Sentara® Health Plans

BEHAVIORAL HEALTH GUIDELINE

ATTENTION DEFICIT DISORDER (ADHD) GUIDELINE

https://www.guideline.gov/summaries/summary/50410/attention-deficit-hyperactivity-disorder-diagnosis-and-management?q=ADHD

Guideline History

Date Approved	1/02
Date Revised	1/04, 12/05, 1/06, 9/06, 1/08, 3/08, 1/10, 1/12, 1/18, 7/22
Date Reviewed	1/16, 7/20, 7/22, 6/24, 6/26
Next Review Date	6/28

These Guidelines are promulgated by Sentara Healthcare (SHC) as recommendations for the clinical management of specific conditions. Clinical data in a particular case may necessitate or permit deviation from these Guidelines. The SHC Guidelines are institutionally endorsed recommendations and are not intended as a substitute for clinical judgment.

Key Points

- Any child age 4 through 18 who presents with academic or behavioral problems and symptoms of inattention, hyperactivity or impulsivity should be evaluated for ADHD.

- Determine whether *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) criteria for ADHD have been met, through administration of standardized questionnaires in more than one setting.

- Evaluation should include assessment for other conditions that might coexist with ADHD including behavioral, developmental and physical conditions.

- Treatment recommendations vary depending on the patient's age:

  Preschool-aged children (4-5 yo): Evidence-based parent- and/or teacher administered behavior therapy as first line of treatment. 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.

  Elementary school-aged children (6-11 yo): Prescribe FDA-approved medications for ADHD and/or evidence-based parent- and/or teacher administered behavior therapy, preferably both.

  Adolescents (12-18 yo): Prescribe FDA-approved medications for ADHD with the assent of the adolescent and may prescribe behavior therapy as treatment for ADHD, preferably both.

- Titrate doses of medication for ADHD to achieve maximum benefit with minimum adverse effects.

- Upon initiation of medication treatment, patients should be seen <u>at least once within 30 days,</u> and for <u>at least 2 additional visits within the following 9 months.</u>

- ADHD is a chronic condition. Management of children and adolescents with ADHD should follow the principles of the chronic care model and the medical home.

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Diagnostic Criteria for ADHD

Inattention, hyperactivity, and impulsivity are the key behaviors of ADHD. To be diagnosed with the disorder, a child must have symptoms for 6 or more months and to a degree that is greater than other children of the same age and negatively impacts directly on social and academic/occupational activities. **Children must have at least 6 symptoms** from either the inattention list or the hyperactivity and impulsivity lists below (or both). **Older adolescents and adults (over age 17 years) must have at least 5 symptoms**. Symptoms must be present before age 12 years.

Children who have symptoms of **inattention** may:

- Be easily distracted, miss details, forget things, and frequently switch from one activity to another
- Have difficulty focusing on one thing
- Become bored with a task after only a few minutes, unless they are doing something enjoyable
- Have difficulty focusing attention on organizing and completing a task or learning something new
- Have trouble completing or turning in homework assignments, often losing things (e.g., pencils, toys, assignments) needed to complete tasks or activities
- Not seem to listen when spoken to
- Daydream, become easily confused, and move slowly
- Have difficulty processing information as quickly and accurately as others
- Struggle to follow instructions.

Children who have symptoms of **hyperactivity** may:

- Fidget and squirm in their seats
- Talk nonstop
- Dash around, touching or playing with anything and everything in sight
- Have trouble sitting still during dinner, school, and story time
- Be constantly in motion
- Have difficulty doing quiet tasks or activities.

Children who have symptoms of **impulsivity** may:

- Be very impatient
- Blurt out inappropriate comments, show their emotions without restraint, and act without regard for consequences
- Have difficulty waiting for things they want or waiting their turns in games
- Often interrupt conversations or others' activities.

http://www.nimh.nih.gov/health/publications/attention-deficit-hyperactivity-disorder
Accessed 2/4/14

Attachment 2

Medications Used to Treat ADHD (alphabetical by class)

For s/e of all stimulants, "Dependency and Abuse" should be listed. It is a boxed warning. Insomnia and Agitation are also common s/e. Psychosis and mania as s/e for most.

NOTE: Some of the medications included on this chart may require prior authorization. **Please check optimahealth.com for the most current information, as requirements may change.**

Generic/ Brand Name	Typical Starting Dose	FDA Max/day	Titration & Timing of Doses	Predominant Adverse Effects	Comments
Amphetamine Preparations					
Short-acting					• Short-acting stimulants often used as initial treatment in small children but have disadvantage of B.I.D. to T.I.D. dosing to control symptoms throughout the day. • Longer-acting stimulants offer greater convenience, confidentiality, and compliance with single daily dosing but may have greater problematic effects on evening appetite and sleep • Adderall XR cap may be opened and sprinkled on soft food • Check BP at each visit due to potential for cardiovascular effects, including hypertension. • For s/e of all stimulants "dependency and abuse" should be listed. It is a boxed warning. insomnia and agitation are also common s/e. Psychosis and mania as s/e for most
Adderall	2.5mg for 3-5 y/o and 5mg for >6yo	40 mg	Increase by 2.5mg increments	Decreased appetite, insomnia, headaches, increased heart rate	
Dexedrine dextroamphetamine DextroStat	4-5 yo: 2.5mg qd 6+: 5mg qd-bid		Increase weekly with 2.5-5 mg tab/dose; am & noon; add 4pm dose as needed		
Long-acting					
Adderall XR		Ages 6-12: 30 mg Ages 13+: 20 mg	May be increased 10 mg daily at weekly intervals.	Decreased appetite, insomnia, headaches, increased heart rate	
Dexedrine Spansule		40 mg	Increased by 5 mg spansule in am only or add 5mg tablets to am dose	Decreased appetite, insomnia, headaches, increased heart rate	
Vyvanse lisdexamphetamine		70 mg	May be increased by 10-20mg/day at weekly intervals	Upper abdominal pain, decreased appetite, dizziness, dry mouth	
Methylphenidate Preparations					
Short-acting					• Short-acting stimulants often used as initial treatment in small children but have disadvantage of B.I.D. to T.I.D. dosing to control symptoms throughout the day. • Methylin is available in chewable tablets and oral solutions. • Longer-acting stimulants offer greater convenience, confidentiality, and compliance with single daily dosing but may have greater problematic effects on evening appetite and sleep • Metadate CD, ritalin LA and Focalin XR may be opened and sprinkled on soft food • Concerta tab should be swallowed whole with liquids • Concerta non-absorbable tab may be seen in stool • For s/e of all stimulants "dependency and abuse" should be listed. It is a boxed warning. insomnia and agitation are also common s/e. Psychosis and mania as s/e for most
Focalin dexmethylphenidate		20 mg	Adjust in increments of 2.5-5 mg weekly	Headache, decreased appetite, restlessness, abdominal pain, increased heart rate	
Methylin Ritalin methylphenidate	4-7yo: 5 mg bid 8+: 10mg bid	30 mg	Increase by 2.5-5 mg/dose (depending on wt) am & noon; add 4pm dose as needed	Decreased appetite, insomnia, headaches, increased heart rate	
Intermediate-acting					
Metadate ER Methylin ER Ritalin SR	20mg SR in am only (considered for use in children tolerating 10mg dose am and noon)	60 mg	Add 5mg-10mg tablet in am and/or at 4pm	Decreased appetite, insomnia, headaches, increased heart rate	
Metadate CD Ritalin LA	6+: 20 mg q am	30 mg	May be increased 10mg daily at weekly intervals		
Long-acting					
Concerta	18mg q am	54 mg 6-12 yo 72 mg >13 yo	May be increased 18 mg daily at weekly intervals, approved up to 72 mg for adolescents	Decreased appetite, insomnia, headaches, increased heart rate	
Daytrana (transdermal system)	6 yo and older: 10 mg patch qd	30 mg	May increase to next transdermal patch size no more frequently than every week	Decreased appetite, insomnia, headaches, increased heart rate, allergic contact dermatitis	
Focalin XR	6+: 5 mg q am	30 mg	Children 6+: adjust in increments of 5 mg weekly	Headache, decreased appetite, restlessness, abdominal pain, increased heart rate	
Quillivant XR	20mg QAM	60mg	May be increased in increments of 10-20mg/day	Increased BP and heart rate, mental/psychiatric symptoms, circulation problems in fingers/toes	• Liquid (reconstituted by pharmacy from powder) • 5mg per mL • Before administering, vigorously shake bottle for at least 10 seconds.

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Medications Used to Treat ADHD (alphabetical by class) continued…

For s/e of all stimulants, "Dependency and Abuse" should be listed. It is a boxed warning. Insomnia and Agitation are also common s/e. Psychosis and mania as s/e for most.

Selective Norepinephrine Reuptake Inhibitor					
Atomoxetine Strattera	0.5 mg/kg/d for 3 d; then 1.2 mg/kg/d	Lesser of 1.4 mg/kg or 100 mg	Children and Adolescents weighing up to 70 kg: After 3 days of dosing, increase 1.2mg/kg/day. Give once daily or may be evenly divided into 2 doses, in morning and evening Patients weighing more than 70 kg: After 3 days of dosing, increase to 80 mg daily or may be evenly divided into 2 doses, in morning and evening	Nausea, vomiting, GI pain, anorexia, dizziness, somnolence, skin rash, pruritis Increased heart rate or blood pressure, urinary retention, rare severe liver injury Capsule should not be opened as atomoxetine is an ocular and mucous membrane irritant	• Not a Schedule II medication • Consider if active substance abuse or severe side effects of stimulants (mood lability, tics) • Monitor closely for suicidal thinking and behavior, clinical worsening, or unusual changes in behavior • The full effect may not be appreciated for up to 4 weeks on a given target dose
Other (selective α-2 adrenergic agonist)					
Intuniv guanfacine	1 mg qd 6 yo and older	4 mg qd	May increase by 1 mg per week.	Drowsiness, dizziness, dry mouth, abdominal pain, constipation	• Swallow whole: chewing or crushing the tablet will markedly enhance the drug's release. • High fat meals will increase absorption of the drug.
Clonidine	6-17 yo <45 kg: 0.05 mg QHS >45 kg: 0.1 mg QHS	27-40.5 kg: 0.2 mg 40.5-45 kg: 0.3 mg >45 kg: 0.4 mg	Titrate in 0.05 mg increments BID, TID, QID Titrate in 0.1 mg increments BID, TID, QID	Drowsiness, hypotension	• Clonidine does not have a specific FDA indication for treatment of ADHD
Kapvay (extended release clonidine)	0.1mg qd	0.4mg	Titrate in increments of 0.1mg/day at weekly intervals until the desired response is achieved. Doses should be taken twice a day, with either an equal or higher split dosage being given at bedtime.	Somnolence, fatigue, insomnia, nightmares, constipation	• Should be discontinued slowly in decrements of no more than 0.1mg every 3-7 days due to potential risk of withdrawal effects. • Only extended release Clonidine has FDA for ADHD

Adapted from:

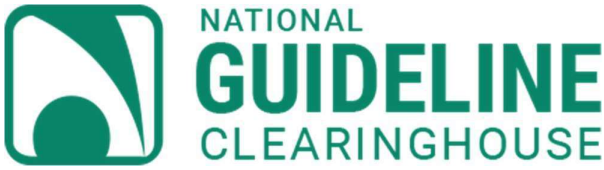
Institutes for Clinical Systems Improvement (ICSI). Behavioral Health Guidelines: ADHD, Attention Deficit Hyperactivity Disorder in Primary Care for School-Age Children & Adolescents, Diagnosis and Management (November, 2011). Retrieved February 5, 2014 from https://ww.icsi.org/_asset/rp1toc/AAP-Suplement.pdf

American Academy of Child and Adolescent Psychiatry. *ADHD: Parents Medication Guide*. Revised July, 2013. Retrieved February 5, 2014. http://www.aacap.org/App_Themes?AACAP/Docs/resource_centers/adhd/adhd_parents_medication_guide_201305.pdf

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General

Guideline Title

Attention deficit hyperactivity disorder: diagnosis and management.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Attention deficit hyperactivity disorder: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb. 41 p. (Clinical guideline; no. 72).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Mental Health. Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Sep. 59 p. (Clinical guideline; no. 72).

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline on attention deficit hyperactivity disorder (ADHD) was originally developed in 2008 by the National Collaborating Centre for Mental Health (NCCMH) on behalf of the National Institute for Health and Care Excellence (NICE). In 2015, the NICE guideline was reviewed, and new evidence relating to the effects of diet on ADHD was found. The guideline was updated by the NICE Clinical Guidelines Update Team as requested by NICE's Guidance Executive. The recommendations below reflect the changes. See the "Availability of Companion Documents" field for the full version of this guidance, including the 2016 addendum, and related appendices.

Recommendations are marked as [new 2016], [2016], or [2008]:

> [new 2016] indicates that the evidence has been reviewed and the recommendation has been added or updated.
> [2016] indicates that the evidence has been reviewed but no change has been made to the recommended action.

[2008] indicates that the evidence has not been reviewed since 2008.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Prerequisites of Treatment and Care for All People with ADHD

People with ADHD require integrated care that addresses a wide range of personal, social, educational, and occupational needs. Care should be provided by adequately trained healthcare and education professionals.

Organisation and Planning of Services

People with ADHD would benefit from improved organisation of care and better integration of paediatric, child, and adolescent mental health services (CAMHS) and adult mental health services. [2008]

Mental health trusts, and children's trusts that provide mental health/child development services, should form multidisciplinary specialist ADHD teams and/or clinics for children and young people and separate teams and/or clinics for adults. These teams and clinics should have expertise in the diagnosis and management of ADHD, and should:

- Provide diagnostic, treatment, and consultation services for people with ADHD who have complex needs, or where general psychiatric services are in doubt about the diagnosis and/or management of ADHD
- Put in place systems of communication and protocols for information sharing among paediatric, child and adolescent, forensic, and adult mental health services for people with ADHD, including arrangements for transition between child and adult services
- Produce local protocols for shared care arrangements with primary care providers, and ensure that clear lines of communication between primary and secondary care are maintained
- Ensure age-appropriate psychological services are available for children, young people, and adults with ADHD, and for parents or carers

The size and time commitment of these teams should depend on local circumstances (for example, the size of the trust, the population covered, and the estimated referral rate for people with ADHD). [2008]

Every locality should develop a multi-agency group, with representatives from multidisciplinary specialist ADHD teams, paediatrics, mental health and learning disability trusts, forensic services, CAMHS, the Children and Young People's Directorate (CYPD) (including services for education and social services), parent support groups and others with a significant local involvement in ADHD services. The group should:

- Oversee the implementation of this guideline
- Start and coordinate local training initiatives, including the provision of training and information for teachers about the characteristics of ADHD and its basic behavioural management
- Oversee the development and coordination of parent-training/education programmes
- Consider compiling a comprehensive directory of information and services for ADHD including advice on how to contact relevant services and assist in the development of specialist teams [2008]

Information, Consent, the Law, and Support for People with ADHD and Their Carers

Many people with ADHD, and their parents or carers, experience stigma and other difficulties because of the symptoms and impairment associated with ADHD and current practice within healthcare and education. The following recommendations have been developed based on the experiences of people with ADHD and their families.

