

CLINICAL PRACTICE GUIDELINES FOR ASSESSMENT AND MANAGEMENT OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER

Authors: Ruchita Shah, Sandeep Grover, Ajit Avasthi

Department of Psychiatry, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Correspondence: drruchitashah@gmail.com

INTRODUCTION

Attention-deficit/ hyperactivity disorder (ADHD) is one of the most common childhood psychiatric disorders. ADHD affects around 5%- 7% of school-aged children. It is a neuro-developmental disorder that runs a chronic course and causes significant impairments across various domains of everyday functioning, such as peer and social functioning, academic and occupational functioning across the lifespan. Besides the patient, ADHD also has significant negative impact on the caregivers. This Guideline seeks to lay out guidelines for effective and comprehensive assessment, diagnosis and management of ADHD. It attempts to update the previous guidelines taking into account current state of evidence that can inform clinical practice. These guidelines ought to be read in conjunction with the earlier version of the treatment guidelines on ADHD as developed and published by the Indian Psychiatric Society in the year 2007.

SCOPE OF THIS DOCUMENT

This Guideline provides a frame work for diagnosis and management of ADHD in children and adolescents aged upto 18 years. In this document, the terms 'child' and 'children' represent all individuals below 18 years of age, unless specified otherwise. The term 'adolescent' represents individuals between 13 to 18 years of age. The term 'pre-schoolers' is used to indicate individuals who are below 6 years of age.-These guidelines may not be applicable to adult patients suffering from ADHD, as their treatment needs may be different. Finally, it is expected that recommendations made will have to be tailored to suit the needs of individual patients.

ASSESSMENT AND EVALUATION

A comprehensive assessment including detailed history, mental state and physical examination is needed to reach the diagnosis and estimate the severity and impact of the disorder on the patient and caregivers. Co-morbid developmental, psychiatric and medical disorders; and psycho-social or environmental factors such as family discord, parenting and parental substance abuse that are directly relevant to the management should be assessed as far as possible. Table-1 presents the components of a comprehensive assessment and Table 2 shows the clinical questions that need to be answered while undertaking the process of assessment.

Table 1 here

Table 2 here

The assessment of pre-schoolers, children and adolescents for ADHD comprise of clinical interviews with parents and the patient, as well as obtaining information directly or indirectly (through parent accounts) from other relevant sources and settings including pre-school, day

care and school. Information from teachers may be obtained by requesting for teacher observation reports (unstructured) or teacher ratings on a structured rating scale (see section on rating scales). Such requests should be sent through parents after explaining to them the need for such information, and seeking their and the child's explicit consent and assent. Parents or the child may be reluctant to initiate such a communication for several reasons; the most important being fear of the child being stigmatized. Clinicians must as far as possible explain to the parents the need of teacher report and how this can aid in assessment, diagnosis and management. If the child and parents are still reluctant, then the clinicians may satisfy themselves through parent and child accounts of symptoms and functioning in the school setting, and review of school work and report cards. Further, in Indian context, the clinician may involve other family members such as grandparents; especially if the child resides in a joint or an extended family. This will provide additional important information, opportunities to understand methods the family uses to handle the problematic behaviors; and expectations and perceptions regarding, and treatment of these behaviours.

It is important to remember that the histories may vary considerably depending upon the informants' own perceptions regarding and tolerance towards such behaviors, their awareness and opportunities for observations. The histories from different sources may complement each other to provide a more complete and realistic picture; hence multi-informant interviews seeking information across various domains of functioning and in various settings is the key.

The process of assessment may require more than one visit. It is an ongoing process, which as far as possible must be continued to be based on multi-informant accounts across multiple settings as for the initial assessment and it should focus on changing needs of the patient and the family.

The diagnosis should preferably be based on the diagnostic criteria as per prevailing nosological systems for the symptoms of inattention, hyperactivity and impulsivity. While establishing the diagnostic criteria-age of onset, persistence and duration of the symptoms must be taken into account. When symptoms are of relatively recent onset, other psychiatric disorders, such as mood or psychotic disorders that may mimic ADHD must be considered. The symptoms must be developmentally inappropriate; it is suggested that the clinician assess the developmental history thoroughly and make a working clinical impression of the mental age of the child or adolescent. When intellectual sub-normality is known or suspected, the rule of thumb is that the symptoms should be inappropriate for the mental age to consider ADHD. Another related consideration is that as a child grows symptom manifestations may change- Pre-schoolers with ADHD are highly overactive (described as 'whirlwind'), do not listen to when called, have no sense of danger, and have short play sequences (of less than 3 minutes), and often leave activities incomplete. As a child reaches primary school, he is found to have difficulty remaining still or calm in situations where he is expected to remain so; for example, in assembly halls and classrooms. Inattention is manifested by brief activities of less than 10 minutes, being forgetful, disorganised and easily distractible. Impulsivity is seen in the form of acting out of turn, interrupting other children, thoughtless rule breaking, intrusions on peers and getting into accidents. During adolescence, the over-activity presents more as inner restlessness and some

fidgetiness instead of the manifest over-activity seen during pre-school and early childhood years. Inattention on the other hand, may manifest as difficulties in organising tasks, procrastinations and frequent missing of deadlines. Impulsivity may manifest as risk taking and substance use. Thus, adolescents may present with problems mainly related to inattention and impulsivity; and a thorough developmental history that traces the symptoms from their onset during childhood may help clarify the diagnosis. Several symptoms are present in two or more settings such as at home, school or pre-school, family and friends, etc. It may be borne in mind that the symptomatic manifestations can vary considerably depending on the context in a given setting. See Table 3 for factors that can affect symptoms of ADHD.

Table 3 here

Next, it is important to assess the impairment caused by the symptoms in different domains of functioning including social and inter-personal, academic or occupational and legal domains. In fact for the diagnosis, it is required that the symptoms should cause impairment in at least one domain. The clinician must attempt to make an overall impression of the severity of ADHD based on the severity and number of symptoms and severity of impairments caused by the symptoms. Additionally, there may be some associated problems that should not by themselves be used as an evidence for ADHD, but if present alongside need to be taken into account while planning management. These problems include defiant or non-compliant behaviors, irritability, mood swings, aggression, temper tantrums, sleep difficulties, clumsiness, mild delays in speech and language and substance abuse or high risk behaviors.

The clinician must as far as possible also assess for the potential effects that ADHD symptoms can have on development. Such effects are seen in cognitive development and academic achievements (for example, chronic inattentiveness leads to years of inadequate learning and hence, affects adversely further learning), social development (children with ADHD may be inattentive to social cues, are impulsive during their interactions with peers and occasionally have lesser opportunities needed for peer interactions due to peer rejection; these all lead to inadequate social development, manifesting as social immaturity), development of self-esteem and self-identity (peer rejection, rejection by adults, constant criticism may all affect the development of self-esteem and identity; though many of these children may appear boisterous).

Differential diagnosis and co-morbidities

It is important to note that the same disorder may be a differential diagnosis or may even be a co-morbid disorder. See Table 4 for co-morbidities seen with ADHD. Table 5 presents clinical points to differentiate ADHD from other developmental and psychiatric disorders. The clinician must as far as possible enquire into developmental and, current and past psychiatric history.

Table 4 here

Table 5 here

In case of pre-schoolers, clinicians must also bear in mind that the so-called symptoms may be developmentally normal or may represent the temperamental characteristics of the child. In the latter case, the clinician should refrain from diagnosing ADHD, but offer parent training for managing difficult behaviors (See section on management; formulating treatment plan for pre-

schoolers). Substance use history should be enquired into, especially while assessing older children and adolescents. This history may be taken from the adolescent by ensuring privacy (Also see section on mental state examination).

It is suggested that the clinician be aware of the problem of diagnostic overshadowing, i.e. symptoms of another disorder are mistakenly subsumed as manifestations of the primary disorder. For example, in a child with hyperactivity and impulsivity with mild intellectual disability, the symptoms are considered to be due to the latter though they are clearly developmentally inappropriate. The clinicians must also recognize the problem of over-diagnosis in presence of other disorders. For example, a child with autism spectrum disorder (ASD) is diagnosed with ADHD, when the symptoms of inattention and hyperactivity are mainly related to social communication and sensory issues of ASD. Detailed and focused clinical interviewing and collecting information across various situations and domains will help the clinician in such circumstances.

Table 6 presents the key clinical points to guide the process of establishing the diagnosis.

Table 6 here

Medical history

Rarely medical disorders may present with behaviors resembling ADHD. Such ADHD like problems may be secondary to head injury, wherein inattention is prominent, thyroid disorders and absence seizures. Rarely ADHD like symptoms may be present in genetic syndromes such as Fragile X or may be secondary to certain medications such as bronchodilators, thyroxine, neuroleptics (causing akathisia) and isoniazid. Epilepsy may be co-morbid especially in children with co-morbid neuro-developmental disorders such as intellectual disability. The clinician must also take specific medical history before prescribing any drug. This should include history of syncope or fainting episodes, exercise intolerance, congenital cardiac malformations or any cardiac surgery.

