical conditions. Left untreated, the condition has a significant impact in the long-term on education resulting in academic failure, and leads to antisocial behaviour, poor self esteem and a significant impact on social functioning.[27,28]

In addition to core symptoms, adolescents with ADHD will exhibit deficits in executive functioning, lower frustration tolerance and emotional responses that are more pronounced than expected. Adolescents with ADHD who are left untreated display significant problems in the long term with poor academic achievement, difficulties in peer interactions, more parent-teen conflict,[29] abuse of illicit substances and experience other mental health problems, including depression, anxiety problems and sleep difficulties.[30-31]

Adults with untreated ADHD demonstrate reduced lifetime earnings, increased illness, lower educational and job status, are often socially isolated, with a higher likelihood of acquiring sexually transmitted diseases and are more likely to become parents at earlier ages compared with their counterparts. Interest in long-term outcomes in adult with ADHD has increased due to the impact it has on work, daily living, family living and relationships.[32-34]

Conclusion

In common with other authors we believe that standardised analyses may lead to firm conclusions about the true prevalence of ADHD, the estimation of which seems impossible to achieved by simply reviewing the existing literature.[35]

Both DSM-IV and ICD-10 criteria will continue to be used for diagnostic purposes for ADHD, although eventually DSM-5 will replace DSM-IV. Although the diagnostic criteria in DSM-5 are fundamentally the same as in DSM-IV.

ADHD guidelines[2,20] suggest person-centered care and tailoring individuals needs in terms of medication and behavioral and psychological interventions are important.

ADHD is potentially a lifelong condition with a profound effect on quality of life.[36-38] Current evidence

supports the premise that, without treatment, people with ADHD often experience poorer long-term outcomes than those without the condition, which may be improved with treatment, but the question remains as to whether the short-term benefits demonstrated by short-term drug or non-pharmacological treatment studies translate directly into long-term outcomes.[27] Further long-term studies are needed.

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Declaration of interests

No conflicts of interest were declared.