Healthcare professionals should develop a trusting relationship with people with ADHD and their families or carers by:

Respecting the person and their family's knowledge and experience of ADHD
Being sensitive to stigma in relation to mental illness [2008]

Healthcare professionals should provide people with ADHD and their families or carers with relevant, age-appropriate information (including written information) about ADHD at every stage of their care. The information should cover diagnosis and assessment, support and self-help, psychological treatment, and the use and possible side effects of drug treatment. [2008]

When assessing a child or young person with ADHD, and throughout their care, healthcare professionals should:

Allow the child or young person to give their own account of how they feel, and record this in the notes
Involve the child or young person and the family or carer in treatment decisions
Take into account expectations of treatment, so that informed consent can be obtained from the child's parent or carer or the young person before treatment is started [2008]

Healthcare professionals working with children and young people with ADHD should be:

Familiar with local and national guidelines on confidentiality and the rights of the child
Able to assess the young person's understanding of issues related to ADHD and its treatment (including Gillick competence)
Familiar with parental consent and responsibilities, child protection issues, the Mental Health Act (2007) and the Children Act (1989) [2008]

Healthcare professionals should work with children and young people with ADHD and their parents or carers to anticipate major life changes (such as puberty, starting or changing schools, the birth of a sibling) and make appropriate arrangements for adequate personal and social support during times of increased need. The need for psychological treatment at these times should be considered. [2008]

Adults with ADHD should be given written information about local and national support groups and voluntary organisations.

Healthcare professionals should ask families or carers about the impact of ADHD on themselves and other family members, and discuss any concerns they may have. Healthcare professionals should:

Offer family members or carers an assessment of their personal, social and mental health needs
Encourage participation in self-help and support groups where appropriate
Offer general advice to parents and carers about positive parent– and carer–child contact, clear and appropriate rules about behaviour, and the importance of structure in the child or young person's day
Explain that parent-training/education programmes do not necessarily imply bad parenting, and that their aim is to optimize parenting skills to meet the above-average parenting needs of children and young people with ADHD [2008]

Training

Healthcare and education professionals require training to better address the needs of people with ADHD.

Trusts should ensure that specialist ADHD teams for children, young people and adults jointly develop age-appropriate training programmes for the diagnosis and management of ADHD for mental health, paediatric, social care, education, forensic and primary care providers and other professionals who have contact with people with ADHD. [2008]

Child and adult psychiatrists, paediatricians, and other child and adult mental health professionals (including those working in forensic services) should undertake training so that they are able to diagnose ADHD and provide treatment and management in accordance with this guideline. [2008]

The Department for Children, Schools and Families should consider providing more education to trainee teachers about ADHD by working with the Training and Development Agency for Schools (TDA) and

relevant health service organisations to produce training programmes and guidance for supporting children with ADHD. [2008]

Care Pathway for the Treatment and Care of People with ADHD

The recommendations below form a care pathway that sets out how children, young people and adults should receive help, treatment and care from different services, from the community (including primary care and education), through to secondary and tertiary services. Most of the recommendations describe the approach for children but some of these also apply to adults. The pathway also covers transition between child and adult services and specific treatment for adults, including those who were first diagnosed with ADHD in adulthood.

Specific recommendations on the use of drugs, monitoring side effects, improving adherence, and discontinuing drug treatment are also provided in the final section.

Identification, Pre-diagnostic Intervention in the Community, and Referral to Secondary Services

Children and young people with behavioural problems suggestive of ADHD can be referred by their school or primary care practitioner for parent-training/education programmes without a formal diagnosis of ADHD. The diagnosis of ADHD in children, young people, and adults should take place in secondary care.

Identification and Referral in Children and Young People with ADHD

Universal screening for ADHD should not be undertaken in nursery, primary, and secondary schools. [2008]

When a child or young person with disordered conduct and suspected ADHD is referred to a school's special educational needs coordinator (SENCO), the SENCO, in addition to helping the child with their behaviour, should inform the parents about local parent-training/education programmes. [2008]

Referral from the community to secondary care may involve health, education, and social care professionals (for example, general practitioners [GPs], paediatricians, educational psychologists, SENCOs, social workers) and care pathways can vary locally. The person making the referral to secondary care should inform the child or young person's GP. [2008]

When a child or young person presents in primary care with behavioural and/or attention problems suggestive of ADHD, primary care practitioners should determine the severity of the problems, how these affect the child or young person and the parents or carers and the extent to which they pervade different domains and settings. [2008]

If the child or young person's behavioural and/or attention problems suggestive of ADHD are having an adverse impact on their development or family life, healthcare professionals should consider:

- A period of watchful waiting of up to 10 weeks
- Offering parents or carers a referral to a parent-training/education programme (this should not wait for a formal diagnosis of ADHD) [2008]

If the behavioural and/or attention problems persist with at least moderate impairment, the child or young person should be referred to secondary care (that is, a child psychiatrist, paediatrician, or specialist ADHD CAMHS) for assessment.

If the child or young person's behavioural and/or attention problems are associated with severe impairment, referral should be made directly to secondary care (that is, a child psychiatrist, paediatrician, or specialist ADHD CAMHS) for assessment. [2008]

Group-based parent-training/education programmes are recommended in the management of children with conduct disorders (see also recommendations about parent-training programmes in the NGC summary of NICE guideline CG158, Antisocial behaviour and conduct disorders in children and young people: recognition, intervention and management, and "Treatment for Pre-school Children" below for the extended use of these programmes to include children with ADHD). [2008]

Primary care practitioners should not make the initial diagnosis or start drug treatment in children or young people with suspected ADHD. [2008]

A child or young person who is currently treated in primary care with methylphenidate, atomoxetine, dexamfetamine, or any other psychotropic drug for a presumptive diagnosis of ADHD, but has not yet been assessed by a specialist in ADHD in secondary care, should be referred for assessment to a child psychiatrist, paediatrician, or specialist ADHD CAMHS as a matter of clinical priority. [2008]

Identification and Referral in Adults with ADHD

Adults presenting with symptoms of ADHD in primary care or general adult psychiatric services, who do not have a childhood diagnosis of ADHD, should be referred for assessment by a mental health specialist trained in the diagnosis and treatment of ADHD, where there is evidence of typical manifestations of ADHD (hyperactivity/impulsivity and/or inattention) that:

- Began during childhood and have persisted throughout life
- Are not explained by other psychiatric diagnoses (although there may be other coexisting psychiatric conditions)
- Have resulted in or are associated with moderate or severe psychological, social and/or educational or occupational impairment [2008]

Adults who have previously been treated for ADHD as children or young people and present with symptoms suggestive of continuing ADHD should be referred to general adult psychiatric services for assessment. The symptoms should be associated with at least moderate or severe psychological and/or social or educational or occupational impairment. [2008]

Diagnosis of ADHD

ADHD is a valid clinical disorder that can be distinguished from coexisting conditions (although it is most commonly comorbid) and the normal spectrum. ADHD differs from the normal spectrum because there are high levels of hyperactivity/impulsivity and/or inattention that result in significant psychological, social, and/or educational or occupational impairment that occurs across multiple domains and settings and persists over time.

A diagnosis of ADHD should only be made by a specialist psychiatrist, paediatrician, or other appropriately qualified healthcare professional with training and expertise in the diagnosis of ADHD, on the basis of:

- A full clinical and psychosocial assessment of the person; this should include discussion about behaviour and symptoms in the different domains and settings of the person's everyday life, and
- A full developmental and psychiatric history, and
- Observer reports and assessment of the person's mental state [2008]

A diagnosis of ADHD should not be made solely on the basis of rating scale or observational data. However, rating scales such as the Conners' rating scales and the Strengths and Difficulties questionnaire are valuable adjuncts, and observations (for example, at school) are useful when there is doubt about symptoms. [2008]

For a diagnosis of ADHD, symptoms of hyperactivity/impulsivity and/or inattention should:

- Meet the diagnostic criteria in Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV) or International Classification of Diseases 10th revision (ICD-10) (hyperkinetic disorder) (the ICD-10 exclusion on the basis of a pervasive developmental disorder being present, or the time of onset being uncertain, is not recommended), and
- Be associated with at least moderate psychological, social, and/or educational or occupational impairment based on interview and/or direct observation in multiple settings, and
- Be pervasive, occurring in two or more important settings including social, familial, educational and/or occupational settings. [2008]

As part of the diagnostic process, include an assessment of the person's needs, coexisting conditions, social, familial, and educational or occupational circumstances, and physical health. For children and young people, there should also be an assessment of their parents' or carers' mental health.

ADHD should be considered in all age groups, with symptom criteria adjusted for age-appropriate changes in behaviour. [2008]

In determining the clinical significance of impairment resulting from the symptoms of ADHD in children and young people, their views should be taken into account wherever possible. [2008]

Post-Diagnostic Advice

After diagnosis people with ADHD and their parents or carers may benefit from advice about diet, behaviour, and general care.

General Advice

Following a diagnosis of ADHD, healthcare professionals should consider providing all parents or carers of all children and young people with ADHD self-instruction manuals, and other materials such as videos, based on positive parenting and behavioural techniques. [2008]

Dietary Advice

Healthcare professionals should stress the value of a balanced diet, good nutrition, and regular exercise for children, young people, and adults with ADHD. [2008]

Do not advise elimination of artificial colouring and additives from the diet as a generally applicable treatment for children and young people with ADHD. [2016]

Ask about foods or drinks that appear to influence hyperactive behaviour as part of the clinical assessment of ADHD in children and young people, and:

- If there is a clear link, advise parents or carers to keep a diary of food and drinks taken and ADHD behaviour
- If the diary supports a relationship between specific foods and drinks and behaviour, offer referral to a dietitian
- Ensure that further management (for example, specific dietary elimination) is jointly undertaken by the dietitian, mental health specialist or paediatrician, and the parent or carer and child or young person [2016]

Do not advise or offer dietary fatty acid supplementation for treating ADHD in children and young people. [2016]

Advise the family members or carers of children with ADHD that there is no evidence about the long-term effectiveness or potential harms of a 'few food' diet for children with ADHD, and only limited evidence of short-term benefits. [new 2016]

Treatment for Children and Young People

Treatment for Pre-School Children

Parent-training/education programmes are the first-line treatment for parents or carers of pre-school children. These programmes are the same as those recommended for the parents or carers of other children with conduct disorder. If more help is needed the child can be referred to a tertiary service.

Drug treatment is not recommended for pre-school children with ADHD. [2008]

Following a diagnosis of ADHD in a child of pre-school age, healthcare professionals should, with the parents' or carers' consent, contact the child's nursery or pre-school teacher to explain:

- The diagnosis and severity of symptoms and impairment

The care plan
Any special educational needs [2008]

Healthcare professionals should offer parents or carers of preschool children with ADHD a referral to a parent-training/education programme as the first-line treatment if the parents or carers have not already attended such a programme or the programme has had a limited effect. [2008]

Group-based parent-training/education programmes, developed for the treatment and management of children with conduct disorders, should be fully accessible to parents or carers of children with ADHD whether or not the child also has a formal diagnosis of conduct disorder (as recommended in the NGC summary of Antisocial behaviour and conduct disorders in children and young people: recognition, intervention and management [NICE guideline CG158]). [2008]

Individual-based parent-training/education programmes (as recommended in the NGC summary of Antisocial behaviour and conduct disorders in children and young people: recognition, intervention and management [NICE guideline CG158]) are recommended in the management of children with ADHD when:

A group programme is not possible because of low participant numbers
There are particular difficulties for families in attending group sessions (for example, because of disability, needs related to diversity such as language differences, parental ill-health, problems with transport, or where other factors suggest poor prospects for therapeutic engagement)
A family's needs are too complex to be met by group-based parent-training/education programmes [2008]

When individual-based parent-training/education programmes for pre-school children with ADHD are undertaken, the skills training stages should involve both the parents or carers and the child. [2008]

Consideration should be given to involving both of the parents or all carers of children or young people with ADHD in parent-training/education programmes wherever this is feasible. [2008]

If overall treatment, including parent-training/education programmes, has been effective in managing ADHD symptoms and any associated impairment in pre-school children, before considering discharge from secondary care healthcare professionals should:

Review the child, with their parents or carers and siblings, for any residual coexisting conditions and develop a treatment plan for these if needed
Monitor for the recurrence of ADHD symptoms and any associated impairment that may occur after the child starts school [2008]

If overall treatment, including parent-training/education programmes, has not been effective in managing ADHD symptoms and any associated impairment in pre-school children, healthcare professionals should consider referral to tertiary services for further care. [2008]

Treatment for School-Age Children and Young People with ADHD and Moderate Impairment

Group-based parent-training/education programmes are usually the first-line treatment for parents and carers of children and young people of school age with ADHD and moderate impairment. This may also include group psychological treatment (cognitive behavioural therapy [CBT] and/or social skills training) for the younger child. For older age groups, individual psychological treatment may be more acceptable if group behavioural or psychological approaches have not been effective, or have been refused. See the section above for recommendations on conducting parent-training/education programmes that also apply to school-age children with ADHD. Drug treatment may be tried next for those children and young people with ADHD and moderate levels of impairment.