Mental state examination

Mental state examination of a pre-schooler or a young child may be carried out concurrently with parent interview. It is important that the clinicians equip themselves with age appropriate play and work materials that would help in building rapport as well as engaging the child in an age appropriate activity. During such observations and interactions, it is suggested clinicians attempt to gauge the general intellectual capacity of the child, language development and verbal and non-verbal communication. The clinician may or may not find evidence of over-activity, impulsivity and inattention during the time of interview as children may perform better when they find tasks interesting or the situation is structured with one-to-one adult interaction as in the clinic. This should not be taken as evidence of absence of ADHD. Also, younger children might not be aware of their problems. Clinicians therefore, should not rely solely on their observations and interview with younger children for diagnosing ADHD. Rather, clinicians may use this opportunity to observe for co-existing disorders including intellectual sub-normality, as well as to observe child-parent interactions. It may reveal over-protective, hostile and critical parent-child interactions, and parents' styles of responding to defiance.

It is desirable that older children and adolescents also be interviewed separately from their parents; this acknowledges their need for autonomy and confidentiality. Adolescents may down play their problems and its impact on their functioning. So, clinician need not focus on ADHD symptoms, but may rather interview the child/ adolescent regarding depressive symptoms and suicidal ideation, peer relations and bullying. Mental state examination should include a formal assessment of form and content of thought, presence of delusions, hallucinations, depressive cognitions, worries, ruminations and obsessive symptoms as far as possible. There may be evidence of low self esteem despite apparent boisterousness. Substance use history should be elicited and history related to other high risk behaviors may be elicited if overall history is indicative of the same. However, such assessments should preferably not be done before a working therapeutic relation has been established with the adolescent or child.

Rating scales

Rating scales and screening instruments may assist in the diagnostic process, but these are neither necessary nor can these replace a good clinical assessment. These include Conner's parent and teacher rating scales; Vanderbilt parent and teacher rating scales and ADHD rating scale – fourth edition. These can be helpful in acquiring structured information from other sources such as teachers. Besides, the rating scales may assist in monitoring treatment response. The scales may over or under diagnose ADHD when co-morbid intellectual disability or ASD is present. Most of the rating scales are expensive and do not have Indian norms, hence, it might be difficult to use these in routine clinical practice. However, more generic instruments such as Strengths and Difficulties Questionnaire and Achenbach's Child Behavior Checklist may be more easily accessible. The clinical global impression (CGI) scales and children's global assessment of functioning scale (CGAS) may be used for baseline assessments and further monitoring.

Psychological testing

Routine psychological testing is not indicated. If intellectual disability is suspected, IQ testing may be conducted. However, in case of severe symptoms, the scores may be erroneously low, and hence, test must be repeated after adequate symptom control. Similarly if specific learning disorder is suspected, the psychological assessment for the same should be carried out after adequate control of ADHD symptom. Play room observation may be assistive when carried out by an experienced clinician. However, it is neither mandatory nor replaces a thorough clinical evaluation. Similarly, neuro-psychological tests such as continuous performance tests are not indicated in routine clinical practice.

Physical investigations

No specific physical investigations are needed or indicated to diagnose ADHD. Neuro-imaging (CT scan, MRI, PET and SPECT scans) and EEG should not be carried out without any specific clinical indication. In cases where lead toxicity is suspected, i.e. when history reveals exposure to lead plumbing or high lead levels in the environment, lead levels should be checked. Thyroid profile should be tested only when clinical features are suggestive of a thyroid disorder.

FORMULATING A TREATMENT PLAN

For a comprehensive treatment plan, factors that need to be taken into account are age and developmental stage of the child, severity of symptoms, domains of functioning affected, how symptoms affect or may affect everyday life, co-morbid developmental, psychiatric and medical disorders, psycho-social risk factors and protective factors, and goals and resources or assets within the child and family. The plan must address as far as possible the child's current psychological, behavioral and educational needs. It is suggested that needs assessment be an ongoing process as needs may change over time. Regular discussions with the children and their family must be carried out to the extent possible regarding the same. Table-7 presents the guiding principles for a comprehensive treatment plan.

Table 7 here

Before starting any treatment for ADHD, it is important to build a working therapeutic alliance with the child and family, take their accounts of perceptions and preferences regarding treatment and offer them information regarding diagnosis and treatment.

Therapeutic alliance

The first step towards management is building a good therapeutic alliance with the child or adolescent and the family. Positive regard for the family's perceptions and concerns is needed. Parents' perceptions regarding diagnosis and treatment may be influenced by other family members, friends, teachers, media and other physicians; and may differ from the clinician's opinion. These perceptions may influence treatment preferences as well as adherence to treatment. For example, parents who consider the behaviors diagnosed as ADHD to be 'normal naughty behavior' or due to the child 'being lazy' may request for only 'counseling' to the child and may not consider medication or parent training as necessary. Family's concerns regarding side effects, and weighing of risk-benefit may not match with that of the clinician's. Inadequate adherence on the prescribed treatment may occur due to any of these reasons, leading to non-response and potentially a breach in alliance and treatment drop-out. Parental expectations from treatment also vary. For example, parents of children with ADHD and co-morbid conduct disorder may expect complete resolution of all the symptoms with a medication and may find the treatment ineffective when such expectations are not realized, again leading to treatment drop-out. The clinician may take into account that the needs identified by the parents and the patient may be often different. For example, the parents may be more concerned about academic performance, while the child may not identify this as an area of concern. Hence, the clinician must as far as possible make an effort to establish alliance with both the child, and his parents, and take into account their perceptions, preferences and expectations. Parents have often been blamed by family, friends or teachers for their child's behaviors or difficulties. They are often emotionally drained and experience burn-out by the time the child is brought to the clinic. The clinician must not blame the parents, must validate their positive and negative experiences with the school, extended family and professional agencies including doctors and offer support. A good therapeutic alliance coupled with psycho-education will help the child and parents take informed treatment decisions. Factors which can enhance therapeutic alliance are shown in Table-8.

Table 8 here

Communication of diagnosis

Before communicating the diagnosis, the clinician may as a minimum ask the parents and other significant family members about their perceptions regarding the causation of the problem behaviours. The clinician may present the diagnosis as a 'brain disorder' or a 'neuro-developmental disorder' with both genetic and environmental influences. The clinician may also briefly present the psycho-social factors that can potentially influence the course and outcome of the disorder (e.g. highly inconsistent parenting, severe family discord). Further, the clinician must as far as possible address guilt and blame amongst the parents, and address the misconceptions regarding ADHD. It may be followed by detailed psycho-education. Also, the clinician must communicate any co-morbid diagnosis, if present. This is essential as treatment considerations and overall course and prognosis may vary depending upon such co-morbidities. It is not uncommon in clinical practice, for parents to feel stigmatized that their child has been given a diagnostic label, and these parents and patients are often apprehensive of and reluctant to liaise with the school, fearing that the child will be labeled by the teachers. Such anticipations are often true in the child's given circumstances. The clinician must acknowledge the same while communicating the diagnosis and educating the child and parents. The clinician must preferably not communicate the diagnosis to the school without the consent of the patient and parents, even if the child was referred to the clinic by the school.

Psycho-education

Psycho-education may be carried out over 2-3 sessions, and should as far as possible be tailored for a given child and the family. The clinician may involve any other significant family members during these sessions or may conduct psycho-education later with them as and when such need is identified. Table 9 presents the rationale for involving extended family members in our context.

Table 9 here

Psycho-education may begin by asking the patient and his family regarding their own understanding of symptoms, their causation and their beliefs regarding treatments. Psycho-education may cover detailed description of core symptoms of hyperactivity/ impulsivity; and inattention and organizational difficulties, including difficulties keeping track of time, poor planning and time management, associated genetic and environmental factors such as pre or perinatal factors, misconceptions regarding ADHD, including that the symptoms are merely due to child's laziness or lack of motivation and available treatment modalities; both pharmacological and non-pharmacological with benefits and risks of each modality. The basic components that may be covered in psychoeducation sessions are given in table-10.

Table 10 here

TREATMENT OPTIONS FOR MANAGEMENT OF ADHD

As with other psychiatric disorders, the treatment options are broadly categorized as non-pharmacological measures, pharmacological interventions and other treatments. See table-11.

Table 11 here

PSYCHO-SOCIAL INTERVENTIONS

Despite the evidence for short term efficacy of medications, treatment with medications has some limitations; partial or no response in a proportion of cases, side effects, not well proven long term efficacy and cost effectiveness, poor adherence and negative perceptions of family and professionals towards medications. Non-pharmacological interventions, on the other hand, if implemented properly and adherently may produce benefits in symptoms as well as functioning in different domains.

Environmental modifications

Environmental modifications include changes made in the environment in one or preferably more settings to either decrease the symptom manifestations or importantly, to decrease the impact of the symptoms. Such modifications should help enhance the performance and functioning of the child.

Such modifications include introducing structure and routine in the child's life. The daily routines such as those related to getting up and getting ready for school, on returning from school, mealtimes and bedtime must be made regular and predictable. The child must be informed in advance of any change in the schedule as well as given reminders during transition. The physical environment must also be structured with 'a place for everything'. Allot a fixed place for almost everything in the house, and particularly for belongings of the patient. Use of verbal prompts and visual cues may be necessary for effective implementation. Parents can help the child in planning and managing their time through use of daily and weekly planners; sticking planners in prominent places such as in the bedroom or near the study table; labelling 'places where things go' (e.g. on bookshelves) and by giving verbal or visual (or both) reminders 3-5 minutes before a transition in routine. For example, the parent may say "5 minutes are left for playing your game", or "after 5 minutes we will start with Maths". Classrooms are ordinarily more structured as compared to home, and the routines are better defined. The teachers can use visual and verbal reminders; and praise to re-inforce the same.