References

1. Ford T, Goodman R, Meltzer H. The British Child and Adolescent Mental Health Survey 1999: the prevalence of DSM-IV disorders. *J Am Acad Child Adolesc Psychiatry* 2003;42:1203–11.
2. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults. Clinical Guideline 72. NICE, 2008.
3. Polanczyk, G, Silva de Lima M, Horta BH, et al. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *Am J Psychiatry* 2007;164:942–8.
4. Skounti M, Philalithis A, Galanakis E. Variation in prevalence of attention deficit hyperactivity disorder worldwide. *Eur J Pediatr* 2007;166(2):117–23.
5. Döpfner M, Breuer D, Wille N, et al; BELLA study group. How often do children meet ICD-10/DSM-IV criteria of attention deficit-/hyperactivity disorder and hyperkinetic disorder? Parent-based prevalence rates in a national sample – results of the BELLA study. *Eur Child Adolesc Psychiatry* 2008;17(Suppl1):59–70.
6. Pineda DA, Lopera F, Palacio JD, et al. Prevalence estimations of attention deficit/hyperactivity disorder: differential diagnoses and co morbidities in a Colombian sample. *Int J Neurosci* 2003;113:49–71.
7. Huntley Z, Maltezos S, Williams C, et al. Rates of undiagnosed attention deficit hyperactivity disorder in London drug and alcohol detoxification units. *BMC Psychiatry* 2012;12:223.
8. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th edn. Washington: APA, 1994
9. The ICD-10 Classification of Mental and Behavioural Disorders. Geneva: World Health Organization, 1992.
10. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th edn. Washington: APA, 2013.
11. Rhodes SM, Coghill D, Matthews K. Acute neuropsychological effects of the psychostimulant methylphenidate in drug naive boys with ADHD. *J Child Psychol Psychiatry* 2006:47;1184 –94.
12. Taylor, E. Overactivity, hyperactivity and hyperkinesis : problems and prevalence. In The Overactive Child: Clinics in Developmental Medicine No. 97 (ed. E. Taylor). London & Oxford: Mac Keith Press & Blackwell, 1986.
13. Taylor EA, Schachar R, Thorley G, et al. Conduct disorder and hyperactivity: I. Separation of hyperactivity and antisocial conduct in British child psychiatric patients. *Br J Psychiatry* 1986;149:760–7.
14. Schwab-Stone M, Fisher P, Piacentini J, et al. The Diagnostic Interview Schedule for Children-Revised Version (DISC-R): II. Test-retest reliability. *J Am Acad Child Adolesc Psychiatry* 1993;32:651–7.
15. Schwab-Stone M, Fallon T, Briggs M, et al. Reliability of diagnostic reporting for children aged 6–11 years: a test-retest study of the Diagnostic Interview Schedule for Children-Revised. *Am J Psychiatry* 1994;151:1048–54.
16. Epstein JN, Willoughby M, Valencia EY, et al. The role of children's ethnicity in the relationship between teacher ratings of attention-deficit/hyperactivity disorder and observed classroom behavior. J *Consult Clin Psycho*l 2005;73:424–34.
17. Schellack N, Meyer HC. The management of attention deficit hyperactivity disorder in children. *S Afr Pharm J* 2012;79(10):12-20.
18. Kendall T, Taylor E, Perez A, et al. Diagnosis and management of attention-deficit / hyperactivity disorder in children, young people, and adults: summary of NICE guidance. *BMJ* 2008;337:a1239.
19. Bolea-Alamañac B, David J Nutt DJ, Marios Adamou M, *et al.* Evidence-based guidelines for the pharmacological management of attention deficit hyperactivity disorder: Update on recommendations from the British Association for Psychopharmacology. *J Psycho pharmacol* 2014;28(3):179-203
20. Scottish Intercollegiate Guidelines Network, 112. Management of attention deficit and hyperkinetic disorders in children and young people. Oct 2009.
21. Joint Formulary Committee. British National Formulary, 64 ed. British Medical Association and Royal Pharmaceutical Society of Great Britain: London, 2012.
22. Pelham WE, Gnagy EM. Psychosocial and combined treatments. *Ment Retard Dev Disabil Res Rev* 1999;5:225–36.
23. Serrano-Troncoso E, Guidi M, Alda-Diez JA. Is psychological treatment efficacious for attention deficit hyperactivity disorder (ADHD)? Review of nonpharmacological treatments in children and adolescents in ADHD. *Actas Esp Psiquiatr* 2013;41(1):44–51.
24 Parker C. Pharmacological treatment for ADHD. P*rogress in Neurology and Psychiatry* 2009;13(4):17–26.
25. Banerjee S. Use of atomoxetine in children and adolescents with ADHD. *Progress in Neurology and Psychiatry* 2009;13(2):18–20.
26. Hodgkins P, Arnold LE, Shaw M, et al. A systematic review of global publication trends regarding long-term outcomes of ADHD. *Frontiers in Psychiatry* 2012;2(article 84):1-18. doi: 10.3389/fpsyt.2011.00084.
27. Shaw M, Hodgkins P, Caci H, et al. A systematic review and analysis of long-term outcomes in attention deficit hyperactivity disorder: effects of treatment and non-treatment. *BMC Medicine* 2012;10:99.
28. Getahun D, Jacobsen SJ, Fassett MJ, et al. Recent trends in childhood attention-deficit/hyperactivity disorder. *JAMA Pediatr* 2013;167(3):282–8.
29. Edwards G, Barkley RA, Laneri M, et al. Parent-adolescent conflict in teenagers with ADHD and ODD. *J Abnorm Child Psychol* 2001;29:557–72.
30. Biederman J, Faraone SV, Lapey K. Comorbidity of diagnosis in attention-deficit hyperactivity disorder. In G. Weiss (Ed.), Attention-deficit hyperactivity disorder, child & adolescent clinics of North America. Philadelphia: PA, 1992.
31. Bartholemew K, Owens J. Sleep and ADHD: A review. *Med Health R I* 2006;89:91–3.
32. Brod M, Schmitt E, Goodman M, et al. ADHD burden of illness in older adults: a life course perspective. *Qual Life Res* 2012;21(5):795-9.
33. Young S, Toone B, Tyson C. Comorbidity and psychosocial profile of adults with attention deficit hyperactivity disorder. P*ers Individ Dif* 2003;35:743–55.
34. Rosler M, Casas M, Konofal E, et al. Attention deficit hyperactivity disorder in adults. *World J Biol Psychiatry* 2010;11:684–98.
35.Skounti M, Philalithis A, Galanakis E. Variations in prevalence of attention deficit hyperactivity disorder worldwide. *Eur J Pediatr.* 2007 Feb;166(2):117-23.
36. National Institute for Health and Care Excellence: Attention deficit hyperactivity disorder: the NICE guideline on diagnosis and management of ADHD in children, young people and adults. British Psychological Society and Royal College of Psychiatrists: Leicester, 2009.
37. American Academy of Pediatrics: Clinical practice guideline: diagnosis and evaluation of the child with attention-deficit/hyperactivity disorder. *Pediatrics* 2000;105:1158–70.
38. Canadian Attention Deficit Hyperactivity Disorder Resource Alliance: Canadian ADHD Practice Guidelines (CAP-Guidelines) Toronto, Canada: Canadian Attention Deficit Hyperactivity Disorder Resource Alliance (CADDRA); 2011.