Drug treatment is not indicated as the first-line treatment for all school-age children and young people with ADHD. It should be reserved for those with severe symptoms and impairment or for those with moderate levels of impairment who have refused non-drug interventions, or whose symptoms have not responded sufficiently to parent-training/education programmes or group psychological treatment. [2008]

Following a diagnosis of ADHD in a school-age child or young person healthcare professionals should, with the parents' or carers' consent, contact the child or young person's teacher to explain:

- The diagnosis and severity of symptoms and impairment
- The care plan
- Any special educational needs [2008]

Teachers who have received training about ADHD and its management should provide behavioural interventions in the classroom to help children and young people with ADHD. [2008]

If the child or young person with ADHD has moderate levels of impairment, the parents or carers should be offered referral to a group parent-training/education programme, either on its own or together with a group treatment programme (CBT and/or social skills training) for the child or young person. [2008]

When using group treatment (CBT and/or social skills training) for the child or young person in conjunction with a parent-training/education programme, particular emphasis should be given to targeting a range of areas, including social skills with peers, problem solving, self-control, listening skills and dealing with and expressing feelings. Active learning strategies should be used, and rewards given for achieving key elements of learning. [2008]

For older adolescents with ADHD and moderate impairment, individual psychological interventions (such as CBT or social skills training) may be considered as they may be more effective and acceptable than group parent-training/education programmes or group CBT and/or social skills training. [2008]

For children and young people (including older age groups) with ADHD and a learning disability, a parent-training/education programme should be offered on either a group or individual basis, whichever is preferred following discussion with the parents or carers and the child or young person. [2008]

When parents or carers of children or young people with ADHD undertake parent-training/education programmes, the professional delivering the sessions should consider contacting the school and providing the child or young person's teacher with written information on the areas of behavioural management covered in these sessions. This should only be done with parental consent. [2008]

Following successful treatment with a parent-training/education programme and before considering discharge from secondary care, the child or young person should be reviewed, with their parents or carers and siblings, for any residual problems such as anxiety, aggression or learning difficulties. Treatment plans should be developed for any coexisting conditions. [2008]

Following treatment with a parent-training/education programme, children and young people with ADHD and persisting significant impairment should be offered drug treatment. [2008]

Treatment for School-Age Children and Young People with Severe ADHD (Hyperkinetic Disorder) and Severe Impairment

The first-line treatment for school-age children and young people with severe ADHD (hyperkinetic disorder) and severe impairment is drug treatment. If the child or young person wishes to refuse medication and/or the parents or carers reject it, a psychological intervention may be tried but drug treatment has more benefits and is superior to other treatments for this group.

In school-age children and young people with severe ADHD, drug treatment should be offered as the first-line treatment. Parents should also be offered a group-based parent-training/education programme. [2008]

Drug treatment should only be initiated by an appropriately qualified healthcare professional with expertise in ADHD and should be based on a comprehensive assessment and diagnosis. Continued prescribing and monitoring of drug therapy may be performed by general practitioners, under shared care arrangements. [2008] (This recommendation is taken from the NICE technology appraisal 98, 'Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder [ADHD] in children and adolescents'. At the time of publication [September 2008], methylphenidate and

atomoxetine did not have UK marketing authorisation for use in children younger than 6 years. Informed consent should be obtained and documented. Licensing arrangements remained unchanged when the guideline was updated [February 2016].)

If drug treatment is not accepted by the child or young person with severe ADHD, or their parents or carers, healthcare professionals should advise parents or carers and the child or young person about the benefits and superiority of drug treatment in this group. If drug treatment is still not accepted, a group parent-training/education programme should be offered. [2008]

If a group parent-training/education programme is effective in children and young people with severe ADHD who have refused drug treatment, healthcare professionals should assess the child or young person for possible coexisting conditions and develop a longer-term care plan. [2008]

If a group parent-training/education programme is not effective for a child or young person with severe ADHD, and if drug treatment has not been accepted, discuss the possibility of drug treatment again or other psychological treatment (group CBT and/or social skills training), highlighting the clear benefits and superiority of drug treatment in children or young people with severe ADHD. [2008]

Following a diagnosis of severe ADHD in a school-age child or young person healthcare professionals should, with the parents' or carers' consent, contact the child or young person's teacher to explain:

- The diagnosis and severity of symptoms and impairment
- The care plan
- Any special educational needs [2008]

Teachers who have received training about ADHD and its management should provide behavioural interventions in the classroom to help children and young people with ADHD. [2008]

Pre-Drug Treatment Assessment

It is important that before starting drug treatment baseline measures of a range of parameters, including height and weight, are taken.

Before starting drug treatment, children and young people with ADHD should have a full pre-treatment assessment, which should include:

- Full mental health and social assessment
- Full history and physical examination, including:
  - Assessment of history of exercise syncope, undue breathlessness and other cardiovascular symptoms
  - Heart rate and blood pressure (plotted on a centile chart)
  - Height and weight (plotted on a growth chart)
  - Family history of cardiac disease and examination of the cardiovascular system
- An electrocardiogram (ECG) if there is past medical or family history of serious cardiac disease, a history of sudden death in young family members, or abnormal findings on cardiac examination
- Risk assessment for substance misuse and drug diversion (where the drug is passed on to others for non-prescription use) [2008]

Drug treatment for children and young people with ADHD should always form part of a comprehensive treatment plan that includes psychological, behavioural, and educational advice and interventions. [2008]

Choice of Drug for Children and Young People with ADHD

Depending on a range of factors such as the presence of coexisting conditions, side effects, and patient preference, the child or young person may be offered methylphenidate, atomoxetine, or dexamfetamine.

W here drug treatment is considered appropriate, methylphenidate, atomoxetine and dexamfetamine are recommended, within their licensed indications, as options for the management of ADHD in children and adolescents. [2008] (This recommendation is taken from the NICE technology appraisal 98,

'Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder [ADHD] in children and adolescents']. At the time of publication [September 2008], methylphenidate and atomoxetine did not have UK marketing authorisation for use in children younger than 6 years. Informed consent should be obtained and documented. Licensing arrangements remained unchanged when the guideline was updated [February 2016].)

The decision regarding which product to use should be based on the following:

- The presence of comorbid conditions (for example, tic disorders, Tourette's syndrome, epilepsy)
- The different adverse effects of the drugs
- Specific issues regarding compliance identified for the individual child or adolescent, for example problems created by the need to administer a mid-day treatment dose at school
- The potential for drug diversion (where the medication is forwarded on to others for non-prescription uses) and/or misuse
- The preferences of the child/adolescent and/or his or her parent or guardian. [2008] (This recommendation is taken from the NICE technology appraisal 98, 'Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder [ADHD] in children and adolescents.' At the time of publication [September 2008], methylphenidate and atomoxetine did not have UK marketing authorisation for use in children younger than 6 years. Informed consent should be obtained and documented). Licensing arrangements remained unchanged when the guideline was updated [February 2016].)

When a decision has been made to treat children or young people with ADHD with drugs, healthcare professionals should consider:

- Methylphenidate for ADHD without significant comorbidity
- Methylphenidate for ADHD with comorbid conduct disorder
- Methylphenidate or atomoxetine when tics, Tourette's syndrome, anxiety disorder, stimulant misuse, or risk of stimulant diversion are present
- Atomoxetine if methylphenidate has been tried and has been ineffective at the maximum tolerated dose, or the child or young person is intolerant to low or moderate doses of methylphenidate [2008]

When prescribing methylphenidate for the treatment of children or young people, modified-release preparations should be considered for the following reasons:

- Convenience
- Improving adherence
- Reducing stigma (because the child or young person does not need to take medication at school)
- Reducing problems schools have in storing and administering controlled drugs
- Their pharmacokinetic profiles [2008]

Alternatively, immediate-release preparations may be considered if more flexible dosing regimens are required, or during initial titration to determine correct dosing levels.

When starting drug treatment children and young people should be monitored for side effects. In particular, those treated with atomoxetine should be closely observed for agitation, irritability, suicidal thinking and self-harming behaviour, and unusual changes in behaviour particularly during the initial months of treatment, or after a change in dose. Parents and/or carers should be warned about the potential for suicidal thinking and self-harming behaviour with atomoxetine and asked to report these to their healthcare professionals. Parents or carers should also be warned about the potential for liver damage in rare cases with atomoxetine (usually presenting as abdominal pain, unexplained nausea, malaise, darkening of the urine or jaundice). [2008]

If there is a choice of more than one appropriate drug, the product with the lowest cost (taking into account the cost per dose and number of daily doses) should be prescribed. [2008] (This recommendation is taken from the NICE technology appraisal 98, 'Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder [ADHD] in children and adolescents.' At the time of publication

[September 2008], methylphenidate and atomoxetine did not have UK marketing authorisation for use in children younger than 6 years. Informed consent should be obtained and documented. Licensing arrangements remained unchanged when the guideline was updated [February 2016].)

Antipsychotics are not recommended for the treatment of ADHD in children and young people. [2008]

Poor Response to Treatment

If there has been a poor response to parent-training/education programmes, psychological treatment, and drug treatment with methylphenidate and atomoxetine, a comprehensive review is required. The following are further options for treatment: higher doses of methylphenidate or atomoxetine; switching to dexamfetamine; further or alternative psychological treatments; or referral to regional specialists for alternative drug treatment.

If there has been a poor response following parent-training/education programmes and/or psychological treatment and treatment with methylphenidate and atomoxetine in a child or young person with ADHD, there should be a further review of:

- The diagnosis
- Any coexisting conditions
- Response to drug treatment, occurrence of side effects and treatment adherence
- Uptake and use of psychological interventions for the child or young person and their parents or carers
- Effects of stigma on treatment acceptability
- Concerns related to school and/or family
- Motivation of the child or young person and the parents or carers
- The child or young person's diet [2008]

Following review of poor response to treatment, a dose higher than that licensed for methylphenidate or atomoxetine should be considered following consultation with a tertiary or regional centre. This may exceed 'British National Formulary' (BNF) recommendations: methylphenidate can be increased to 0.7 mg/kg per dose up to three times a day or a total daily dose of 2.1 mg/kg/day (up to a total maximum dose of 90 mg/day for immediate release; or an equivalent dose of modified-release methylphenidate) (refer to the note in the original guideline document for information on stimulant dose equivalents); atomoxetine may be increased to 1.8 mg/kg/day (up to a total maximum dose of 120 mg/day). The prescriber should closely monitor the child or young person for side effects. [2008]

Dexamfetamine should be considered in children and young people whose ADHD is unresponsive to a maximum tolerated dose of methylphenidate or atomoxetine. [2008]

In children and young people whose ADHD is unresponsive to methylphenidate, atomoxetine and dexamfetamine, further treatment should only follow after referral to tertiary services.

Further treatment may include the use of medication unlicensed for the treatment of ADHD (such as bupropion, clonidine, modafinil and imipramine) or combination treatments (including psychological treatments for the parent or carer and the child or young person). The use of medication unlicensed for ADHD should only be considered in the context of tertiary services. [2008] (*Note*: At the time of publication [September 2008], bupropion, clonidine, modafinil and imipramine did not have UK marketing authorisation for use in children and young people with ADHD. Informed consent should be obtained and documented. Licensing arrangements remained unchanged when the guideline was updated [February 2016].)

A cardiovascular examination and electrocardiogram (ECG) should be carried out before starting treatment with clonidine in children or young people with ADHD. [2008]

Transition to Adult Services

Young people with ADHD receiving treatment and care from CAMHS or paediatric services should normally be transferred to adult services if they continue to have significant symptoms of ADHD or other coexisting

conditions that require treatment. Transition should be planned in advance by both referring and receiving services. If needs are severe and/or complex, use of the care programme approach should be considered.

A young person with ADHD receiving treatment and care from CAMHS or paediatric services should be reassessed at school-leaving age to establish the need for continuing treatment into adulthood. If treatment is necessary, arrangements should be made for a smooth transition to adult services with details of the anticipated treatment and services that the young person will require. Precise timing of arrangements may vary locally but should usually be completed by the time the young person is 18 years. [2008]

During the transition to adult services, a formal meeting involving CAMHS and/or paediatrics and adult psychiatric services should be considered, and full information provided to the young person about adult services. For young people aged 16 years and older, the care programme approach (CPA) should be used as an aid to transfer between services. The young person, and when appropriate the parent or carer, should be involved in the planning. [2008]

After transition to adult services, adult healthcare professionals should carry out a comprehensive assessment of the person with ADHD that includes personal, educational, occupational and social functioning, and assessment of any coexisting conditions, especially drug misuse, personality disorders, emotional problems and learning difficulties. [2008]

Treatment of Adults with ADHD

Drug treatment is the first-line treatment for adults with ADHD with either moderate or severe levels of impairment. Methylphenidate is the first-line drug. Psychological interventions without medication may be effective for some adults with moderate impairment, but there are insufficient data to support this recommendation. If methylphenidate is ineffective or unacceptable, atomoxetine or dexamfetamine can be tried. If there is residual impairment despite some benefit from drug treatment, or there is no response to drug treatment, CBT may be considered. There is the potential for drug misuse and diversion in adults with ADHD, especially in some settings, such as prison, although there is no strong evidence that this is a significant problem.

For adults with ADHD, drug treatment should be the first-line treatment unless the person would prefer a psychological approach. [2008] (At the time of publication [September 2008], methylphenidate, dexamfetamine and atomoxetine did not have UK marketing authorisation for use in adults with ADHD. However atomoxetine is licensed for adults with ADHD when the drug has been started in childhood. Informed consent should be obtained and documented. Licensing arrangements remained unchanged when the guideline was updated [February 2016].)

Drug treatment for adults with ADHD should be started only under the guidance of a psychiatrist, nurse prescriber specialising in ADHD, or other clinical prescriber with training in the diagnosis and management of ADHD. [2008]

Before starting drug treatment for adults with ADHD a full assessment should be completed, which should include:

- Full mental health and social assessment
- Full history and physical examination, including:
  - Assessment of history of exercise syncope, undue breathlessness, and other cardiovascular symptoms
  - Heart rate and blood pressure (plotted on a centile chart)
  - Weight
  - Family history of cardiac disease and examination of the cardiovascular system
- An ECG if there is past medical or family history of serious cardiac disease, a history of sudden death in young family members or abnormal findings on cardiac examination
- Risk assessment for substance misuse and drug diversion [2008]

Drug treatment for adults with ADHD should always form part of a comprehensive treatment programme

that addresses psychological, behavioural and educational or occupational needs. [2008]

Following a decision to start drug treatment in adults with ADHD, methylphenidate should normally be tried first. [2008]

Atomoxetine or dexamfetamine should be considered in adults unresponsive or intolerant to an adequate trial of methylphenidate (this should usually be about 6 weeks). Caution should be exercised when prescribing dexamfetamine to those likely to be at risk of stimulant misuse or diversion. [2008] (At the time of publication [September 2008], methylphenidate, dexamfetamine and atomoxetine did not have UK marketing authorisation for use in adults with ADHD. However atomoxetine is licensed for adults with ADHD when the drug has been started in childhood. Informed consent should be obtained and documented. Licensing arrangements remained unchanged when the guideline was updated [February 2016].)