Adult supervision may help the child, especially when on boring or mentally demanding tasks such as homework. The parent or teacher may give a simple reminder to the child when he goes off task. Such reminder may be verbal or physical or both; for e.g., a tap on the shoulder and telling him, "Read the fifth question" or asking him, "so, where were we?"

While studying, minimise distractions around; for e.g. make the child sit away from traffic, away from the TV room. The study table may be in the corner of the room, away from the windows and doors (preferably child's back facing the door), with only the books, which the child is suppose to read at that time with no other distraction on the table, with no distraction on the walls which are being faced by the child and no other child in the room to distract the child. The house should be as quiet as possible. The parent/supervisor should preferably sit with the child. Presence of toys and other screen media around should be avoided. Parents may increase stimulation of the material related to task to improve attention through use of highlighters, i.e. use colours to highlight important points. If listening to any genre of instrumental music helps the child improve his on-task attention, it may be tried.

Children may be provided with break times in middle of lengthy or boring tasks. The break may be of around 5 minutes after every 15-20 minutes of being on-task or lesser in younger children or when the adult senses increase in fidgetiness. The parent may request the child to carry out a household chore like fetching water or shovelling or any task that helps the child use his physical energy. In school, the teacher may ask the child to distribute copies or fetching something from the other classroom. Children may also be allowed to stand and work, if that helps them to remain on-task. The child must be given adequate opportunities to channelise their excessive energy, for example, by participating in physical sports such as cycling, running, swimming or football.

For some children, extra time to complete work, decreasing work loads (these children take much more time in completing their work as compared to peers, not because they do not know, but because of their problem of inattention), giving smaller assignments focusing on must-knows and use of word processors may help improve their performance and their self esteem. Some schools may be open to use of these strategies. Only the Indian Certificate of Secondary Education (ICSE) Board allows for some of these accommodations, but these must be recommended only in conjunction with other treatments and must not be used as a sole measure.

In any case, every attempt should be made after obtaining consent, to liaise with the school. As a minimum, it should be conveyed to the school teachers that ADHD is a valid diagnosis and use of certain environmental modifications and strategies will help the child. Every effort should be made to enlist their support. See the section on 'Liasing with the school' for detailed discussion.

Table 12 summarises the environmental modifications that can be instituted at home and school.

Table 12 here

Parent training intervention

Individual or group parent training programs are generally skills based and aim at imparting such skills to parents that they are able to implement behavioral strategies effectively. Parents must be explicitly told that referral for parent training does not mean that their parenting is faulty; rather the training would help them in learning strategies for particularly difficult and extraordinary situation that they are facing. Other significant members of the family may be involved in such programs, if needed.

The clinician must remember while dealing with the parents and family, that a parent might himself or herself have ADHD with its resultant attentional and organisational difficulties and impulsivity, or may have other psychopathology (e.g. depression) that may hinder the effective implementation of the strategies. Also, some families may be better suited for individual training. The indications for individual parental training include co-morbid conduct problems or disorder, family psychopathology, intellectual disability in parent, language difficulties or difficulties in therapeutic engagement due to any reason.

Most parent training programs are carried out over 8-10 weekly sessions if individual and 10-20 sessions if group training. It must cover psycho-education, environmental modifications, effective communication methods, behavioural management strategies (may include token

economy), anticipating and preparing for unstructured situations, taking care of self and may include liaising with teachers. Environmental modifications specific to ADHD have been presented in detail in the earlier section. Effective communication includes effective ways of instructing (clear, short, long instructions simplified into steps), re-phrasing statements, focusing on positives while communicating, decreasing critical comments and establishing consistency between what is said and what is done (no empty promises or warnings regarding consequences). The behavioral principles used are: setting of clear rules, consistency, use of immediate rewards, followed by use of delayed rewards contingent upon desirable behaviors, withdrawal of rewards or response cost contingent upon undesirable behaviors; rewards and cost being proportionate to the behavior. Consistency should be employed across time (i.e. a parent being consistent over time across situations) and across individuals (i.e. there must be consistency between both the parents; and also grandparents if applicable). Above all, parents must be encouraged to focus on their child's and their own strengths and inculcate healthy parent-child interactions. Parents must also be encouraged to appreciate their own and the child's efforts through regular positive feedback. Feedback should also be sought regularly from the parents and difficulties faced by them in implementing the strategies must be addressed regularly. Table-13 presents the components of a parent training intervention manualised at PGIMER, Chandigarh.

Table-13 here

Cognitive behavior therapy

In case of older children and adolescents, who have benefited from environmental modifications and parent training and/or use of medications, but still have significant impairments in specific domains, cognitive behavior therapy may be considered. For example, there may be problems in peer functioning or social functioning, or problems in academics due to poor time management. For example, the cognitive behavior therapy may focus on enhancing social skills in dealing with peers, time management, problem solving, dealing with and expressing feelings and self-control and anger management.

Cognitive training

Cognitive training may improve working memory, but it is not yet well researched if this translates into improved academic functioning.

PHARMACOLOGICAL INTERVENTIONS

Basic considerations

The treatment should as far as possible be tailored to the individual needs based on current level of symptom severity and impairment, and improvements, if any gained by the non-pharmacological measures. Factors that may need to be taken into account include variations in bioavailability and pharmacokinetic profiles of different preparations so as to avoid reduced effects or excessive side effects, co-existing neuro-developmental or psychiatric or physical disorders, specific treatment needs, and risk of drug misuse or diversion. Diversion occurs when someone in the patient's circle who has access to the medication uses it without prescription, usually for recreational purposes or to enhance performance.

Baseline assessment before starting a medication

Weight and height should be measured and plotted on the World Health Organization (WHO) or Indian Association of Paediatrics (IAP) weight for age and height for age growth charts respectively along with Body mass Index (BMI). Baseline assessment of appetite, diet and sleep should be done and recorded.

Specific medical and family history that takes into account contra-indications for specific medications should be reviewed. This history must include that of exercise intolerance or shortness of breath during exercise that is excessive as compared to peers, or syncope or fainting episodes on exertion or in response to sudden noise or fright, congenital heart disease or previous cardiac surgery, rapid, regular palpitations that stop and start suddenly, or chest pain suggestive of cardiac origin. Family history of sudden young (less than 40 years of age) cardiac death should be specifically enquired into. A cardiologist's opinion should be sought before starting the medication if any of these are present. Heart rate and blood pressure must be measured in the patient at rest. The blood pressure must be measured using age-appropriate cuffs and plotted on age adjusted percentile charts. Alternately, heart rate and blood pressure may be compared with the normal range for age. If the baseline heart rate is more than 100 beats per minute or systolic or diastolic blood pressure is more than the 95th percentile, or more than normal for age, it should be repeated twice within 10 minutes. If there is persistent tachycardia (> 100 beats per minute) or systolic or diastolic blood pressure is > 95th percentile or there are signs of heart failure or a murmur is heard on auscultation, an electrocardiogram (ECG) should be done and a cardiologist opinion should be sought. There is no recommendation for routine baseline ECG, except when a tricyclic antidepressant (TCA) is considered. TCAs are however, third line drugs and should be avoided due to their side effect profile.

History of seizures of any kind and of tics must be specifically looked for.

Liver enzymes, i.e., alanine transferase (ALT) and aspartate transferase (AST) levels should be done at baseline if atomoxetine is to be prescribed.

Parents must be explained about the effect of medications on the symptoms, i.e., which symptoms will improve with medications and which will not improve with medications. Parents also must be explained about the available options, possible side effects with different medications and given the choice to select a specific agent.

Medications

Stimulants

The stimulant medications with maximum evidence for ADHD include methylphenidate, dexamphetamine and lisdexamphetamine. Methylphenidate is the only stimulant available in India. There are several different formulations of methylphenidate available in the Indian market. These include immediate release (short acting), sustained / extended release (intermediate acting) and osmotic-controlled release oral delivery system, i.e. OROS (long acting) preparations (Table-14). Methylphenidate - immediate release (IR) has a relatively short half life, with a duration of action of about 1-4 hours. Maximum drug concentration occurs at about 1-2 hours after oral administration, and this is the time of maximum effect also. Due to short half life, IR preparations need twice or thrice daily dosing. Sustained/ extended release preparations have a duration of action of about 6-8 hours, while the OROS preparation has duration of action of 12

hours. Due to their longer half lives, the intermediate acting (sustained preparations) and long acting (OROS) need single dosing in the morning and may improve adherence as compared to IR preparation. There is marked individual variability in dose response relation, and optimal dose titration aiming at maximum response with minimal or acceptable level of side effects must be done for each individual patient.

Non-stimulants

The non-stimulants that have evidence for ADHD in children and adolescents include atomoxetine, clonidine, guanfacine, tricyclic anti-depressants, modafinil and bupropion and desipramine. Out of these, clonidine extended release and guanfacine are not available in India.

Atomoxetine is a selective noradrenaline reuptake inhibitor, taken as once daily dose in the morning. Some individuals may benefit by dividing the daily dose and taking it twice daily, once in morning and second dose at late afternoon or early evening. Atomoxetine is metabolised by CYP2D6 enzyme, hence, poor metabolisers may have more side effects and there are chances of drug-drug interactions. Atomoxetine has evidence of greater efficacy than other non-stimulant drugs. Clonidine is an alpha 2 noradrenergic agonist taken in 3-4 divided daily doses as extended release clonidine is not available currently in India.

TCAs, modafinil and bupropion are considered third line drugs. TCAs are generally not recommended due to their side effect profile.

Table-14 here

Initiating medication

If a medication has to be started, the child and parents must again be apprised of the specific side effects, monitoring and any precautions, as the case may be. In case of stimulants and atomoxetine, appetite suppression and sleep difficulties may become a concern in the initial part of the treatment itself. Hence, specific advice regarding meals and sleep hygiene may be given. In case of clonidine, parents must be specifically advised regarding the risk of rebound hypertension with abrupt discontinuation of the drug; so doses of clonidine should not be missed. Medications should be started at a low dose (as indicated in Table 14); and side effects and improvement must be monitored after each increment. Stimulants are Schedule X drugs; retailers cannot sell without a license and except on and in accordance with the prescription of a Registered Medical Practitioner; and are supposed to retain a copy of the prescription for a period of two years. The clinician must mention clearly the exact number of days for which the prescription is given.

Initial monitoring

During the phase of dose titration, the child should preferably be seen every week/ once in 2 weeks. The clinician must gauge improvement vis-a-vis side effects. Improvement may be rated on a structured scale or on a simple instrument such as CGI. If possible, ratings may be obtained from the teachers at 2-4 weekly intervals. Specific enquiries should be made regarding the onset of improvement noted after intake of medication (for example about 60 minutes after the morning dose) and duration of such improvement (for example, till 11am). Parents and teachers may report that the child is disruptive in the class during afternoons. This may be due to

tiredness or wearing off of the drug's effects. Such reporting will aid the clinician to titrate the dose or change the dosing pattern.

Specific enquiries should be made regarding side effects. This should be done both from parents and the child. Some older children and adolescents report that they do not like the drug effect, and feel they are not themselves. Such concerns may affect adherence to the medication and should be addressed. The child's sleep patterns and food intake should be asked about. Appetite suppression and reduced food intake may be a major concern for the parents. Weight should be measured on every visit during titration and plotted on the for-age charts.

Continued monitoring

Response to medications must be reviewed across different settings and domains of functioning. Specific enquiries should be made regarding side effects. The child's sleep patterns and food intake should be asked about. Weight should be measured on every visit during titration, and thereafter every 3 months. Height should be measured every 3-6 months. Both weight and height should be plotted on the for-age charts and monitored over time. Heart rate and blood pressure should be measured on every visit. Stimulants may increase the pulse rate and blood pressure, while clonidine can cause orthostatic hypotension. Liver enzymes should be monitored periodically if atomoxetine has been started.

Adequate trial

A 6 week trial of methylphenidate at an adequate dose if taken with good adherence may be considered as adequate. Time to response for atomoxetine is longer than that for stimulants. Hence, it may be continued at an adequate dose for at least 12 weeks with good adherence for an adequate trial.

Improving medication adherence

Besides response to the medication and its tolerability, other important factors that may affect adherence are multiple dosing, stigma especially if the child needs to take a dose during the school hours, perceptions of patients and families regarding medications and cost. Cost of the medication and that of multiple visits to the hospital during drug titration and for later follow ups may be a major practical hindrance.

In case of inadequate adherence due to multiple dosing, sustained release or OROS preparations may be prescribed. OROS preparations are relatively more expensive. A sustained release preparation with additional immediate release doses as required may be another option. Ongoing discussions related to efficacy, side effects and patient and family preferences are necessary and should be carried out regularly as far as possible.

Drug Holidays

Drug holidays are planned breaks in taking medications, usually during periods when the child is expected to have lesser demands for performance. These can be short, over weekends, or longer, during summer vacations. Drug holidays may reduce adverse events and give opportunities for improvement in appetite and catch up growth. During drug holidays, the symptoms may or may not worsen. Longer drug holidays also provide with opportunities to assess for ongoing need for medications. Weekend drug holidays are more appropriate for stimulant drugs, where such holidays do not cause any advertent effect such as rebound

hypertension with clonidine. However, drug holidays increase the chances of non-adherence (unplanned discontinuation or missing of doses) during non 'holiday' periods.

Discontinuation of medication

The need for continued medication should be reviewed at least once a year. The benefits, impact on functioning including academics, side effects, effects of missed doses, planned dose reductions and periods of no treatment and any psycho-social treatment in place and its effects as well as patient and family preferences are the factors to be taken into account. A few clinical signs that indicate that ADHD has remitted include, lack of any need to adjust dose despite robust growth, lack of deterioration when a dose of stimulant medication is missed or able to concentrate during drug holidays. Consider trial periods of stopping or reducing the medication dose if benefit-risk analysis suggests that it may be appropriate. Vacations are probably a good time to attempt withdrawal of medications. However, parents should be advised to assign the child in some cognitively demanding tasks (such as solving math problems, reading a book) to confirm that improvements persist despite being medication free.

Managing drug side effects

Table 15 presents the side effects of ADHD medications, along with guidance on monitoring for and management of these side effects.

Table 15 here

Managing sleep problems associated with ADHD

Behavioral problems such as bedtime resistance, sleep onset delay, effect of psychiatric comorbidity and sleep disorders may contribute to sleep difficulties in children with ADHD. It is suggested that pre-treatment or baseline sleep patterns, including behavioral patterns around bedtime routines be evaluated. Bedtime resistance include behaviors such as the child refusing to get ready for bed, refusing to remain in bed or requiring a parent to be present at bedtime is often the result of parental difficulties in limit setting and managing behaviors. It is suggested that sleep hygiene measures and behavioral interventions for healthier bedtime routines be instituted. These may include avoiding evening naps, having a regular bedtime, calming bedtime routine, darkened room, comfortable bed and no loud noises that promote sleep, and avoiding electronic media or screen use in the evening and adults also not using screens in the bedroom. In individual cases, low dose clonidine or melatonin (3 mg in children and 3-6 mg in adolescents) may be used for sleep onset delay. Sleep studies including polysomnography are only indicated for specific sleep related disorders, and not routinely.

EVIDENCE

Medications

In pre-schoolers, there is some evidence of short term efficacy of stimulants, however, there are serious concerns regarding side effects, especially related to appetite and growth suppression. In children > 6 years and adolescents, stimulants, atomoxetine and clonidine have been shown to be significantly more efficacious than placebo. Stimulants have been shown to be superior to non-stimulants and have good short term efficacy, though evidence for long term efficacy is inadequate. There is not adequate evidence of differences in efficacy or side effects between the different formulations of methylphenidate. The main advantage of longer acting formulations

over the short acting is in single versus multiple dosing that may result in lesser stigma associated with taking a dose in school and better adherence. Amongst non-stimulants, atomoxetine has greater evidence of efficacy with effect sizes though lower than stimulants, better than the other non-stimulants. There is evidence of efficacy for clonidine, though effect sizes are smaller than that for atomoxetine. Amongst tricyclic antidepressants, desipramine has the largest evidence of efficacy but the medication has considerable cardiac side effects.

Psychosocial interventions

In pre-schoolers, there is enough evidence for group and individual parent training interventions. In children > 6 years and adolescents, there is evidence of efficacy for parent training interventions; and in older children and adolescents for other psycho-social interventions also.

Comparing medication and psychosocial interventions

There is no robust evidence directly comparing medications with psycho-social interventions. In pre-schoolers, there is evidence of efficacy for both medications and psycho-social interventions, with more concerns about side effects with the medications. In children > 6 years of age and adolescents, there is evidence of efficacy for both medications and psycho-social interventions. There is some evidence of possibly *differential effects* of the two modalities; with the drug more efficacious for the core symptoms whereas non-pharmacological interventions more efficacious in improving associated behavioral problems and functioning. Though the effect sizes for medications, especially stimulants are greater than those for psycho-social interventions, it is probable that this is because of the outcome measures studied; ADHD symptom specific outcomes versus more generic outcomes regarding behavioral problems and functioning.

Combination Treatments

There is no evidence that combination of two medications offers any advantage over a single medication. Additionally, there are more side effects; and hence should be avoided. Combination of medication with psycho-social intervention has been found to be more efficacious than psycho-social intervention alone. Adding psycho-social intervention to the medication treatment may offer specific benefits and so, must be instituted when indicated. Besides evidence of possibly differential effects of the two modalities; there is also some evidence that addition of psycho-social interventions may facilitate dose reduction and discontinuation of medication on follow up.

OTHER INTERVENTIONS

Diet and exercise

It is suggested that all children and adolescents be advised regarding need for nutritious and balanced diet; and physical exercise.

Exclusion of food preservatives and additives and Elimination or oligoantigenic (few foods) diets

There is not enough evidence for special diets such as exclusion of food additives and preservatives, or elimination of several potential antigens as in the oligo-antigenic diets as stand alone treatments in the management of ADHD. There is limited evidence of short-term benefits; and not enough evidence of long-term effectiveness or harms of elimination diets. If it is suspected that specific foods increase the symptoms, it is suggested that parents be advised to

maintain detailed diet diaries and any elimination of specific food be attempted only in consultation with an expert dietician. It may take weeks to months for tailoring an oligoantigenic diet through series of re-introduction of foods; and requires close collaboration between the dietician, clinician and the family and patient. IgG blood tests are not helpful in selecting foods for elimination. The clinical utility of dietary interventions may be explored in individual cases, bearing in mind difficulties in practical implementation such as preparation of special foods in a household with several members, parents' control over child's diet, motivation of child and family as well as expenses towards preparation of additive-free or anitgen free foods.