When starting drug treatment, adults should be monitored for side effects. In particular, people treated with atomoxetine should be observed for agitation, irritability, suicidal thinking and self-harming behaviour, and unusual changes in behaviour, particularly during the initial months of treatment, or after a change in dose. They should also be warned of potential liver damage in rare cases (usually presenting as abdominal pain, unexplained nausea, malaise, darkening of the urine, or jaundice). Younger adults aged 30 years or younger should also be warned of the potential of atomoxetine to increase agitation, anxiety, suicidal thinking, and self-harming behaviour in some people, especially during the first few weeks of treatment. [2008]

For adults with ADHD stabilised on medication but with persisting functional impairment associated with the disorder, or where there has been no response to drug treatment, a course of either group or individual CBT to address the person's functional impairment should be considered. Group therapy is recommended as the first-line psychological treatment because it is the most cost effective. [2008]

For adults with ADHD, CBT may be considered when:

- The person has made an informed choice not to have drug treatment
- Drug treatment has proved to be only partially effective or ineffective or the person is intolerant to it
- People have difficulty accepting the diagnosis of ADHD and accepting and adhering to drug treatment
- Symptoms are remitting and psychological treatment is considered sufficient to target residual (mild to moderate) functional impairment [2008]

Where there may be concern about the potential for drug misuse and diversion (for example, in prison services), atomoxetine may be considered as the first-line drug treatment for ADHD in adults. [2008] (At the time of publication [September 2008], methylphenidate, dexamfetamine and atomoxetine did not have UK marketing authorisation for use in adults with ADHD. However atomoxetine is licensed for adults with ADHD when the drug has been started in childhood. Informed consent should be obtained and documented. Licensing arrangements remained unchanged when the guideline was updated [February 2016].)

Drug treatment for adults with ADHD who also misuse substances should only be prescribed by an appropriately qualified healthcare professional with expertise in managing both ADHD and substance misuse. For adults with ADHD and drug or alcohol addiction disorders there should be close liaison between the professional treating the person's ADHD and an addiction specialist. [2008]

Antipsychotics are not recommended for the treatment of ADHD in adults. [2008]

How to Use Drugs for the Treatment of ADHD

Good knowledge of the drugs used in the treatment of ADHD and their different preparations is essential (refer to the BNF and summaries of product characteristics). It is important to start with low doses and titrate upwards, monitoring effects and side effects carefully. Higher doses may need to be prescribed to some adults. The recommendations on improving adherence in children and young people may also be of use in adults.

General Principles

Prescribers should be familiar with the pharmacokinetic profiles of all the modified-release and immediate-release preparations available for ADHD to ensure that treatment is tailored effectively to the individual needs of the child, young person or adult. [2008]

Prescribers should be familiar with the requirements of controlled drug legislation governing the prescription and supply of stimulants. [2008]

During the titration phase, doses should be gradually increased until there is no further clinical improvement in ADHD (that is, symptom reduction, behaviour change, improvements in education and/or relationships) and side effects are tolerable. [2008]

Following titration and dose stabilisation, prescribing and monitoring should be carried out under locally agreed shared care arrangements with primary care. [2008]

Side effects resulting from drug treatment for ADHD should be routinely monitored and documented in the person's notes. [2008]

If side effects become troublesome in people receiving drug treatment for ADHD, a reduction in dose should be considered. [2008]

Healthcare professionals should be aware that dose titration should be slower if tics or seizures are present in people with ADHD. [2008]

Initiation and Titration of Methylphenidate, Atomoxetine, and Dexamfetamine in Children and Young People

During the titration phase, symptoms and side effects should be recorded at each dose change on standard scales (for example, Conners' 10-item scale) by parents and teachers, and progress reviewed regularly (for example, by weekly telephone contact and at each dose change) with a specialist clinician. [2008]

If using methylphenidate in children and young people with ADHD aged 6 years and older:

- Initial treatment should begin with low doses of immediate-release or modified-release preparations consistent with starting doses in the BNF
- The dose should be titrated against symptoms and side effects over 4 to 6 weeks until dose optimisation is achieved
- Modified-release preparations should be given as a single dose in the morning
- Immediate-release preparations should be given in two or three divided doses [2008]

If using atomoxetine in children and young people with ADHD aged 6 years and older:

- For those weighing up to 70 kg, the initial total daily dose should be approximately 0.5 mg/kg; the dose should be increased after 7 days to approximately 1.2 mg/kg/day
- For those weighing more than 70 kg, the initial total daily dose should be 40 mg; the dose should be increased after 7 days up to a maintenance dose of 80 mg/day
- A single daily dose can be given; two divided doses may be prescribed to minimise side effects [2008]

If using dexamfetamine in children and young people with ADHD:

- Initial treatment should begin with low doses consistent with starting doses in the BNF
- The dose should be titrated against symptoms and side effects over 4 to 6 weeks
- Treatment should be given in divided doses increasing to a maximum of 20 mg/day
- For children aged 6 to 18 years, doses up to 40 mg/day may occasionally be required [2008]

Initiation and Titration of Methylphenidate, Atomoxetine, and Dexamfetamine in Adults

In order to optimise drug treatment, the initial dose should be titrated against symptoms and side effects over 4 to 6 weeks. [2008]

During the titration phase, symptoms and side effects should be recorded at each dose change by the prescriber after discussion with the person with ADHD and, wherever possible, a carer (for example, a spouse, parent or close friend). Progress should be reviewed (for example, by weekly telephone contact and at each dose change) with a specialist clinician. [2008]

If using methylphenidate in adults with ADHD:

- Initial treatment should begin with low doses (5 mg three times daily for immediate-release preparations; the equivalent dose for modified-release preparations)
- The dose should be titrated against symptoms and side effects over 4 to 6 weeks
- The dose should be increased according to response up to a maximum of 100 mg/day
- Modified-release preparations should usually be given once daily and no more than twice daily
- Modified-release preparations may be preferred to increase adherence and in circumstances where there are concerns about substance misuse or diversion
- Immediate-release preparations should be given up to four times daily [2008]

If using atomoxetine in adults with ADHD:

- For people with ADHD weighing up to 70 kg, the initial total daily dose should be approximately 0.5 mg/kg; the dose should be increased after 7 days to approximately 1.2 mg/kg/day
- For people with ADHD weighing more than 70 kg, the initial total daily dose should be 40 mg; the dose should be increased after 7 days up to a maintenance dose of 100 mg/day
- The usual maintenance dose is either 80 or 100 mg, which may be taken in divided doses
- A trial of 6 weeks on a maintenance dose should be allowed to evaluate the full effectiveness of atomoxetine [2008]

If using dexamfetamine in adults with ADHD:

- Initial treatment should begin with low doses (5 mg twice daily)
- The dose should be titrated against symptoms and side effects over 4 to 6 weeks
- Treatment should be given in divided doses
- The dose should be increased according to response up to a maximum of 60 mg/day
- The dose should usually be given between two and four times daily [2008]

Monitoring Side Effects and the Potential for Misuse in Children, Young People and Adults

Healthcare professionals should consider using standard symptom and side effect rating scales throughout the course of treatment as an adjunct to clinical assessment for people with ADHD. [2008]

In people taking methylphenidate, atomoxetine, or dexamfetamine:

- Height should be measured every 6 months in children and young people
- Weight should be measured 3 and 6 months after drug treatment has started and every 6 months thereafter in children, young people, and adults
- Height and weight in children and young people should be plotted on a growth chart and reviewed by the healthcare professional responsible for treatment [2008]

If there is evidence of weight loss associated with drug treatment in adults with ADHD, healthcare professionals should consider monitoring body mass index and changing the drug if weight loss persists. [2008]

Strategies to reduce weight loss in people with ADHD, or manage decreased weight gain in children, include:

- Taking medication either with or after food, rather than before meals
- Taking additional meals or snacks early in the morning or late in the evening when the stimulant

effects of the drug have worn off
Obtaining dietary advice
Consuming high-calorie foods of good nutritional value [2008]

If growth is significantly affected by drug treatment (that is, the child or young person has not met the height expected for their age), the option of a planned break in treatment over school holidays should be considered to allow 'catch-up' growth to occur. [2008]

In people with ADHD, heart rate and blood pressure should be monitored and recorded on a centile chart before and after each dose change and routinely every 3 months. [2008]

For people taking methylphenidate, dexamfetamine and atomoxetine, routine blood tests and ECGs are not recommended unless there is a clinical indication. [2008]

Liver damage is a rare and idiosyncratic adverse effect of atomoxetine and routine liver function tests are not recommended. [2008]

For children and young people taking methylphenidate and dexamfetamine, healthcare professionals and parents or carers should monitor changes in the potential for drug misuse and diversion, which may come with changes in circumstances and age. In these situations, modified-release methylphenidate or atomoxetine may be preferred. [2008]

In young people and adults, sexual dysfunction (that is, erectile and ejaculatory dysfunction) and dysmenorrhoea should be monitored as potential side effects of atomoxetine. [2008]

For people taking methylphenidate, dexamfetamine or atomoxetine who have sustained resting tachycardia, arrhythmia or systolic blood pressure greater than the 95th percentile (or a clinically significant increase) measured on two occasions should have their dose reduced and be referred to a paediatrician or adult physician. [2008]

If psychotic symptoms (for example, delusions and hallucinations) emerge in children, young people and adults after starting methylphenidate or dexamfetamine, the drug should be withdrawn and a full psychiatric assessment carried out. Atomoxetine should be considered as an alternative. [2008]

If seizures are exacerbated in a child or young person with epilepsy, or de novo seizures emerge following the introduction of methylphenidate or atomoxetine, the drug should be discontinued immediately. Dexamfetamine may be considered as an alternative in consultation with a regional tertiary specialist treatment centre. [2008]

If tics emerge in people taking methylphenidate or dexamfetamine, healthcare professionals should consider whether:

The tics are stimulant-related (tics naturally wax and wane)
Tic-related impairment outweighs the benefits of ADHD treatment

If tics are stimulant-related, reduce the dose of methylphenidate or dexamfetamine; consider changing to atomoxetine, or stop drug treatment. [2008]

Anxiety symptoms, including panic, may be precipitated by stimulants, particularly in adults with a history of coexisting anxiety. Where this is an issue, lower doses of the stimulant and/or combined treatment with an antidepressant used to treat anxiety can be used; switching to atomoxetine may be effective. [2008]

Improving Adherence to Drug Treatment

For children and young people with ADHD, the strategies outlined in the recommendations below should be considered to improve treatment adherence. Similar strategies, adapted for age, may be considered for adults.

Communication between the prescriber and the child or young person should be improved by educating

parents or carers and ensuring there are regular three-way conversations between prescriber, parent or carer and the child or young person. For adults with ADHD, and with their permission, a spouse, partner, parent, close friend or carer wherever possible should be part of these conversations. Clear instructions about how to take the drug should be offered in picture or written format, which may include information on dose, duration, side effects, dosage schedule, the need for supervision and how this should be done. [2008]

Healthcare professionals should consider suggesting peer-support groups for the child or young person with ADHD and their parents or carers if adherence to drug treatment is difficult or uncertain. [2008]

Simple drug regimens (for example, once-daily modified-release doses) are recommended for people with ADHD. [2008]

Healthcare professionals should encourage children and young people with ADHD to be responsible for their own health, including taking their medication as required, and support parents and carers in this endeavour. [2008]

Healthcare professionals should advise parents or carers to provide the child or young person with visual reminders to take medication regularly (for example, alarms, clocks, pill boxes, or notes on calendars or fridges). [2008]

Healthcare professionals should advise children and young people and their parents or carers that taking medication should be incorporated into daily routines (for example, before meals or after brushing teeth). [2008]

Where necessary, healthcare professionals should help parents or carers develop a positive attitude and approach in the management of medication, which might include praise and positive reinforcement for the child or young person with ADHD. [2008]

Duration, Discontinuation, and Continuity of Treatment in Children and Young People

It is advisable to review each year whether the child or young person needs to continue drug treatment and to ensure that the long-term pattern of use is tailored to the person's needs, preferences and circumstances.

Following an adequate treatment response, drug treatment for ADHD should be continued for as long as it remains clinically effective. This should be reviewed at least annually. The review should include a comprehensive assessment of clinical need, benefits, and side effects, taking into account the views of the child or young person, as well as those of parents, carers, and teachers, and how these views may differ. The effect of missed doses, planned dose reductions and brief periods of no treatment should be taken into account and the preferred pattern of use should also be reviewed. Coexisting conditions should be reviewed, and the child or young person treated or referred if necessary. The need for psychological and social support for the child or young person and for the parents or other carers should be assessed. [2008]

Drug holidays are not routinely recommended; however, consideration should be given to the parent or carer and child or young person with ADHD working with their healthcare professional to find the best pattern of use, which may include periods without drug treatment. [2008]

Duration, Discontinuation and Continuity of Treatment in Adults

Following an adequate response, drug treatment for ADHD should be continued for as long as it is clinically effective. This should be reviewed annually. The review should include a comprehensive assessment of clinical need, benefits, and side effects, taking into account the views of the person and those of a spouse, partner, parent, close friends, or carers wherever possible, and how these accounts may differ. The effect of missed doses, planned dose reductions and brief periods of no treatment should be taken into account and the preferred pattern of use should also be reviewed. Coexisting conditions should be reviewed, and the person treated or referred if necessary. The need for psychological, social, and occupational support for the person and their carers should be assessed. [2008]

An individual treatment approach is important for adults, and healthcare professionals should regularly review (at least annually) the need to adapt patterns of use, including the effect of drug treatment on coexisting conditions and mood changes. [2008]

Definitions

2008 Guideline

Not applicable

2016 Update

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Committee makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Committee is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Recommendations That Must (or Must Not) Be Followed

The Committee usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the Committee uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Recommendations That Should (or Should Not) Be Followed – a 'Strong' Recommendation

The Committee uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the Committee is confident that an intervention will not be of benefit for most patients.