Omega fatty acids and nutritional supplements

There is inconclusive evidence for use of omega fatty acids or any micronutrient or nutritional supplements for treatment of ADHD, and hence, it is suggested that such dietary supplements may not be prescribed for this purpose routinely till further good quality evidence emerges.

Neurofeedback

Though small studies indicate that neurofeedback may have some positive effects on core symptoms and neuropsychological functions, well designed studies and meta-analysis have failed to show the same. Overall, there is not adequate evidence to support neurofeedback for treatment of ADHD.

LIAISON WITH SCHOOL

It is suggested that liaison with the school be a continual activity. First and all subsequent contacts with the school should be after parental and patient's consent and as far as possible contact should be made through the parents. It is sound clinical practice to acknowledge the school's strengths while dealing with the index child, taking teacher's observational report and follow up feedbacks. Teacher reports and parent reports may give insights into different areas of impairment and in different settings. A good alliance with the teachers will set the stage to communicate the diagnosis and that it is a valid disorder; and suggest environmental modifications that a teacher can easily implement in the classroom. Efficient and sensitive teachers do encourage these children to exploit their other potentials and use verbal reinforcements effectively, while minimally using punishment. These children often are bullied or are bullies themselves, and school intervention can be very helpful in either case. Besides clinicians liaising with the school, parents may be advised to liaise with the child's teachers and use the parent-teacher daily report cards. These report cards aid in implementing the behavior principles more consistently and across the two settings.

STEPS IN MANAGING ADHD

Factors determining the steps in management of ADHD

The evidence for medications is limited in pre-schoolers; whereas there are genuine concerns regarding the side effects of the medications. There is enough evidence for group and individual parent training interventions. Keeping these in mind, pre-schoolers must first be offered psycho-social interventions.

In children > 6 years of age and adolescents, there is evidence of efficacy for both medications and psycho-social interventions. Medications appear to be more efficacious in improving the core symptoms of ADHD and psycho-social interventions in improving associated behavioral

problems and functioning in specific domains. In mild ADHD, environmental modifications usually suffice alone; while in severe ADHD, medications may be necessary. In the latter case, following some response with the medication, psycho-social interventions may be indicated for specific problems or impairments in specific domains. In case of moderate ADHD, parent training where available must be offered first.

Besides the evidence for efficacy and side effects, and severity of ADHD, the other important factors that determine the strategies in managing ADHD include co-morbidities, current needs, patient and family's preferences, affordability and availability. Table 16 lists the factors determining the steps in management of ADHD.

Table-16 here

Steps in management of ADHD

Figure 1 presents the algorithm for managing ADHD. It is expected that the plan and steps may have to be tailored to suit the needs of an individual patient. Psycho-education and support to the child and family must as far as possible be provided to all individuals. Medication is not the first line of management in pre-schoolers and those aged less than 6 years as there are concerns regarding tolerability and safety. Also, it is often difficult to differentiate a difficult temperament from ADHD in toddlers. Parent training interventions that include environmental modifications as well as behavioral management may be offered instead. The training may be given as group training or individual training. The clinician must consider addressing any factors that may hinder the effective implementation of the parent training intervention.

For school aged children and adolescents, it is suggested that environmental modifications be advised first. Despite the implementation of environmental modifications or in cases where the severity is so marked that such implementation is quite difficult, choose the next line of management based on the severity. In children with mild to moderate level of severity, offer parent training and school interventions. If the response is not good or parent training intervention is not available and severity is at least of moderate level, offer medications. If ADHD is severe, medications must be offered. The sequencing of medications considering response, contra-indications, side effects affordability and availability is preferably stimulant followed by atomoxetine followed by clonidine.

For all individuals who respond on a given treatment, continue with the same, along with periodic review and monitoring. In children and adolescents who have responded on a medication, but still have impairments in a specific domain, offer additional focused psycho-social intervention. For example, an adolescent having impairments in peer functioning, offer social skills training. In case of response to a psycho-social intervention, continue with periodic booster sessions and monitoring.

In case of inadequate response on a medication, check for non-adherence. Ensure adherence after addressing the child and family's concerns regarding the medication; these may include side effects, cost and stigma. If child is adherent on the medication, optimize the dose while monitoring for side effects. If despite an adequate trial, there is inadequate response, consider changing the drug. Family may prefer psycho-social intervention following a failed medication trial; in that case, it must be offered, if available after again discussing the benefits and risks of

each modality of treatment. If there is inadequate response after adequate medication trials, review the diagnosis, manage co-morbidities (for example, conduct disorder), may add parent training intervention. In case of inadequate response following parent training intervention, first check for and address adherence to the interventions. If despite this, there is inadequate response, offer medication alone or in combination with the psycho-social intervention. Table-17 lists out the factors related to inadequate response to pharmacological or non-pharmacological intervention.

Besides the medication or parent training and other child focused psycho-social interventions, ongoing liaison with the school must be carried out with consent of child and parents. School liaison strategies must be attempted. Review of teacher-implemented environmental modifications and behavioral management strategies must be made periodically, along with teacher reports regarding child's problems and progress.

Figure 1 here

Table-17 here

Review and discontinuation of treatment

The clinician must perform ongoing reviews regarding improvement, tolerability and needs of the child and family. The management plan may be altered in accordance with changing needs as outlined in earlier sections.

Further, the clinician must review the need for ongoing treatment at least once a year. For this, response to treatment, functioning in various domains and maintenance of response despite periods of planned or unplanned discontinuation of treatment must be considered. As during initial assessment, assessment of symptoms and functioning at this stage must involve multiple informants (preferably, must involve teachers) and must be done across settings. The child and family must be involved in discussions regarding possibility of discontinuation and risks and benefits thereof, including chances of relapse, though definitely not inevitable and improvement in side effects. Discontinuation must be attempted during low stress periods such as during vacations. Discontinuation of medications has been dealt with in detail in an earlier section. In case of psycho-social intervention, it is expected that some benefits may persist beyond the training programs. However, booster sessions may be required or focused strategies such as life skills or time management may be required. In case a child is on drug and non-drug treatment, the former may be discontinued first. The children and adolescents and their families must be advised ongoing reviews despite discontinuation of treatment. The clinician must monitor for relapse of symptoms or any impairments in functioning that need to be addressed.

SPECIAL CIRCUMSTANCES

In case of co-morbid tic disorder, anxiety disorders, obsessive compulsive disorder and ASD, the same medication may be started as for children and adolescents without any co-morbidity. However, drug titration must be slower and special attention should be paid to side effects. Clonidine or atomoxetine may be a good choice in case of co-morbid tic disorder; while atomoxetine may be a good choice in case of co-morbid anxiety disorder although there is no good evidence for avoiding methylphenidate.

In case of children with co-morbid intellectual disability or ASD, tolerability is an important consideration. Some children with developmental disabilities experience irritability, withdrawal or agitation and apparent worsening of symptoms. In such children, the diagnosis of ADHD should be re-visited and the medication should be stopped. A non-stimulant medication may be started.

In case of psychosis or bipolar disorder co-existing with ADHD, the psychosis or mood disorder should be treated first, and after resolution of the symptoms, a review of diagnosis of ADHD should be made. The clinician should assess the need for medication and then may start a stimulant or a non-stimulant drug weighing the risks and benefits in the individual case and considering drug interactions.

In case of co-morbid depression, the clinician must assess the severity of depression, presence of suicidal attempts or strong suicidal intent, and contribution of depressive symptoms to the overall global clinical severity. If any of these are present, depression should be treated first. In case of severe depression or suicidal ideas or attempts, inpatient management may be warranted depending on the individual circumstances. On the other hand, if depression is not severe with mild neuro-vegetative symptoms, suicidal ideas but without strong intent and ADHD symptoms are thought to contribute more than depressive symptoms to overall clinical severity, ADHD must be treated first. Often, the depressive symptoms and dysphoria may be related to the ADHD and resolve with effective treatment of ADHD.

In case of co-morbid substance dependence, treatment of ADHD and substance dependence should be instituted simultaneously. The clinician must assess the risk of medication misuse and diversion. If this risk is high, a non-stimulant may be used.

If co-morbid conduct disorder or oppositional defiant disorder are present, parent training directed towards the behavioural problems in addition to ADHD focused parent training should be commenced. Also, risk of medication misuse and diversion should be assessed and a non-stimulant drug may be started. Risperidone in low doses may be started particularly for aggression. Refer to CPG on Conduct Disorder for its management.

REFERENCES

1. American Academy of Child and Adolescent Psychiatry. Practice Parameter for the Assessment and Treatment of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder. *J Am Acad Child Adolesc Psychiatry*. 2007; 46(7):894-921.
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.). 2013; APA, Washington DC.
3. Barkley RA. Taking charge of ADHD: the complete, authoritative guide for parents. 2005; Guilford Press, New York.
4. Bolea-Alamañac B, Nutt DJ, Adamou M, et al. Evidence-based guidelines for the pharmacological management of attention deficit hyperactivity disorder: update on recommendations from the British Association for Psychopharmacology. *J Psychopharmacol*. 2014; 28: 179-203.