Recommendations That Could Be Followed

The Committee uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

A National Institute for Health and Care Excellence (NICE) pathway titled "Attention deficit hyperactivity disorder overview" is available from the NICE W eb site.

Scope

Disease/Condition(s)

Attention deficit hyperactivity disorder (ADHD) and related diagnoses*

*Hyperkinetic disorder (International Classification of Diseases, 10th revision [ICD-10] is considered, along with the three Diagnostic and Statistical Manual of Mental Disorders, 4th Edition [Text Revision] [DSM-IV] ADHD subtypes)

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Nutrition

Pediatrics

Psychiatry

Psychology

Intended Users

Advanced Practice Nurses

Dietitians

Nurses

Occupational Therapists

Patients

Pharmacists

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Social W orkers

Students

Guideline Objective(s)

2008 Guideline

To provide recommendations on the diagnosis and treatment of attention deficit hyperactivity disorder (ADHD) in children, young people, and adults

To assist clinicians, people with ADHD, and their carers by identifying the merits of particular treatment approaches where the evidence from research and clinical experience exists

Specifically, the guideline aims to:

- Examine the validity of the diagnostic construct of ADHD

Evaluate the role of specific pharmacological agents and non-pharmacological, psychological, and psychosocial interventions in the treatment and management of ADHD
Evaluate the role of specific services and systems for providing those services in the treatment and management of ADHD
Integrate the above to provide best-practice advice on the care of people with a diagnosis of ADHD through the different phases of illness, including the initiation and maintenance of treatment for the chronic condition, the treatment of acute episodes and the promotion of well-being
Consider economic aspects of various interventions for ADHD

2016 Update

To evaluate the clinical effectiveness and cost-effectiveness of elimination and restriction diets and of dietary supplementation with polyunsaturated fatty acids (PUFAs) on children and young people with ADHD

Target Population

Children (aged 3 to 11 years), young people (aged 12 to 18 years), and adults with a diagnosis of attention deficit hyperactivity disorder (ADHD) and related diagnoses

Interventions and Practices Considered

1. Identification, pre-diagnostic intervention, and referral to secondary services
2. Diagnosis of attention deficit hyperactivity disorder (ADHD) including clinical and psychosocial assessment, developmental and psychiatric history, observer reports, and assessment of mental state
3. Post-diagnostic advice including general and dietary advice
4. Treatment of pre-school children including referral to parent-training/education program (group- or individual-based)
5. Treatment for school-age children and young people with moderate impairment (referral to parent-training/education program either on its own or together with cognitive behavioural therapy and social skills training)
6. Management of school-age children and young people with severe impairment and adults
    - Pre-drug treatment assessment (mental health assessment, full history and physical examination, electrocardiogram, risk assessment for substance misuse)
    - Methylphenidate, atomoxetine, or dexamfetamine therapy (including drug initiation and titration, improving adherence, monitoring for side effects and misuse)
    - Cognitive behavioural therapy/social skills training
    - Review and management of poor response to initial treatment
    - Transition to adult services

Note: The following interventions were considered but not recommended: universal screening for ADHD, eliminating artificial colouring and additives from the diet as a treatment for ADHD, fatty acid supplementation for treating ADHD, drug treatment for pre-school children with ADHD, drug treatment as first-line therapy for school-age children and young people with moderate impairment, and antipsychotics for treatment of ADHD.

Major Outcomes Considered

2008 Guideline

Sensitivity and specificity of diagnostic measures
Clinical effectiveness
Attention deficit hyperactivity disorder (ADHD) symptoms
Conduct problems

Social skills
Emotional outcomes
Self-efficacy
Reading attainment
Mathematics attainment
Nonresponse to treatment
Adverse effects of stimulants
Cost-effectiveness

2016 Update

ADHD symptom severity (rated by the parent, teacher or self-rated)
Academic performance
Functional status
Side effects (limited to: gastrointestinal symptoms, change in weight/height, change in appetite, change in sleep pattern, headache)
Number of participants
Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline on attention deficit hyperactivity disorder (ADHD) was originally developed in 2008 by the National Collaborating Centre for Mental Health (NCCMH) on behalf of the National Institute for Health and Care Excellence (NICE). In 2015, the NICE guideline was reviewed, and new evidence relating to the effects of diet on ADHD was found. The guideline was updated by the NICE Clinical Guidelines Update Team as requested by NICE's Guidance Executive. See the "Availability of Companion Documents" field for the full version of this guidance, including the 2016 addendum, and related appendices.

2008 Guideline

Systematic Clinical Literature Review

The aim of the clinical literature review was to identify and synthesise relevant evidence from the literature systematically in order to answer the specific clinical questions developed by the Guideline Development Group (GDG).

Methodology

A stepwise, hierarchical approach was taken to locating and presenting evidence to the GDG. The NCCMH developed this process based on methods set out in The Guidelines Manual (NICE, 2006) and after considering recommendations from a range of other sources. These included:

Clinical Policy and Practice Program of the New South Wales Department of Health (Australia)

Clinical Evidence Online
The Cochrane Collaboration
Grading of Recommendations: Assessment, Development, and Evaluation (GRADE) W orking Group
New Zealand Guidelines Group
National Health Service (NHS) Centre for Reviews and Dissemination
Oxford Centre for Evidence-Based Medicine
Oxford Systematic Review Development Programme
Scottish Intercollegiate Guidelines Network (SIGN)
United States Agency for Healthcare Research and Quality

The Review Process

After the scope was finalised, a more extensive search for systematic reviews and published guidelines was undertaken. Existing NICE guidelines were updated where necessary.

Searches for evidence were updated between 6 and 8 weeks before the stakeholder consultation. After this point, studies were included only if they were judged by the GDG to be exceptional (for example, the evidence was likely to change a recommendation).

The Search Process for Questions Concerning Interventions

For questions related to interventions, the initial evidence base was formed from well-conducted randomised controlled trials (RCTs) that addressed at least one of the clinical questions (the review process is illustrated in Flowchart 1 of the full version of the guideline). Although there are a number of difficulties with the use of RCTs in the evaluation of interventions in mental health, the RCT remains the most important method for establishing treatment efficacy. For other clinical questions, searches were for the appropriate study design.

All searches were based on the standard mental health related bibliographic databases (EMBASE, MEDLINE, PsycINFO, Cochrane Library, ERIC) for all trials potentially relevant to the guideline. If the number of citations generated from this search was large (more than 5000), existing systematic reviews and question-specific search filters were developed to restrict the search while minimising loss of sensitivity.

W here the evidence base was large, recent high-quality English-language systematic reviews were used primarily as a source of RCTs (see Appendix 10 in the full guideline appendices for quality criteria used to assess systematic reviews). In some circumstances, however, existing data sets were utilised. W here this was the case, data were cross-checked for accuracy before use. New RCTs meeting inclusion criteria set by the GDG were incorporated into the existing reviews and fresh analyses performed.

After the initial search results had been scanned liberally to exclude irrelevant papers, the review team used a purpose built 'study information' database to manage both the included and the excluded studies (eligibility criteria were developed after consultation with the GDG). For questions without good-quality evidence (after the initial search), a decision was made by the GDG about whether to (a) repeat the search using subject-specific databases (for example, CINAHL, AMED, SIGLE or PILOTS), (b) conduct a new search for lower levels of evidence, or (c) adopt a consensus process. Future guidelines will be able to update and extend the usable evidence base starting from the evidence collected, synthesised and analysed for this guideline.

In addition, searches were made of the reference lists of all eligible systematic reviews and included studies, as well as the list of evidence submitted by stakeholders. Known experts in the field (see Appendix 5 in the full guideline appendices), based both on the references identified in early steps and on advice from GDG members, were sent letters requesting relevant studies that were in the process of being published. In addition, the tables of contents of appropriate journals were periodically checked for relevant studies.

The Search Process for Questions of Diagnosis and Prognosis

For questions related to diagnosis and prognosis, the search process was the same as described above, except that the initial evidence base was formed from studies with the most appropriate and reliable design to answer the particular question. That is, for questions about diagnosis, the initial search was for systematic reviews and meta-analyses as well as cross-sectional, factor analytic, genetic and diagnostic studies; for questions about prognosis, it was for cohort studies of representative patients. In situations where it was not possible to identify a substantial body of appropriately designed studies that directly addressed each clinical question, a consensus process was adopted.

Search Filters

Search filters developed by the review team consisted of a combination of subject heading and free-text phrases. Specific filters were developed for the guideline topic, and where necessary, for each clinical question. In addition, the review team used filters developed for systematic reviews, RCTs and other appropriate research designs (see Appendix 8 in the full guideline appendices).

Study Selection

All primary-level studies included after the first scan of citations were acquired in full and re-evaluated for eligibility at the time they were being entered into the study information database (see Appendix 9 in the full guideline appendices for screen shots of the database). Specific eligibility criteria were developed for each clinical question and are described in the relevant clinical evidence chapters. Eligible systematic reviews and primary-level studies were critically appraised for methodological quality (see Appendix 10 in the full version of the guideline for the quality checklists). The eligibility of each study was confirmed by at least one member of the appropriate topic group.

For some clinical questions, it was necessary to prioritise the evidence with respect to the UK context (that is, external validity). To make this process explicit, the topic groups took into account the following factors when assessing the evidence:

Participant factors (for example, gender, age, ethnicity)
Provider factors (for example, model fidelity, the conditions under which the intervention was performed and the availability of experienced staff to undertake the procedure)
Cultural factors (for example, differences in standard care and differences in the welfare system).

It was the responsibility of each topic group to decide which prioritisation factors were relevant to each clinical question in light of the UK context and then decide how they should modify their recommendations.

Unpublished Evidence

The GDG used a number of criteria when deciding whether or not to accept unpublished data. First, the evidence must have been accompanied by a trial report containing sufficient detail to assess the quality of the data properly. Second, the evidence must be submitted with the understanding that data from the study and a summary of the study's characteristics would be published in the full guideline. Therefore, the GDG did not accept evidence submitted as commercial in confidence. Having said that, the GDG recognised that unpublished evidence submitted by investigators might later be retracted by those investigators if the inclusion of such data would jeopardize publication of their research.

Health Economics Methods

Search Strategy

For the systematic review of economic evidence on treatments for ADHD the standard mental-health-related bibliographic databases (EMBASE, MEDLINE, CINAHL and PsycINFO) were searched. For these databases, a health economics search filter adapted from the Centre for Reviews and Dissemination at the University of York was used in combination with a general filter for ADHD. Additional searches were performed in specific health economics databases (National Health Service Economic Evaluation Database [NHS EED], Office of Health Economics, Health Economics Evaluation Database [OHE HEED]), as well as in the Health Technology Assessment (HTA) database. For the HTA and NHS EED databases, the general

filter for ADHD was used. OHE HEED was searched using a shorter, database-specific strategy. Initial searches were performed in June 2006. The searches were updated regularly, with the final search conducted 5 weeks before the consultation period.

In parallel to searches of electronic databases, reference lists of eligible studies and relevant reviews were searched by hand. Studies included in the clinical evidence review were also screened for economic evidence.

The systematic search for economic evidence resulted in 47 potentially relevant studies. Full texts of all potentially eligible studies (including those for which relevance/eligibility was not clear from the abstract) were obtained. These publications were then assessed against a set of standard inclusion criteria by the health economists, and papers eligible for inclusion were subsequently assessed for internal validity. The quality assessment was based on the checklists used by the *British Medical Journal* to assist referees in appraising full and partial economic analyses (see Appendix 12 in the full guideline appendices).

Selection Criteria

The following inclusion criteria were applied to select studies identified by the economic searches for further analysis:

No restriction was placed on language or publication status of the papers.
Studies published from 1990 onwards were included. This date restriction was imposed in order to obtain data relevant to current healthcare settings and costs.
Only studies from Organisation for Economic Co-operation and Development countries were included, as the aim of the review was to identify economic and health-related quality of life (HRQoL) information transferable to the UK context.
Selection criteria based on types of clinical conditions and patients were identical to the clinical literature review.
Studies were included provided that sufficient details regarding methods and results were available to enable the methodological quality of the study to be assessed, and provided that the study's data and results were extractable. Poster presentations or abstracts were in principle excluded; however, they were included if they reported additional data from studies which had already been published elsewhere and met the inclusion criteria, or if they contained appropriate input data required for economic modelling that were not otherwise available.
Full economic evaluations that compared two or more relevant options and considered both costs and consequences (that is, cost-effectiveness analysis, cost-utility analysis, cost-consequences analysis or cost-benefit analysis) were included in the review. HRQoL studies were included if they reported utility weights appropriate to use in a cost-utility analysis.

2016 Update

Evidence Review

Methods

A systematic review of the literature was conducted, as specified in the review protocol in Appendix C of the guideline addendum (see the "Availability of Companion Documents" field). The protocol was developed in consultation with the topic expert members, and then reviewed by the core Committee members, before the review was carried out. The following outcomes were considered important for decision making: ADHD symptom severity (rated by the parent, teacher or self-rated), academic performance, functional status, side effects (limited to: gastrointestinal symptoms, change in weight/height, change in appetite, change in sleep pattern, headache), number of participants and quality of life.

A systematic search was conducted (see Appendix D of the guideline addendum for databases and search terms). The titles and abstracts were screened and full-text version of articles that were identified as potentially relevant were obtained and reviewed against the criteria specified in the review protocol (see Appendix C of the guideline addendum).

Results for Question 1

The systematic search identified 2364 articles. The titles and abstracts were screened and 34 articles were identified as potentially relevant. Full-text versions of these articles were obtained and reviewed against the criteria specified in the review protocol (Appendix C of the guideline addendum). Of these, 32 were excluded as they did not meet the criteria, and 2 met the criteria and were included.

Review Question 2

What is the clinical and cost-effectiveness of dietary supplementation with polyunsaturated fatty acids (PUFAs) in children and young people with ADHD?

Results for Question 2

The systematic search identified 1184 articles. The titles and abstracts were screened and 56 articles were identified as potentially relevant. Full-text versions of these articles were obtained and reviewed against the criteria specified in the review protocol (see Appendix C of the guideline addendum). Of these, 41 were excluded as they did not meet the criteria, and 15 met the criteria and were included.

Health Economic Evidence Review

A systematic literature search was undertaken to identify health economic evidence within published literature relevant to both review questions. The evidence was identified by conducting a broad search relating to restriction diets, elimination diets, and dietary supplements (polyunsaturated fatty acids) in the NHS EED and the HTA database. The search also included Medline and EMBASE databases based on the review protocol using an economic filter.

Studies published in languages other than English were not reviewed. The search was conducted on 2 July 2015. The health economic search strategies are detailed in Appendix J of the guideline addendum. The health economist also sought out relevant studies identified by the surveillance review or Committee members.

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost-utility, cost-effectiveness, cost-benefit and cost-consequence analyses) and comparative costing studies that address the review question in the relevant population were considered potentially includable as economic evidence. Studies that only reported burden of disease or cost of illness were excluded. Literature reviews, abstracts, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

Results of the Economic Literature Review

Five hundred ninety articles were identified by the search. All articles were excluded based on title and abstract. No studies were included in the economic literature review for both review questions. The flowchart summarising the number of studies included and excluded at each stage of the review process can be found in Appendix K of the guideline addendum. No full-text versions of the articles were obtained so there are no excluded economic studies list provided in the appendices of the guideline addendum.

Number of Source Documents

2008 Guideline

Not stated

2016 Update

Clinical Evidence

Question 1: Two articles were included.
Question 2: Fifteen articles were included.

See Appendix E of the guideline addendum (see the "Availability of Companion Documents" field) for the clinical review flowchart.

Health Economic Evidence

No studies were included in the economic literature review.

See Appendix K of the guideline addendum for the economic review flowchart.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline on attention deficit hyperactivity disorder (ADHD) was originally developed in 2008 by the National Collaborating Centre for Mental Health (NCCMH) on behalf of the National Institute for Health and Clinical Excellence (NICE). In 2015, the NICE guideline was reviewed, and new evidence relating to the effects of diet on ADHD was found. The guideline was updated by the NICE Clinical Guidelines Update Team as requested by NICE's Guidance Executive. See the "Availability of Companion Documents" field for the full version of this guidance, including the 2016 addendum, and related appendices.

2008 Guideline

Clinical Effectiveness

Data Extraction

Outcome data were extracted from all eligible studies, which met the quality criteria, into RevMan 4.2.10 (Review Manager, The Cochrane Centre, 2003) or Word tables.

Studies with factor analysis were quality assessed using a checklist elaborated and agreed by the Guideline Development Group (GDG) members.

For each outcome, a hierarchy of most suitable outcome measures was agreed upon by the GDG members. If a study reported more than one relevant outcome measure for a given outcome, only the measure with the highest hierarchy was included in the meta-analysis.

For a given outcome (continuous and dichotomous), where more than 50% of the number randomised to any group were not accounted for by trial authors, the data were excluded from the review because of the risk of bias. Where possible, however, dichotomous efficacy outcomes were calculated on an intention-to-treat basis (that is, a 'once-randomised-always-analyse' basis). This assumes that those participants who ceased to engage in the study – from whatever group – had an unfavourable outcome. This meant that the 50% rule was not applied to dichotomous outcomes where there was good evidence that those participants who ceased to engage in the study were likely to have an unfavourable outcome (in this case, early withdrawals were included in both the numerator and denominator). Adverse effects were entered into Review Manager as reported by the study authors because it was usually not possible to determine whether early withdrawals had an unfavourable outcome. For the outcome 'leaving the study early for any reason', the denominator was the number randomised.

Synthesising the Evidence

Where possible, meta-analysis was used to synthesise the evidence using Review Manager. If necessary, reanalyses of the data or sub-analyses were used to answer clinical questions not addressed in the original studies or reviews.

Dichotomous outcomes were analysed as relative risks (RR) with the associated 95% confidence interval (CI). A relative risk (also called a risk ratio) is the ratio of the treatment event rate to the control event rate. An RR of 1 indicates no difference between treatment and control.

The CI shows with 95% certainty the range within which the true treatment effect should lie and can be used to determine statistical significance. If the CI does not cross the 'line of no effect', the effect is statistically significant.

Continuous outcomes were analysed as weighted mean differences (WMD), or as a standardised mean difference (SMD) when different measures were used in different studies to estimate the same underlying effect. If provided, intention-to-treat data, using a method such as 'last observation carried forward', were preferred over data from completers.

To check for consistency between studies, both the I^2 test of heterogeneity and a visual inspection of the forest plots were used. The I^2 statistic describes the proportion of total variation in study estimates that is due to heterogeneity.

Study characteristics tables, generated automatically from the study database, were used to summarise general information about each study (see Appendix 17 in the full version of the guideline). Where meta-analysis was not appropriate and/or possible, the reported results from each primary-level study were also presented in the included studies table (and included, where appropriate, in a narrative review).

Presenting the Data to the GDG

Study characteristics tables and, where appropriate, forest plots generated with Review Manager were presented to the GDG in order to prepare a GRADE (Grading of Recommendations Assessment, Development and Evaluation) evidence profile table for each review and to develop recommendations.

GRADE Evidence Profile Tables

A GRADE evidence profile was used to summarise both the quality of the evidence and the results of the evidence synthesis (see Table 4 in the full version of the guideline for an example of an evidence profile). For each outcome, quality may be reduced depending on the study design, limitations (based on the quality of individual studies; see Appendix 10 in the full guideline appendices for the quality checklists), inconsistency, indirectness (that is, how closely the outcome measures, interventions and participants match those of interest), and imprecision (based on the CI around the effect size). For observational

studies, the quality may be increased if there is a large effect, plausible confounding would have changed the effect, or there is evidence of a dose-response gradient (details would be provided under the other considerations column). Each evidence profile also included a summary of the findings: number of patients included in each group, an estimate of the magnitude of the effect, and the overall quality of the evidence for each outcome.

Forest Plots

Each forest plot displayed the effect size and CI for each study as well as the overall summary statistic. The graphs were organised so that the display of data in the area to the left of the 'line of no effect' indicated a 'favourable' outcome for the treatment in question.

Refer to Section 3.5 in the full version of the guideline for more information.

Cost-effectiveness

Data Extraction

Data were extracted by the health economist using a standard economic data extraction form (see Appendix 13 in the full guideline appendices [see the "Availability of Companion Documents" field]).

Presentation of Economic Evidence

The characteristics and results of all economic studies included in the review are provided in the form of evidence tables in Appendix 14 in the full guideline appendices.

Focus Group Methodology

Besides making recommendations based on the clinical and cost-effectiveness of interventions for attention deficit hyperactivity disorder (ADHD), an important function of developing this guideline was understanding the experience of ADHD from the service user's point of view.

In order to provide sufficient breadth of context and depth of understanding of children's views on taking stimulant medicine, the NCCMH commissioned the London School of Economics to undertake a qualitative focus group study with children and young people on their perceptions of their use of stimulant medication, together with a review of the available literature on young people's experiences.

Data Collection

Semi-structured focus groups were used to collect data about how children and young people experience stimulant medication. Allowing children to describe their experiences through qualitative interviews has been found to be both reliable and valid, and there is compelling evidence to suggest that children are competent research participants.

Thirteen children were interviewed as part of a series of focus groups. Three children were interviewed one-to-one, either because they were unable to attend the focus groups or because they preferred to be interviewed individually. Written informed consent was obtained from one parent and also from the participant. Parents were also asked to complete a basic demographic questionnaire.

Data Analysis

All interviews were digitally recorded, transcribed and analysed using rigorous qualitative coding practices that meet established criteria of validity and relevance to qualitative health research. Focus groups were coded using content analysis. The coding process captured the data on two analytic levels: individual concepts were coded first, and then these concepts were grouped together under higher order themes. Systematic coding meant that it was possible to code at both the individual level and at the group level. Group-level data were represented in the frequency with which concepts and themes were expressed by group members. Transcript excerpts elucidated the meaning of codes.

A coding frame was drawn up by the lead author of the study, and validated within a coding team. The coding team applied the same codes to a transcript in order to discuss their definition and validity. This

discussion resulted in refinements to the structure of categories and sub-categories, as well as refinements to individual codes.

The coding team was able to reach agreement on the validity of a majority of codes.

Refer to Sections 3.6 and 3.7 in the full guideline appendices for additional information.

2016 Update

Evidence Review

Many of the outcomes for both review questions were reported as change measures from baseline (for example, change in ADHD symptom severity). Some studies did not report this measure directly, but instead reported the measure at baseline and at follow up for each group. In these situations the reviewer calculated the mean change from baseline and imputed the standard deviation for this measure.

When more than one study assessed an outcome for a given comparison, data were combined using pair-wise meta-analyses. The Mantel-Haenszel and inverse variance methods were used for dichotomous and continuous outcomes, respectively. A random effects model was chosen because the treatment effects were unlikely to be identical across studies due to differences in baseline ADHD severity and the heterogeneity in interventions across studies. The I^2, chi^2 and tau^2 statistics were calculated to assess heterogeneity. Forest plots showing the outcome of these meta-analyses are shown in Appendix I of the guideline addendum.

The degree of heterogeneity was assessed, and 95% CIs were examined to determine whether serious inconsistency was present, using the methods described by the GRADE working group. Indirectness was assessed by noting whether the evidence directly applied to the review question; the outcome 'number of participants leaving the study early' was judged to have serious indirectness because it was a surrogate measure for treatment acceptability. Imprecision was assessed by determining whether 95% CIs incorporated clinically important harm, no effect and clinically important benefit. If all three were incorporated in the CI, imprecision was judged very serious. If two of the three were incorporated, imprecision was considered serious. Other factors such as publication bias were also considered, but none gave rise to serious uncertainty.

The GRADE default minimally important differences were used (0.75 and 1.25 for dichotomous outcomes, and -0.5 and 0.5 SMDs for continuous outcomes). Published minimally important differences were sought for all outcomes via an internet search and through consulting the topic expert members, but none were found.

Question 1

Data were not available to assess any of the subgroup effects specified in the review protocol (age, comorbid learning disability, neurological or behavioural disorder, ADHD severity).

The quality of evidence for each outcome for each comparison was appraised using the approach recommended by the GRADE working group (for full GRADE profiles, see Appendix H of the guideline addendum). All included studies were randomised controlled trials. Both included studies were unblinded; parents, teachers and clinicians were aware of group allocation. This was considered a very serious risk of bias for subjective outcomes rated by an unblinded observer (e.g., ADHD symptom severity) and a serious risk of bias for outcomes that could be objectively measured (e.g., number of participants leaving the study early). Inconsistency (the variability in the 8 results from different trials) was only assessed when data were combined in a meta-analysis.

Question 2

Data were not available to assess any of the subgroup effects specified in the review protocol. However, the included studies consisted of a mixture of studies assessing the effectiveness of a combination of omega 3 and 6 polyunsaturated fatty acids (PUFAs) and studies assessing the effectiveness of omega 3 PUFAs alone. These groups of studies considered as separate subgroups in the meta-analyses and tests

for subgroup differences were used to assess the evidence for the presence of a subgroup effect. The tests for subgroup differences were not significant in any case. Therefore the overall effect was reported in the results of the analyses.

Different studies used different doses of PUFAs. Initially the Committee planned to perform subgroup analyses for studies using different doses. However, the composition and doses of PUFAs used differed markedly across all studies and so this approach was not possible. Instead, the studies were ordered in the forest plots showing the results of the meta-analyses according to omega 3 dose from low to high, and the dose for each study is indicated in order to give a qualitative indication of the effect of dose on each outcome.

The quality of evidence for each outcome for each comparison was appraised using the approach recommended by the GRADE working group (for full GRADE profiles, see Appendix H of the full guideline addendum). All included studies were randomised controlled trials. Reasons for downgrading for risk of bias typically included a lack of blinding of participants, parents or outcome assessors. This was considered a very serious risk of bias for subjective outcomes rated by an unblinded observer (e.g., ADHD symptom severity) and a serious risk of bias for outcomes that could be objectively measured (e.g., number of participants leaving the study early) or when only some of the studies contributing to an outcome were affected. Randomisation methods and allocation concealment was assessed across studies. Many studies had unclear randomisation methods and methods for ensuring allocation concealment, but this was not judged sufficient to warrant downgrading for risk of bias. Similarly, some studies had moderate dropout rates and did not perform an intention to treat analysis, but as drop-out rates were similar across groups in all cases, this was not considered a serious risk of bias. Inconsistency (the variability in the results from different trials) was only assessed when data were combined in a meta-analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Expert Consensus (Nominal Group Technique)

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline on attention deficit hyperactivity disorder (ADHD) was originally developed in 2008 by the National Collaborating Centre for Mental Health (NCCMH) on behalf of the National Institute for Health and Care Excellence (NICE). In 2015, the NICE guideline was reviewed, and new evidence relating to the effects of diet on ADHD was found. The guideline was updated by the NICE Clinical Guidelines Update Team as requested by NICE's Guidance Executive. See the "Availability of Companion Documents" field for the full version of this guidance, including the 2016 addendum, and related appendices.

2008 Guideline

The Guideline Development Group (GDG)

The GDG consisted of: professionals in clinical child and adolescent psychiatry, clinical child and adolescent psychology (and neuropsychology), psychiatry for learning disorders, developmental paediatrics, paediatrics (neurodisability), general practice and nursing; academic experts in child and adolescent psychiatry, paediatric medicine research, forensic clinical psychology, and education; service users and carers. In order to ascertain the experiences of children and young people of stimulant medication for ADHD, the NCCMH commissioned a focus group study. The guideline development process was supported by staff from the NCCMH, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GDG, managed the process and contributed to

drafting the guideline.

Guideline Development Group Meetings

Twenty GDG meetings were held between March 2006 and May 2008. During each day-long GDG meeting, in a plenary session, clinical questions and clinical evidence were reviewed and assessed and recommendations formulated and reviewed.