5. Canadian Attention Deficit Hyperactivity Disorder Resource Alliance (CADDRA): Canadian ADHD Practice Guidelines, Third Edition, 2011; CADDRA, Toronto ON.
6. Catalá-López F, Hutton B, Núñez-Beltrán A, et al. The pharmacological and non-pharmacological treatment of attention deficit hyperactivity disorder in children and adolescents: A systematic review with network meta-analyses of randomised trials. *Glud C, ed. PLoS ONE.* 2017;12(7):e0180355. doi:10.1371/journal.pone.0180355.
7. Cortese S, Holtmann M, Banaschewski T, Buitelaar J, Coghill D, Danckaerts M,, et al. Practitioner Review: Current best practice in the management of adverse events during treatment with ADHD medications in children and adolescents. *J Child Psychol Psychiatry.* 2013;54: 227–246
8. Cortese S, Vincenzi B, Angriman M. Identifying and managing sleep disorders associated with ADHD. *Neuropsychiatry.* 2012; 2:393–405
9. Cortese S, Ferrin M, Brandeis D, Holtmann M, Aggensteiner P, Daley D, et al. Neurofeedback for Attention-Deficit/Hyperactivity Disorder: Meta-Analysis of Clinical and Neuropsychological Outcomes From Randomized Controlled Trials. *J Am Acad Child Adolesc Psychiatry.* 2016; 55: 444 - 455
10. Daniel F, Guan C, Wong CJM, Ng KH, Cheok CCS, Kiing JSH, et al. Academy of Medicine- Ministry of Health Clinical Practice Guidelines: Attention Deficit Hyperactivity Disorder. *Singapore Med J.* 2014; 55(8): 411-415doi: 10.11622/smedj.2014098
11. Ferrin M, Sonuga-Barke E, Daley D, Danckaerts M, van der Oord S, Buitelaar JK. Non-pharmacologic treatments for Attention deficit hyperactivity disorder. In Eds. Zepf FD. *IACAPAP Textbook of Child and Adolescent Mental Health.* 2015 Available at: <http://iacapap.org/iacapap-textbook-of-child-and-adolescent-mental-health>
12. Gautam S, Batra L, Gaur N, Meena PS. Clinical Practice Guidelines for the Assessment and Treatment of Attention- Deficit/Hyperactivity Disorder. *Indian Psychiatric Society,* 2007.
13. Gillies D, Sinn JKH, Lad SS, Leach MJ, Ross MJ. Polyunsaturated fatty acids (PUFA) for attention deficit hyperactivity disorder (ADHD) in children and adolescents. *Cochrane Database of Systematic Reviews* 2012, Issue 7. Art. No.: CD007986. DOI: 10.1002/14651858.CD007986.pub2
14. Maia CRM, Samuele C, Arthur C, Deakin TK, Polanczyk GV, et al. Long-Term Efficacy of Methylphenidate Immediate-Release for the Treatment of Childhood ADHD: A Systematic Review and Meta-Analysis. *J AttenDisord.* 2017, Vol. 21(1) 3– 13
15. Moriyama TS, Cho AJM, Verin RE, Fuentes J, Polanczyk GV. Attention deficit hyperactivity disorder. In Eds. Zepf FD. *IACAPAP Textbook of Child and Adolescent Mental Health.* 2015. Available at: <http://iacapap.org/iacapap-textbook-of-child-and-adolescent-mental-health>
16. National Institute for Health and Care Excellence. Antisocial behaviour and conduct disorders in children and young people: recognition and management. London: NICE; 2013
17. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder: diagnosis and management. London: NICE; 2018

18. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder in children and young people: clonidine. London: NICE; 2013
19. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder (update). [B] Evidence reviews for information and support for people with ADHD. Evidence review. London: NICE; 2018
20. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder (update). [C] Evidence reviews for pharmacological efficacy and sequencing pharmacological treatment. Evidence review. London: NICE; 2018
21. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder (update). [D] Evidence reviews for safety of pharmacological treatment. Evidence review. London: NICE; 2018
22. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder (update). [E] Evidence reviews for efficacy of non-pharmacological treatment and the impact of adverse events associated with non-pharmacological treatments of ADHD. Intervention evidence review. London: NICE; 2018
23. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder (update). [F] Evidence reviews for combined pharmacological and non-pharmacological treatments review. Intervention evidence review. London: NICE; 2018
24. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder (update). [G] Evidence reviews for adherence to treatment (pharmacological and non-pharmacological). Evidence review. London: NICE; 2018
25. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder (update). [H] Evidence reviews for the principles for discussion when starting, adjusting and discontinuing pharmacological treatment for ADHD. Evidence review. London: NICE; 2018
26. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder (update). [I] Withdrawal from pharmacological treatment and drug holidays. Evidence review. 2018
27. National Institute for Health and Care Excellence. Sleep disorders in children and young people with attention deficit hyperactivity disorder melatonin. Evidence summary. London: NICE; 2013
28. National Institute for Health and Care Excellence. The NICE guideline on diagnosis and management of ADHD in children, young people and adults. London: NICE; 2009
29. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder Clinical Guideline Addendum 72.1 Methods, evidence and recommendations. London: NICE; 2016
30. Osland ST, Steeves TDL, Pringsheim T. Pharmacological treatment for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders. Cochrane Database of Systematic Reviews 2018, 6. Art. No.: CD007990. DOI: 10.1002/14651858.CD007990.pub3.

31. Osland ST, Steeves TDL, Pringsheim T. Pharmacological treatment for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders. *Cochrane Database of Systematic Reviews* 2018, Issue 6. Art. No.: CD007990. DOI: 10.1002/14651858.CD007990.pub3.
32. Otasowie J, Castells X, Ehimare UP, Smith CH. Tricyclic antidepressants for attention deficit hyperactivity disorder (ADHD) in children and adolescents. *Cochrane Database of Systematic Reviews* 2014, Issue 9. Art. No.: CD006997. DOI: 10.1002/14651858.CD006997.pub2.
33. Pelsler LM, Frankena K, Toorman J, Rodrigues Pereira R (2017) Diet and ADHD, Reviewing the Evidence: A Systematic Review of Meta-Analyses of Double-Blind Placebo-Controlled Trials Evaluating the Efficacy of Diet Interventions on the Behavior of Children with ADHD. *PLoS ONE* 12(1): e0169277.
34. Shah R, Sharma A, Grover S, Sachdeva D, Chakrabarti S, Avasthi A. PGIMER Manual Parent training for families of children with attention deficit/ hyperactivity disorder.
35. Sonuga-Barke E, Brandeis D, Ferrin M, Holtmann, M, Stevenson J. Nonpharmacological Interventions for ADHD: Systematic Review and Meta-Analyses of Randomized Controlled Trials of Dietary and Psychological Treatments. *Am J Psychiatry* 2013; 170:275–289
36. Sonuga-Barke E, Taylor E. ADHD and hyperkinetic disorder. In EdsThaparA et al. *Rutter's Child and Adolescent Psychiatry*. Sixth edition. Blackwell Publishing Limited. USA, 2015
37. Taylor E, Döpfner M, Sergeant J, et al. European clinical guidelines for hyperkinetic disorder — first upgrade. *Eur Child Adolesc Psychiatry* 2004; 13(Suppl 1): 1/7-1/30.
38. Taylor E, Sonuga-Barke E. Disorders of attention and activity. In EdsRutter M et al. *Rutter's Child and Adolescent Psychiatry*. Fifth edition. Blackwell Publishing Limited. USA, 2008.
39. World Health Organisation. The 11th Revision of the International Classification of Diseases (ICD-11) Beta draft. Available at: <http://www.who.int/classifications/icd/revision/en>
40. World Health Organisation. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva, 1992
41. Young S, Amarasinghe JM. Practitioner Review: Non-pharmacological treatments for ADHD: A lifespan approach. *Journal of Child Psychology and Psychiatry* 2010;51:116–33

Table 1: Components of a comprehensive assessment and evaluation (text in parenthesis may be used as a guide for assessment)

Core components

1. Establishing diagnosis through detailed history from multiple informants
2. Developmental and psychiatric history (for differential diagnosis and co-morbidities)
3. Medical history (for co-morbidities and contra-indications for medications)
 - a. Comorbid physical disorders: Include tics, seizures, malnutrition, thyroid abnormalities
 - b. Contra-indications: Syncope, exercise intolerance
4. Substance use history
5. Family history (Family h/o ADHD, other developmental, psychiatric and physical disorders; family history of young, i.e. <40 years age sudden cardiac deaths if planning to prescribe a drug)
6. Treatment history (past treatment contacts and experiences, type of treatment, drug dose, formulation, dosing schedule, adherence, response, side effects and perceptions, use of drug holidays, treatment adherence, premature termination of treatment, etc.)
7. Sleep patterns and appetite (pre-treatment baseline night sleep and day time naps; baseline history of appetite and food intake)
8. Psycho-social history (environmental factors, perceptions and expectations regarding diagnosis and treatment, family psychopathology and family resources)
9. Dysfunction: domains involved (academic, family, social, interpersonal, legal, peer relationship, occupational), severity of illness
10. Impact of illness on the patient: secondary depression, perpetuator of bullying, or a bully victim, stigma, parental abuse (psychological, physical and neglect)
11. Impact of illness on the life of caregivers: burden, distress, burnout, psychiatric/psychological burden, stigma
12. Strengths (physical, psychological, cognitive or creative attributes of the child that can be considered as assets; e.g. good in a sport, coloring or sketching, obedient and respectful of elders)
13. Assessment of current needs (to be assessed across various domains such as psychological, social and academic)
14. Physical examination (for co-morbidities and contra-indications; pre-treatment baseline assessments)
15. Mental state examination (to assess for any other psychopathology such as depressive cognitions, suicidal ideas, delusions and hallucinations)