Topic Groups

The GDG divided its workload along clinically relevant lines to simplify the guideline development process, and GDG members formed smaller topic groups to undertake guideline work in that area of clinical practice. Topic group 1 covered questions relating to diagnosis and assessment; topic group 2 covered psychological interventions; topic group 3 covered pharmacological interventions; topic group 4 covered education interventions; and topic group 5 covered dietary interventions. These groups were designed to manage the large volume of evidence appraisal efficiently before presenting it to the GDG as a whole. Each topic group was chaired by a GDG member with expert knowledge of the topic area (one of the healthcare professionals). Topic groups refined the clinical definitions of treatment interventions, reviewed and prepared the evidence with the systematic reviewer before presenting it to the GDG as a whole, and helped the GDG to identify further expertise in the topic. Topic group leaders reported the status of the group's work as part of the standing agenda. They also introduced and led the GDG discussion of the evidence review for that topic and assisted the GDG Chair in drafting that section of the guideline relevant to the work of each topic group.

Service Users and Carers

Individuals with direct experience of services gave an integral service-user focus to the GDG and the guideline. The GDG included carers and a service user. They contributed as full GDG members to writing the clinical questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology associated with ADHD, and bringing service-user research to the attention of the GDG. In drafting the guideline, they contributed to the editing of the first draft of the guideline's introduction and to the writing of Chapter 4, and identified recommendations from the perspective of service users and carers.

Refer to Section 3.3 in the full version of the guideline for additional information on special advisers and national and international experts.

Clinical Questions

Clinical questions were used to guide the identification and interrogation of the evidence base relevant to the topic of the guideline. The questions were developed using a modified nominal group technique. The process began by asking each topic group of the GDG to submit as many questions as possible. The questions were then collated and refined by the review team. The GDG members were then asked to rate each question for importance. At a subsequent meeting, the GDG Chair facilitated a discussion to further refine the questions. The results of this process were then discussed and consensus reached about which questions would be of primary importance and which would be secondary. The GDG aimed to address all primary questions, while secondary questions would only be covered time permitting.

See Appendix 6 in the full guideline appendices (see the "Availability of Companion Documents" field) for the list of the clinical questions.

The Review Process

The review team, in conjunction with the GDG, developed an evidence map that detailed all comparisons necessary to answer the clinical questions. The initial approach taken to locating primary-level studies depended on the type of clinical question and availability of evidence.

The GDG decided which questions were best addressed by good practice based on expert opinion, which questions were likely to have a good evidence base and which questions were likely to have little or no

directly relevant evidence. Recommendations based on good practice were developed by informal consensus of the GDG. For questions with a good evidence base, the review process depended on the type of clinical question. For questions that were unlikely to have a good evidence base, a brief descriptive review was initially undertaken by a member of the GDG.

Forming the Clinical Summaries and Recommendations

Once the GRADE profile tables relating to a particular clinical question were completed, summary tables incorporating important information from the GRADE profiles were developed. Finally, the systematic reviewer in conjunction with the topic group lead produced a clinical evidence summary.

Once the GRADE profiles and clinical summaries were finalised and agreed by the GDG, the associated recommendations were drafted, taking into account the trade-off between the benefits and downsides of treatment as well as other important factors. These included economic considerations, values of the GDG and society, and the group's awareness of practical issues.

Method Used to Answer a Clinical Question in the Absence of Appropriately Designed, High-Quality Research

In the absence of level-I evidence (or a level that is appropriate to the question), or where the GDG were of the opinion (on the basis of previous searches or their knowledge of the literature) that there was unlikely to be such evidence in this guideline, an informal consensus process was adopted. This process focused on those questions that the GDG considered a priority.

Informal Consensus

The starting point for the process of informal consensus was that a member of the topic group identified, with help from the systematic reviewer, a narrative review that most directly addressed the clinical question. Where this was not possible, a brief review of the recent literature was initiated.

This existing narrative review or new review was used as a basis for beginning an iterative process to identify lower levels of evidence relevant to the clinical question and to lead to written statements for the guideline. The process involved a number of steps:

A description of what is known about the issues concerning the clinical question was written by one of the topic group members.
Evidence from the existing review or new review was then presented in narrative form to the GDG and further comments were sought about the evidence and its perceived relevance to the clinical question.
Based on the feedback from the GDG, additional information was sought and added to the information collected. This may include studies that did not directly address the clinical question but were thought to contain relevant data.
If, during the course of preparing the report, a significant body of primary-level studies (of appropriate design to answer the question) were identified, a full systematic review was conducted. At this time, subject possibly to further reviews of the evidence, a series of statements that directly addressed the clinical question were developed.
Following this, on occasions and as deemed appropriate by the GDG, the report was then sent to appointed experts outside the GDG for peer review and comment. The information from this process was then fed back to the GDG for further discussion of the statements.
Recommendations were then developed and could also be sent for further external peer review. After this final stage of comment, the statements and recommendations were again reviewed and agreed upon by the GDG.

2016 Update

This update was developed based on the process and methods described in the Guidelines Manual 2014 (see the "Availability of Companion Documents" field).

The guidelines are updated using a standing Committee of healthcare professionals, research

methodologists and lay members from a range of disciplines and localities. For the duration of the update the core members of the Committee are joined by additional members who have specific expertise in the topic being updated, hereafter referred to as 'topic expert members'.

Review Questions

Question 1

What is the clinical and cost-effectiveness of elimination/restriction diets in children and young people with ADHD?

Question 2

What is the clinical and cost-effectiveness of dietary supplementation with polyunsaturated fatty acids, (PUFAs) in children and young people with ADHD?

The wording used in the recommendations in the guideline denotes the certainty with which the recommendations were made. Some recommendations were made with more certainty than others. Recommendations are based on the trade-off between the benefits and harms of an intervention, whilst taking into account the quality of the underpinning evidence. See the "Rating Scheme for the Strength of the Recommendations" field.

Rating Scheme for the Strength of the Recommendations

2008 Guideline

Not applicable

2016 Update

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Committee makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Committee is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Recommendations That Must (or Must Not) Be Followed

The Committee usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the Committee uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Recommendations That Should (or Should Not) Be Followed – a 'Strong' Recommendation

The Committee uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the Committee is confident that an intervention will not be of benefit for most patients.

Recommendations That Could Be Followed

The Committee uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

2008 Guideline

The following economic issues relating to diagnosis and management of children, young people and adults with attention deficit hyperactivity disorder (ADHD) were identified by the Guideline Development Group (GDG) in collaboration with the health economist as primary key issues that should be considered in the guideline:

- The cost-effectiveness of parent training for pre-school age children and cognitive behavioural therapy (CBT) for older children and young people
- The cost-effectiveness of CBT for adults with ADHD
- The relative cost-effectiveness of different pharmacological interventions for children and adults with ADHD
- The cost-effectiveness of intensive medication management for children
- The relative cost-effectiveness of psychological, pharmacological and combination therapies for children

In addition, literature on health-related quality of life (HRQoL) of children and adults with ADHD was systematically searched to identify studies reporting appropriate utility weights that could be utilised in a cost-utility analysis.

The economic evidence identified by the health economics systematic review is summarised in the respective chapters of the guideline, following presentation of the clinical evidence. The characteristics and results of all economic studies included in the review are provided in the form of evidence tables in Appendix 14 in the full guideline appendices (see "Availability of Companion Documents"). Results of additional economic modelling undertaken alongside the guideline development process are also presented in the relevant chapters.

2016 Update

In the Absence of Economic Evidence

When no relevant economic studies were found from the economic literature review, and de novo modelling was not feasible or prioritised, the Committee made a qualitative judgement about cost-effectiveness by considering expected differences in resource use between options and relevant UK National Health Service (NHS) unit costs, alongside the results of the clinical review of effectiveness evidence. The UK NHS costs reported in the guideline were those presented to the Committee and they were correct at the time recommendations were drafted; they may have been revised subsequently by the time of publication. However, the Committee has no reason to believe they have been changed substantially.

Refer to the "Trade-off between net health benefits and resource use" sections in the guideline addendum (see the "Availability of Companion Documents" field).

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

2008 Guideline

The guideline was validated through two consultations.

The first draft of the guideline (The full guideline, National Institute for Clinical Excellence [NICE] guideline and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG).
The final consultation draft of the full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

2016 Update

Not stated

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type and quality of evidence supporting each review question are described in evidence profiles in the full version of the guideline and the guideline addendum (see the "Availability of Companion Documents" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of attention deficit hyperactivity disorder

Recommendations were drafted, taking into account the trade-off between the benefits and downsides of treatment as well as other important factors. Refer to the discussion sections of the full version of guideline and the "Trade-off between benefits and harms" sections in the guideline addendum (see the "Availability of Companion Documents" field) for details about benefits of specific interventions.

Potential Harms

2008 Guideline

Adverse Effects of Medications

Growth (height and weight) can be affected by drug treatment and needs to be monitored during treatment.
Patients treated with atomoxetine should be closely observed for agitation, irritability, suicidal thinking and self-harming behaviour, and unusual changes in behaviour, particularly during the initial months of treatment or after a change in dose. Parents and/or carers should be warned about the potential for suicidal thinking and self-harming behaviour with atomoxetine and asked to report these to their healthcare professionals. Parents or carers should also be warned about the potential for liver damage in rare cases with atomoxetine (usually presenting as abdominal pain, unexplained nausea, malaise, darkening of the urine, or jaundice).
In young people and adults, sexual dysfunction (that is, erectile and ejaculatory dysfunction) and dysmenorrhoea should be monitored as potential side effects of atomoxetine.
People taking methylphenidate, dexamfetamine, or atomoxetine who have sustained resting tachycardia, arrhythmia, or systolic blood pressure greater than the 95th percentile (or a clinically significant increase) measured on two occasions should have their dose reduced and be referred to a

paediatrician or adult physician.
If psychotic symptoms (for example, delusions and hallucinations) emerge in children, young people, and adults after starting methylphenidate or dexamfetamine, the drug should be withdrawn and a full psychiatric assessment carried out. Atomoxetine should be considered as an alternative.
If seizures are exacerbated in a child or young person with epilepsy, or de novo seizures emerge following the introduction of methylphenidate or atomoxetine, the drug should be discontinued immediately. Dexamfetamine may be considered as an alternative in consultation with a regional tertiary specialist treatment centre.
Anxiety symptoms, including panic, may be precipitated by stimulants, particularly in adults with a history of coexisting anxiety.
There is a potential for drug misuse and diversion in children and young people taking methylphenidate and dexamfetamine.

The "Monitoring Side Effects and the Potential for Misuse in Children, Young People and Adults" section in the "Major Recommendations" field provides additional information on adverse effects of stimulants.

2016 Update

Recommendations were drafted, taking into account the trade-off between the benefits and downsides of treatment as well as other important factors. Refer to the discussion sections of the full version of guideline and the "Trade-off between benefits and harms" sections in the guideline addendum (see the "Availability of Companion Documents" field) for additional details about harms of specific interventions.

Contraindications

Contraindications

2008 Guideline

To reduce the risk of seizures, bupropion is contraindicated in patients with a current seizure disorder or any history of seizures, with current or previous diagnosis of bulimia or anorexia nervosa, with a known central nervous system (CNS) tumour, and those experiencing abrupt withdrawal from alcohol or benzodiazepines.
Analysis looking at outcomes at the end of treatment for subgroups with comorbid anxiety and disruptive behaviour (oppositional defiant disorder or conduct disorder) pointed to some impacts on treatment effects. All Multimodal Treatment Study of Children with ADHD (MTA) interventions including community care were found to be effective in the subgroup with ADHD and comorbid anxiety. For subgroups with attention deficit hyperactivity disorder (ADHD) only or ADHD and disruptive behaviour (oppositional defiant disorder or conduct disorder), medication was favoured – whether alone or in combination with behavioural treatment – but behavioural treatment alone may be contraindicated. For the subgroup with ADHD and both anxiety and disruptive behaviour, there was evidence of an advantage of combined treatment, particularly with respect to overall impairment and functioning.

2016 Update

Not applicable

Qualifying Statements

Qualifying Statements

- The recommendations in this guideline represent the view of the National Institute for Health and

Care Excellence (NICE), arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The application of the recommendations in this guideline is not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

- Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.
- This guideline assumes that prescribers will use a drug's summary of product characteristics to inform their decisions for individual people. At the time of publication (September 2008), methylphenidate, atomoxetine and dexamfetamine did not have UK marketing authorisation for the treatment of adults with attention deficit hyperactivity disorder (ADHD). However, atomoxetine is licensed for use in adults with ADHD when treatment with the drug began in childhood. At the time of publication, methylphenidate and atomoxetine did not have UK marketing authorisation for use in children younger than 6 years. Prescribers should advise people with ADHD and their parents or carers of the implications of prescribing unlicensed or 'off-label' drugs. Informed consent should be obtained and documented.
- For all recommendations, NICE expects that there is discussion with the person about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also 'Patient-centred care' in the guideline addendum [see the "Availability of Companion Documents" field]).

Implementation of the Guideline

Description of Implementation Strategy

See the "Organisation and Planning of Services" section in the "Major Recommendations" field.

Additionally, tools and resources to help users put the guidance into practice are available on the National Institute for Health and Care Excellence Web site (see all the "Availability of Companion Documents" field.)