Supportive or only if indicated

1. Rating scales (baseline assessment and monitoring treatment response)
2. Psychological testing (e.g. IQ assessment, only if indicated)
3. Physical investigations (e.g. Lead levels; only if indicated)

Table 2: Clinical questions to be answered in the process of assessment

1. Is there presence of symptoms of inattention/ overactivity / impulsivity?
2. What has been the onset and course of these complaints?
3. Are the symptoms age-appropriate?
4. Are there global developmental delays? If so, are the symptoms appropriate to the level of 'mental-age' or stage of development
5. Are the symptoms persistent (present more often than not)?
6. Are the symptoms causing impairment in more than one setting (e.g. home, school)?
7. How severe are the symptoms and the impairment?
8. Are there associated developmental and/or other psychiatric problems?
9. Are there any associated medical problems?
10. What are the genetic and environmental risk factors?
11. Relevant psychosocial factors, parenting, parenting stress & parents' perceptions and experiences regarding diagnosis and treatment
12. Strengths or assets of the child and family and any protective or positive environmental factors (e.g. supportive school environment)

Table 3: factors that may affect symptom manifestations of ADHD

Signs of ADHD may be minimal or absent if

- child is engaged in a one to one interaction (as with the clinician),
- in a novel setting (such a clinic),
- under close supervision (as in private tuitions),
- is being frequently rewarded for appropriate behaviors,
- is engaged in especially interesting activity or
- getting consistent external stimulation, often with rewards (as while watching TV or playing video games).

Inattention is more evident when

- tasks are lengthy, boring or monotonous
- depends on the demands for attention that the tasks/ environment make

The symptoms can vary with both internal and external motivation, type of activity (interesting versus boring), demands that the task makes for attention, adult supervision, one to one interaction as well as with fatigue and time of the day.

Table 4: Co-morbidities seen with ADHD

Developmental: Intellectual disability, speech and language disorders, learning disorders, motor co-ordination disorders, autism spectrum disorders, tic disorders

Psychiatric: Oppositional defiant disorder, conduct disorder, mood and anxiety disorders, psychotic disorders, substance use disorders

Medical: Epilepsy, tics, seizures, malnutrition, thyroid abnormalities

Table 5: Clinical features for differentiating ADHD from other disorders

Differential diagnosis	Clinical features that help in differentiating
Oppositional defiant disorder and conduct disorder	<ul style="list-style-type: none"> • Symptoms of ADHD usually pre-date the symptoms of defiant disorders • However, in extremely severe cases of ADHD, defiance may seem to start very soon after the onset of ADHD. • It may at times be clinically difficult to separate out the two; though a good chronological history may help. • However, a diagnosis of ADHD should not be made when there is presence of defiance in absence of the core symptoms of ADHD.
Intellectual disability (ID)	<ul style="list-style-type: none"> • In children with ID, apparent inattentiveness and difficulty to follow instructions can be better explained by a lack of comprehension • In case of suspected co-morbidity, symptoms suggestive of ADHD must be clearly developmentally inappropriate.
Specific learning disorders (SLD)	<ul style="list-style-type: none"> • Academic difficulties in SLD are quite persistent while in ADHD the performance can be strikingly variable • Children with ADHD may engage in reading or writing as leisure activities (e.g. reading fiction) in contrast to those with specific learning disorders • It is clinically a good practice to first treat ADHD and then assess for specific learning disorders if these appear to be co-existent.
Autism spectrum disorders (ASDs)	<ul style="list-style-type: none"> • increased motor activity of ASDs is characterized by repetitive, stereotyped movements as against the hyperactivity of ADHD • Several behaviors mimicking ADHD may be due to sensory issues and deviant socio-emotional reciprocity
Tic disorders	<ul style="list-style-type: none"> • Prolonged observation helps in differentiating complex motor tics seen in Tourette’s disorder from the increased motor activity and fidgetiness seen in ADHD.
Mania	<ul style="list-style-type: none"> • Symptoms are of a relatively recent onset • Definite change from pre-morbid state • Increased activity in mania is goal directed; that of ADHD is not • Presence of symptoms such as inflated self-esteem and grandiosity
Depression	<ul style="list-style-type: none"> • Symptoms are of a relatively recent onset • Definite change from pre-morbid state

	<ul style="list-style-type: none"> • Symptoms other than irritability and agitation, such as decreased interest in pleasurable activities
Psychosis	<ul style="list-style-type: none"> • Symptoms are of a relatively recent onset • Definite change from pre-morbid state • Presence of delusions and hallucinations
Anxiety disorders	<ul style="list-style-type: none"> • Inattentiveness, lack of concentration and generalized hyperarousal may be seen in anxiety disorders; but presence of other cognitive (e.g. worry) and behavioral symptoms (e.g. autonomic arousal) may be present
Obsessive compulsive disorder	<ul style="list-style-type: none"> • Compulsive behaviors are repetitive, goal directed and often ritualistic • Concurrent obsessions may be present

Table 6: Key clinical points to guide the process of establishing the diagnosis

<ol style="list-style-type: none"> 1. Multi-informant; each informant may add a different dimension to the history 2. Assess symptoms across multiple settings 3. Compare the reported symptoms to developmentally normal levels of inattention, activity and impulsivity 4. Symptom manifestation may change with development 5. Symptoms may vary with internal and external motivation, re-inforcers, close supervision, one to one interaction, time of the day, and fatigue 6. Symptoms are not due to merely defiance or lack of comprehension or are specific to a particular task or due to another psychiatric disorder 7. Assess impairment in multiple domains 8. Assess effects on development in various domains 9. Make an impression of overall severity of the disorder
--

Table 7: Principles to guide formulation of a comprehensive treatment plan

<ol style="list-style-type: none"> 1. The main objectives of a treatment plan must be to alleviate symptoms as well as improve functioning in various domains of functioning 2. It should be needs-based, individualised and may change over time 3. Consider the level of symptoms and impairments in functioning across settings and domains of functioning 4. Consider co-morbid developmental, psychiatric and medical disorders 5. Consider psycho-social and environmental protective and risk factors 6. Consider patient's and family's perceptions regarding treatment and their treatment preferences 7. Consider family's resources including financial resources

Table 8: Important points to remember while building therapeutic alliance

1. Positive regard for all involved in the care of the child
2. Parental (and family's) perceptions regarding diagnosis and treatment may differ from that of the clinician's.
3. Parental expectations may differ from realistic goals that can be achieved.
4. Parents have often experienced blame and guilt before reaching the clinic. Validate their experiences and feelings; offer support.
5. Child or adolescent's needs may be different from those identified by the parents. Establish a working therapeutic alliance with both the parties.

Table 9: Rationale for involving extended family members in the Indian context

1. Parental perceptions regarding diagnosis and treatment may be influenced by the extended family.
2. It is common for parents to take treatment decisions jointly with grandparents and members of extended family, even when residing as nuclear families.
3. Treatment adherence; both for pharmacological and non-pharmacological modalities will be affected at least partially by other significant elders in the family. For example, much of the behavioural management is dependent upon the consistency shown in implementing the strategies by all the significant adults in the child's life. Behavioral management through parent training may fail, if grandparents who stay in the same household are not involved pro-actively.
4. Involving other members may mitigate blame and conflict amongst them. For example, family members often hold each other responsible for ineffective or punitive or excessively liberal disciplining, and hence, the child's 'misbehaviors'.

Table 10: Components of psycho-education

1. Take feedback about their understanding about the symptoms/diagnosis and expectation from treatment
2. Information about prevalence: ADHD is seen world-wide with global estimates of 5% -7% in school aged children. Higher prevalence rate in clinic population
3. Possible etiological factors:
 - a. ADHD is a neuro-developmental disorder; i.e. a state arising out of problems in development of the brain.
 - b. Like many other psychiatric and developmental problems, the problems are at the level of neuro-chemicals and neural connections between different regions of the brain.
 - c. Genetic and environmental factors (such as low birth weight and pre-

maturity) are associated with ADHD.

d. Symptoms are neither child's fault nor parents' fault.

4. Discuss how parental factors can contribute in manifestation of symptoms, continuation, and influence the course of the disorder
5. Symptoms of the disorder: The core symptoms are inattention (difficulty in sustained attention), hyperactivity (problem of too much behavior) and impulsivity (problem of acting without thinking or controlling impulses), with a likely central problem in self-control (behavior) or response inhibition). Core symptoms must be described with examples.
6. Symptoms are usually present since early childhood; manifestations may change over time with age.
7. Symptoms cause impairments in different domains of functioning; may increase probability of high risk behaviors and substance use.
8. Co-morbid developmental, psychiatric and physical disorders may be present.
9. Long term course is variable; ADHD may be a life-long disorder in a significant proportion of individuals
10. Long term outcomes including risk of substance use are known to improve with treatment; while co-morbid disorders, drug or alcohol use in family, other psychological or socio-environmental risk factors may lead to worse outcomes.
11. No specific investigations needed to diagnose; ADHD is a clinical diagnosis.
12. Treatment consists of medications and non-medication interventions including behaviour training programs.
13. Discuss evidence for, and benefits and risks of each modality of treatment (For e.g. benefits of drug on the core symptoms of ADHD, along with side effects of the medication may be explained; benefits of parent training programs but the risk of ineffective implementation due to factors such as parental psychopathology and preferences that may lead to unresponsiveness may be explained).
14. If a child has co-morbid disorder, include discussion on how it may affect the course and treatment choices in that child.

Table 11: Modalities of intervention for ADHD

PSYCHO-SOCIAL INTERVENTIONS

- A. Environmental modifications
- B. Parent training intervention
- C. Cognitive behavior therapy
- D. Cognitive training

PHARMACOLOGICAL INTERVENTIONS

- A. Stimulants
- B. Non-stimulants

OTHER MEASURES

- A. Diet and exercise
- B. Exclusion and Elimination / few food diets
- C. Omega fatty acid and nutritional supplements
- D. Neuro-feedback

Table 12: Environmental modifications to minimise distraction, improve attention and channelize energy

- Structured routine
- Structure the physical environment
- Assist the child in learning time management
- Use reminders and planners
- Increase supervision by adults
- Minimize distraction in the environment while studying
- Improve attention on the task by using highlighters
- Listening to instrument music: can help in improving attention in some patients
- Short breaks at regular intervals
- Allow activity during breaks to channelize the excessive energy
- Providing extra time to complete work, decreasing the work load, giving small assignments
- If feasible, informing the teacher through parents about the problem and their role in the management

Table 13: Components of PGIMER Manual: 'Parent training for families of children with attention deficit/ hyperactivity disorder'

1. Psycho-education
2. Parenting and communication: 3 Ps (Patience, Persistence, Special Play Time) and 4Cs of communication (Clear, specific and short instructions, Consistency between what is said and done, across adults, over time and in different situations); Catch them good and Cut down critical comments)
3. Dealing with Inattention – disorganisation through structure and routines
 - a. Helping him to make sense of time: Structuring the day
 - b. Helping in organising: Structure the physical environment (Home and room)
 - c. Helping in organising: Use of visual cues and prompts
 - d. Preparing in advance for daily routines
 - e. Helping in sustaining attention: Decrease off task distractibility, increase on task stimulation
 - f. Helping in sustaining attention: External motivators; and immediate and powerful rewards
4. Attention enhancing tasks
5. Managing hyperactivity through environmental modifications

6. Home point (token economy) system (setting the rules)
7. Home point system (to reinforce desirable behaviours)
8. Home point system (Response cost/ penalty) and time outs
9. Anticipating and preparing in advance
10. Liaising with the School; Teacher-parent note

Table 14: Medications available in India for management of ADHD

	Formulation	Starting doses	Maximum recommended dose
STIMULANTS			
Methylphenidate Immediate release (Duration of action: 1-4 hours)	Tablets, 10 mg	5mg once or b.i.d	Max. 60 mg
Methylphenidate Intermediate release (Duration of action: 6-8 hours)	Tablets, 10 mg, 18mg, 20 mg	10mg q.a.m.	Max 60 mg
Methylphenidate Long acting (OROS) (Duration of action: 12 hours)	Tablets, 18 mg, 36 mg, 54 mg	18 mg q.a.m.	72 mg
NON-STIMULANTS			
Atomoxetine	Tablet, capsule, 10mg, 18 mg, 25 mg, 40 mg	<70 kg; 0.5 mg/kg/day >70 Kg; 40 mg/day	Lesser of 1.2 mg/kg/day or 80 mg
Clonidine	Tablet 0.1 mg	< 45 kg, 0.05 mg q.h.s., titrate in 0.05 mg increments b.i.d., t.i.d., q.i.d >45 kg 0.1 mg q.h.s., titrate in 0.1 mg increments b.i.d., t.i.d., q.i.d	27-40.5 kg; 0.2 mg, 40.5-45 kg; 0.3 kg; >45kg; 0.4 mg

Table 15: Side effects with medications and their management

	Commonly seen with	Monitoring	Initial management	Management if side effects persist despite initial
--	--------------------	------------	--------------------	--

				management
Appetite suppression	Methylphenidate Atomoxetine	Weight every visit during titration and once every 3 months thereafter; height every 3-6 months	<ul style="list-style-type: none"> • Differentiate between pre-treatment eating problems from medication induced • Medication should be taken either with or after meals and not before meals • Breakfast and late evening meal should be high on calories and nutrition 	<ul style="list-style-type: none"> • Dose reduction • Discontinuing medication on weekends to prevent weight loss • Changing to another class of medication
Growth retardation	Methylphenidate Possibly with atomoxetine	Same as above	<ul style="list-style-type: none"> • If the trajectory of growth is suppressed and the child lags behind peers significantly (on for age charts) on weight or height, risk-benefit ratio should be weighed. • Dosage reduction • Institute weekend and longer drug holidays for catch up growth • Changing the class of medication • Stop the drug 	<ul style="list-style-type: none"> • If growth suppression persists or growth parameters are below the critical thresholds even after stopping the drug (roughly below the third percentile and growth velocity falling 2 centile lines over 1 year), refer to a pediatric endocrinologist
Tachycardia and rise in blood pressure	Methylphenidate Atomoxetine	Measure heart rate and blood pressure every visit during titration, and once every 3 months	<ul style="list-style-type: none"> • If there is sustained tachycardia of more than 120 beats per minute or systolic blood pressure or diastolic blood pressure more than 95th percentile measured on 2 occasions, reduce the dose and refer to a cardiologist. 	<ul style="list-style-type: none"> • ECG and echocardiography may be needed to assess for arterial hypertension and ruling out secondary causes of the same. If the BP > 95th percentile even after institution of treatment for hypertension, then stop the medication
Orthostatic hypotension (Fall in systolic blood pressure of at least 20 mm HG or in diastolic blood pressure of 10 mm Hg within 3 minutes of standing)	Clonidine	Same as above. Measure blood pressure for orthostatic fall	<ul style="list-style-type: none"> • General measures to prevent fall • Dose reduction • Divide the doses with frequent monitoring 	<ul style="list-style-type: none"> • Change of medication • Stop the medication
Insomnia	Methylphenidate	Sleep onset,	<ul style="list-style-type: none"> • Differentiate 	<ul style="list-style-type: none"> • Add low dose clonidine

		duration and quality	<p>between pre-existing sleep problems and post-medication.</p> <ul style="list-style-type: none"> • Sleep hygiene measures and healthy bedtime routines • Take stimulant medications prior to 3.00 pm • Reduce dose, especially evening dose of stimulant 	<p>or melatonin at night</p> <ul style="list-style-type: none"> • Change medication
Sedation	Clonidine	Sleep onset, duration and quality; daytime sedation	<ul style="list-style-type: none"> • Shift higher dose to night time • Reduce dose 	Stop or change medication
Tics (New onset)	Methylphenidate	Monitor for tics	<ul style="list-style-type: none"> • First consider if tics are related to the medication or not; because tics naturally wax and wane and may be coincidental; if possible observe for a prolonged period, e.g. 3 months • Weigh the risk-benefits, impairment due to tics vis-a-vis impairment due to ADHD symptoms and discuss same with child and parents • Dose reduction • Planned discontinuation of stimulant • Change to atomoxetine or clonidine 	If tics persist, start clonidine or low dose antipsychotic
Mania/Psychosis	Methylphenidate	Monitor for side effects	<ul style="list-style-type: none"> • Stop the medication 	<ul style="list-style-type: none"> • If symptoms persist, treat psychosis/ mania. • After symptom resolution, start another ADHD medication if there is need for pharmacological treatment • Stimulants may be best avoided, especially if

				the episode was stimulant induced.
Seizures (New onset)	Methylphenidate	Same as above	<ul style="list-style-type: none"> • Stop the medication • Neurologist referral and assessment for cause of seizure • If the drug seems to be innocuous it may be gradually re-introduced with continued monitoring. • If seizures appear to be drug induced, start another medication after reviewing the need for medication 	
Suicidal behaviour	Atomoxetine	Ask patients about suicidal or aggressive ideas or impulses	<ul style="list-style-type: none"> • Stop the medication • High risk management • New onset symptoms must be closely monitored – patient may need admission • ADHD medication from a different class may be started; do not start atomoxetine 	
Mood lability and aggression	Atomoxetine	Same as above	Same as above	
Hepatotoxicity (If suspected either clinically or on investigations)	Atomoxetine	Monitor liver enzymes	<ul style="list-style-type: none"> • Stop medication • Medical referral and management • ADHD medication from a different class may be started; do not start atomoxetine 	

Footnote: If a medication is stopped due to side effects, monitor ADHD symptoms and the side effects; review again the need for medication for ADHD; and if there is need, then start with a medication from a different class

Table 16: Factors determining the steps in management of ADHD

Age of the child
Severity of ADHD (consider symptoms and impairments in various domains)
Co-morbidities and contra-indications
Side effect profile and tolerability
Current needs of child and family
Preferences of child and family

Availability
Affordability

Table 17: Factors related to inadequate response to pharmacological or non-pharmacological interventions

Poor adherence
Sub-optimal dosing
Co-morbidities (for example, conduct disorder)
Mismatch between needs and target goals of treatment
Mis-diagnosis