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Attention deficit hyperactivity disorder: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb. 41 p. (Clinical guideline; no. 72).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Feb

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Guideline Development Group

Composition of Group That Authored the Guideline

2008 Guideline

Guideline Development Group Members: Professor Eric Taylor (*Chair*), Head of Department of Child and Adolescent Psychiatry, Institute of Psychiatry, King's College London; Dr Tim Kendall (*Facilitator, Guideline Development Group*), Joint Director, The National Collaborating Centre for Mental Health, Deputy Director, Royal College of Psychiatrists Research and Training Unit, Consultant Psychiatrist and Medical Director, Sheffield Care Trust; Professor Philip Asherson, Professor of Molecular Psychiatry and Honorary Consultant Psychiatrist, MRC Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London; Mr Simon Bailey (2006-2007), Service User Representative; Dr Karen Bretherton, Consultant Psychiatrist for Children with Learning Disabilities, Child and Adolescent Mental Health Services, Leicestershire Partnership NHS Trust; Ms Amy Brown (2006-2007), Research Assistant, The National Collaborating Centre for Mental Health; Ms Liz Costigan (2006-2007), Project Manager, The National Collaborating Centre for Mental Health; Mr Alan Duncan, Systematic Reviewer, The National Collaborating Centre for Mental Health; Dr Val Harpin, Consultant Paediatrician (Neurodisability), Ryegate Children's Centre, Sheffield Children's NHS Foundation Trust; Professor Chris Hollis, Professor of Child and Adolescent Psychiatry, Division of Psychiatry, University of Nottingham, Queens Medical Centre, Nottingham; Dr Daphne Keen, Consultant Developmental Paediatrician, Developmental Paediatrics, St George's Hospital, London; Ms Angela Lewis (2007-2008), Research Assistant, The National Collaborating Centre for Mental Health; Dr Ifigeneia Mavranezouli, Senior Health Economist, The National Collaborating Centre for Mental Health; Dr Christine Merrell, Education Specialist, Curriculum, Evaluation and Management Centre, Durham University, Durham; Ms Diane Mulligan, Carer Representative; Dr Alejandra Perez, Systematic Reviewer, The National Collaborating Centre for Mental Health; Dr Catherine Pettinari (2007-2008), Centre Manager, The National Collaborating Centre for Mental Health; Ms Noreen Ryan, Nurse Consultant, Child and Adolescent Mental Health Services, Bolton NHS Hospital Trust, Bolton; Dr Nicola Salt, General Medical Practitioner, Thurleigh Road Surgery, London; Dr Kapil Sayal, Senior Lecturer in Child and Adolescent Psychiatry, Institute of Mental Health and University of Nottingham, Nottingham; Ms Linda Sheppard (2006-2007), Carer Representative; Ms Sarah Stockton, Information Scientist, The National Collaborating Centre for Mental Health; Dr Clare Taylor, Editor, The National Collaborating Centre for Mental Health; Dr Geoff Thorley, Head Clinical Child and Adolescent Psychologist, Child and Adolescent Mental Health Service, Leicestershire Partnership NHS Trust, Leicester; Ms Jenny Turner (2006-2007), Research Assistant, The National Collaborating Centre for Mental Health; Professor Peter Tymms, Professor of Education and Director of the Curriculum, Evaluation and Management Centre, Durham University, Durham; Dr Miranda Wolpert (2006-2007), Director, CAMHS Evidence Based Practice Unit, University College London and Anna Freud Centre, London; Professor Ian Wong, Professor of Paediatric Medicine Research, Centre for Paediatric Pharmacy Research, The School of Pharmacy, London; Dr Susan Young, Senior Lecturer in Forensic Clinical Psychology, Institute of Psychiatry, King's College London, Honorary Consultant Clinical and Forensic Psychologist, Broadmoor Hospital, West London Mental Health Trust

<u>2016 Update</u>

Standing Committee (Core Members): Susan Bewley (*Chair*), Professor of Complex Obstetrics, Kings College London; Gita Bhutani, Clinical Psychologist, Lancashire Care NHS Foundation Trust; Simon Corbett, Cardiologist, University Hospital Southampton NHS Foundation Trust; Gail Fortes Mayer, Commissioner, John Graham Consultant Oncologist & Trust Cancer Lead Clinician, Taunton & Somerset Hospital; Peter Hoskin, Consultant in Clinical Oncology, Mount Vernon Hospital; Roberta James, Programme Lead, Scottish Intercollegiate Guidelines Network (SIGN); Jo Josh, Lay member; Asma Khalil, Obstetrician, St George's Hospital University London; Manoj Mistry, Lay member; Amaka Offiah, Reader in Paediatric Musculoskeletal Imaging and Honorary Consultant Paediatric Radiologist, University of Sheffield; Mark Rodgers, Research Fellow, University of York; Nicholas Steel, Clinical Senior Lecturer in Primary Care, Norwich Medical School; Sietse Wieringa, General Practitioner, Barts & the London School of Medicine & Dentistry

Standing Committee (Topic Expert Committee Members): Bernadette Ashton, Lay Member; David Edwards, GP; Nicole Horwitz, Community Paediatrician; Paul McArdle, Child and Adolescent Psychiatrist; Sarah Owen, Dietician; Noreen Ryan, Nurse

Financial Disclosures/Conflicts of Interest

2008 Guideline

To minimise and manage any potential conflicts of interest, and to avoid any public concern that commercial or other financial interests have affected the work of the Guideline Development Group (GDG) and influenced guidance, members of the GDG must declare as a matter of public record any interests held by themselves or their families which fall under specified categories. These categories include any relationships they have with the healthcare industries, professional organisations and organisations for people who misuse drugs and their families and carers.

Individuals invited to join the GDG were asked to declare their interests before being appointed. To allow the management of any potential conflicts of interest that might arise during the development of the guideline, GDG members were also asked to declare their interests at each GDG meeting throughout the guideline development process. The interests of all the members of the GDG are listed in Appendix 2 of the full version of the guideline (see the "Availability of Companion Documents" field), including interests declared prior to appointment and during the guideline development process.

2016 Update

See Appendix B in the guideline addendum (see the "Availability of Companion Documents" field) for information on declaration of interest.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Mental Health. Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Sep. 59 p. (Clinical guideline; no. 72).

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site. Also available for download in eBook and ePub formats from the NICE Web site.

Availability of Companion Documents

The following are available:

Attention deficit hyperactivity disorder. Evidence update. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. 28 p. (Evidence update; no. 45). Available from the National Institute for Health and Care Excellence (NICE) Web site.

Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults. Full guideline. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009. 664 p. (Clinical guideline; no. 72). Available from the NICE Web site.

Attention deficit hyperactivity disorder: diagnosis and management. Full guideline appendices. London (UK): National Institute for Health and Care Excellence (NICE); 2009. (Clinical guideline; no. 72). Available from the NICE Web site.

Attention deficit hyperactivity disorder. Full guideline addendum. London (UK): National Institute for

Health and Care Excellence (NICE); 2016 Feb. 140 p. (Clinical guideline; no. 72). Available from the NICE W eb site.

Attention deficit hyperactivity disorder. Costing report. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Sep. 36 p. (Clinical guideline; no. 72). Available in from the NICE W eb site.

Attention deficit hyperactivity disorder. Costing template. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. Various p. (Clinical guideline; no. 72). Available from the NICE W eb site.

Attention deficit hyperactivity disorder: a guide to management in adults and children. Online educational tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. Various p. (Clinical guideline; no. 72). Available from the NICE W eb site.

Attention deficit hyperactivity disorder. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb. Various p. (Clinical guideline; no. 72). Available from the NICE W eb site.

The guidelines manual 2007. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Apr. Available from the NICE archive W eb site.

Developing NICE guidelines: the manual. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Oct. 240 p. Available from the NICE W eb site.

Patient Resources

The following is available:

Attention deficit hyperactivity disorder: diagnosis and management. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2008 Sep 1. 18 p. Available in English and W elsh from the National Institute for Health and Care Excellence (NICE) W eb site. Also available for download in eBook and ePub formats from the NICE W eb site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This summary was completed by ECRI Institute on February 15, 2010. An evidence update was completed by the developer in July 2013 and this summary was updated by ECRI Institute on October 30, 2013. This summary was updated by ECRI Institute on April 7, 2014 following the U.S. Food and Drug Administration advisory on Methylphenidate ADHD Medications. This summary was updated by ECRI Institute on July 23, 2015 following the U.S. Food and Drug Administration advisory on the Daytrana Patch (methylphenidate transdermal system). This summary was updated by ECRI Institute on November 10, 2016.

The National Institute for Health and Care Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their clinical guidelines with the intention of disseminating and facilitating the implementation of that guidance. NICE has not yet verified this content to confirm that it accurately reflects that original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE clinical guidelines are prepared in relation to the National Health Service in England and W ales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk.

Copyright Statement

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Readers with questions regarding guideline content are directed to contact the guideline developer.

Attachment 3

Attention Deficit Hyperactivity Disorder (ADHD) Resources/Community Support Groups

The American Academy of Child and Adolescent Psychiatry http://www.aacap.org/

Children and Adults with ADD (CHADD) http://www.chadd.org/

National Center for Learning Disabilities http://www.ncld.org/

National Institute of Mental Health (NIMH)
http://www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml

National Institute of Neurological Disorders and Stroke
http://www.ninds.nih.gov/disorders/adhd/adhd.htm

These guidelines are promulgated by Sentara Health Plans as recommendations for the clinical management of specific conditions. Clinical data in a particular case may necessitate or permit deviation from these guidelines. The Sentara Health Plans guidelines are institutionally endorsed recommendations and are not intended as a substitute for clinical judgment.

Attachment 4

Attention Deficit Hyperactivity Disorder (ADHD)

References

American Academy of Pediatrics. *ADHD: Clinical practice guideline for the Diagnosis, evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents.* Pediatrics Volume 128, Number 5, November 2011. www.pediatrics.org/cgi/doi/10.1542/peds.2011-2654

American Psychiatric Association. Diagnostic & Statistical Manual of Mental Disorders, 5th Edition. DSM-5. American Psychiatric Publishing (APPI), 2014. www.psych.org

National Committee for Quality Assurance (NCQA). Follow-Up Care for Children Prescribed ADHD Medication (ADD). HEDIS 2018, Vol. 2 pp. 174-178. Washington, D.C.: NCQA. www.ncqa.org

National Institute for children's Health Quality (NICHQ). Vanderbilt Assessment Scales. http://www.nichq.org/childrens-health/adhd/resources/vanderbilt-assessment-scales

Multi-Health Systems Inc. (MHS). Conners Comprehensive Behavior Rating Scales™ (CBRS). http://www.mhs.com/product.aspx?gr=cli&prod=cbrs&id=overview

UPDATES FOR TREATMENT OF ADHD IN CHILDREN 2026:

The systematic review showed that standardized rating scales that include input from multiple sources (e.g., youth, parents, and teachers) across multiple settings can inform clinical decision making. In head-to-head comparisons, the diagnostic accuracy of parent rating scales was better than the accuracy of neuropsychological tests of executive functioning (e.g., the Continuous Performance Test).

The diagnostic performance of biomarkers, EEGs, and magnetic resonance imaging scans varied greatly across studies. The ability of these tools to aid in clinical diagnosis for ADHD remains unclear. The FDA-approved stimulant medications methylphenidate and amphetamine and the non-stimulant medications atomoxetine, viloxazine, clonidine, and guanfacine significantly improved ADHD symptoms. These medications had comparable effect sizes. They also had similar side effects; for example, appetite suppression, commonly associated with stimulants, was also associated with use of most non-stimulants.

Psychosocial treatments, parent support, neurofeedback, and nutritional interventions may exert considerably weaker effects on ADHD symptoms than pharmacological treatments. Very few of the non-medication studies have employed precisely the same interventions, which limited conclusions about effectiveness.

The use of combined pharmacological and psychosocial treatments was not systematically superior to monotherapy (i.e., either pharmacological or psychosocial interventions alone). However, few studies evaluated the use of combined treatments.

The systematic review did not find enough evidence to determine the effectiveness of using combinations of medications versus using a single medication.

Clinical practice guidelines for ADHD are available from the American Academy of Pediatrics (AAP).[4] The current guidelines recommend using multiple sources of information to determine whether *The Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) (DSM-5) criteria for diagnosing ADHD have been met.

The guidelines still recommend screening for ADHD in school aged children, but the updated information also recommend screening for common comorbid conditions, including emotional or behavioral conditions, developmental conditions, and physical conditions. The AAP guidelines recommend the use of FDA-approved medications to treat ADHD. Finally, referrals to appropriate subspecialists are recommended when a primary care provider does not have experience with diagnosing and treating comorbid conditions.

This systematic review was commissioned to inform the process of updating the AAP's ADHD guidelines.

This Evidence Update is based on a systematic review that included findings from 550 studies published between 1980 and June 2023. The review team conducted strength of evidence and applicability assessments for key outcomes.

SOURCES:

1. © 2011–2025 Patient-Centered Outcomes Research Institute. "Attention-Deficit/Hyperactivity Disorder (ADHD): Diagnosis and Treatment in Children and Adolescents (A Systematic Review)." Updated December 15, 2025. https://www.pcori.org/research-results/2021/attention-deficit-hyperactivitydisorder-diagnosis-and-treatment-children-and-adolescents-systematic-review

2. Peterson BS, Trampush J, Maglione M, et al. ADHD Diagnosis and Treatment in Children and Adolescents. This systematic review was supported by PCORI through a research partnership with AHRQ. Rockville, MD: AHRQ Publication No. 24EHC003. Washington, DC: PCORI Publication No. 2023-SR-03; 2024 https://doi.org/10.23970/AHRQEPCCER267

3. Danielson ML, Claussen AH, Bitsko RH, et al. ADHD prevalence among US children and adolescents in 2022: diagnosis, severity, co-occurring disorders, and treatment. J Clin Child Adolesc Psychol. 2024;53(3):343-360. https://doi.org/10.1080/15374416.2024.2335625

4. Wolraich ML, Hagan JF Jr, Allan C, et al. Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. Pediatrics. 2019;144(4):e20192528. https://doi.org/10.1542/peds.2019-2528

NEW ADHD MEDICATIONS SINCE LAST UPDATE:

For pediatric ADHD:

There ARE newer stimulant options, but:

- Others are better delivery systems, not new drug classes The biggest advances:
- Longer-acting coverage
- Smoother pharmacokinetics
- More formulation choices (patch, liquid, ODT)

The field is shifting toward:

- personalized medication selection
- combining stimulant+ non-stimulant strategies

There are not any new drugs since last update but new delivery.

These are still methylphenidate or amphetamine at the core, but improved pharmacokinetics:

- **Jornay PM** -taken at night, works the next morning
- **Adhansia XR / Mydayis / Cotempla XR-ODT / Dyanavel XR**
- **Liquid, chewable, orally dissolving tablets**

👉 These are **reformulations,** not new molecules [ryansultan.com]

🔬 Potential upcoming stimulant

- **CTx-1301**
  - Dexmethylphenidate-based
  - Designed as a **true once-daily, full-day coverage stimulant**
  - In late-stage FDA review (as of 2025-2026) [streetwise...eports.com]

Trend:

- New stimulants aim for:

16+ hourcoverage

Fewer rebound/crash effects

Lower abuse/diversion potential [doctronic.ai]

Sources:
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