CLINICAL PRACTICE GUIDELINES

October 2008

MOH/P/PAK/173.08(GU)

MANAGEMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS

MINISTRY OF HEALTH MALAYSIA

MALAYSIAN PSYCHIATRIC ASSOCIATION

ACADEMY OF MEDICINE MALAYSIA

This guideline is meant to be a guide for clinical practice, based on the best available evidence at the time of development. Adherence to this guideline may not necessarily guarantee the best outcome in every case. Every health care provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

Review of the Guidelines
This guideline was issued in 2008 and will be reviewed in 2012 or sooner if new evidence becomes available.

CPG Secretariat
Health Technology Assessment Section
Medical Development Division
Ministry of Health Malaysia
4th Floor, Block E1, Parcel E
62590, Putrajaya.

Electronic version available on the following website:
http://www.moh.gov.my
http://www.acadmed.org.my
http://www.psychiatry-malaysia.org
http://www.mpaeds.org.my

GUIDELINE DEVELOPMENT

The development group for this guideline consist of child and adolescent psychiatrists, general psychiatrists, paediatricians, family medicine specialists, a clinical psychologist, a pharmacist, special needs educator, and an occupational therapist. The members of the development group are from the Ministry of Health Malaysia, Ministry of Education, Ministry of Higher Education Malaysia and the private sector. During the process of development of this guideline, there was active involvement of a review committee comprising child and adolescent psychiatrists, general psychiatrists, paediatricians, public health specialists both from the government and private sector as well as non-governmental organisations (NGOs).

This is the first guideline by the Ministry of Health that have included participation from non healthcare professionals who are involved in the care of children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD).

Literature search was carried out at the following electronic databases: International Health Technology Assessment Websites, PUBMED, Cochrane Database of Systematic Reviews (CDSR), Journal full text via OVID search engine, PsycINFO, Biomedical Reference Collection, Comprehensive Database of Abstracts of Reviews of Effectiveness, Psychology and Behavioural Sciences Collection, Cochrane Controlled Trials Registered, CINAHL, Academic Search Premier, ERIC, PsycARTICLES via EBSCO search engine. In addition, the reference lists of all relevant articles retrieved were searched to identify further studies. The following free text terms or MeSH terms were used either singly or in combination: *attention deficit hyperactivity disorder; ADHD; pharmacotherapy; hyperkinetic; risk factors; causal; television; diet; sugar; psychopathology; co-morbid; assessment; Conduct Disorder; autism; rating scale; teacher report; diagnostic criteria; DSM IV; ICD 10; differential diagnosis; history; physical examination; laboratory diagnosis; diagnosis; family counselling; family therapy; psycho-education; non-pharmacological; social skill; self management; behaviour management; CBT; cognitive therapy; play therapy; parent education; parent training; parent knowledge; parent counselling; knowledge; parental training; family treatment; school based intervention; medication counselling; preschooler medication; stimulant medication; treatment adherence; effectiveness; adverse effects.*

Reference was also made to other guidelines on the Management of Attention Deficit Hyperactivity Disorder including the Scottish Intercollegiate Guideline Network - National Guideline on Attention Deficit and Hyperkinetic Disorder in Children and Young People 2001, University of Michigan Health System

Guidelines for Clinical Care - on Attention Deficit Hyperactivity Disorder 2005, Institute for Clinical System Improvement Health Care Guidelines on Diagnosis and Management of Attention Hyperactivity Disorder in Primary Care for School Age Children and Adolescence 2005, Cincinnati Children's Hospital Medical Center - Evidence Based CPG on Outpatient Evaluation and Management of Attention Deficit/Hyperactivity Disorder 2004, American Academy Of Pediatrics Clinical Practice Guideline - Diagnosis and Evaluation of the Child With Attention-Deficit/Hyperactivity Disorder 2000, New Zealand Guidelines for the Assessment and Treatment of Attention-Deficit/ Hyperactivity Disorder 2001, AACAP Practice Parameter for the Assessment and Treatment of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder 2007 and The European Clinical Guidelines for Hyperkinetic Disorder- first update European Child & Adolescent Psychiatry 2004.

This guideline is based largely on the findings of systematic reviews and meta-analyses in the literature, taking into consideration local practices.

The clinical questions were divided into major subgroups and members of the development group were assigned individual topics within these subgroups. The group members met a total of 15 times throughout the development of the guideline. All literature retrieved was appraised by at least two members and presented and discussed during group meetings. All statements and recommendations formulated were agreed by both the development group and the review committee. Where the evidence was insufficient the recommendations were derived by consensus of the development group and the review committee.

The articles were graded using the modified version of the criteria used by the Catalonia Agency for Health Technology Assessment and Research (CAHTAR) Spain, while the grading of recommendation in this guideline was modified from the Scottish Intercollegiate Guidelines Network (SIGN).

The draft guideline was posted on the Ministry of Health Malaysia website for comment and feedback. This guideline has also been presented to the Technical Advisory Committee for Clinical Practice Guidelines, and the Health Technology Assessment and Clinical Practice Guidelines Council, Ministry of Health Malaysia and was reviewed and approved.

OBJECTIVE

To provide evidence-based guidelines in the assessment and management of ADHD in children and adolescents.

CLINICAL QUESTIONS

- What is ADHD?
- What are the risk factors?
- How is ADHD recognized and diagnosed?
- What are the associated co-morbidities?
- How is ADHD treated?
- What is the pharmacological treatment?
- How should pre-schoolers be managed?
- What are the non-pharmacological treatment modalities?
- Is there a role for alternative therapy?
- When and to whom do primary care providers and teachers refer?
- What is the follow-up plan?
- Can treatment be stopped?

TARGET POPULATION

This guideline is developed for the Management of ADHD in children and adolescents under the age of 18. Management of associated co-morbidities (e.g. mental retardation, pervasive developmental disorders) are not included.

TARGET GROUP / USERS

This guideline is applicable to all health care professionals involved in treating patients with ADHD, i.e. primary care doctors, medical officers, nurses, medical assistants, paediatricians, psychiatrists, psychologists / counsellors, social workers, pharmacists, speech therapists, occupational therapists, as well as educators.

GUIDELINE DEVELOPMENT GROUP

Chairperson

Dr. Toh Chin Lee
Senior Consultant Child & Adolescent Psychiatrist
Department of Psychiatry and Mental Health
Hospital Kuala Lumpur, Kuala Lumpur

Members (alphabetical order)

A/Prof Dr. Aili Hanim Hashim
Consultant Child & Adolescent Psychiatrist
Psychiatry Adolescent & Child Unit
Department of Psychological Medicine
University Malaya Medical Center, Petaling Jaya

Ms. Cheong Sau Kuan
Lecturer & Clinical Psychologist
Sunway University College
Bandar Sunway, Selangor

Dr. Eni Rahaiza Muhd Ramli
Consultant Child & Adolescent Psychiatrist
Department of Psychiatry & Mental Health
Hospital Taiping, Perak

Dr. Fauziah Mohammed
Head of Department and Senior Consultant
Child & Adolescent Psychiatrist
Department of Psychiatry & Mental Health
Hospital Tengku Ampuan Rahimah Klang,
Selangor

Dr. Farahidah Md Dai
Consultant Child & Adolescent Psychiatrist
Department of Psychiatry & Mental Health
Hospital Umum Sarawak, Kuching

Dr. Ibrahim Abu Samah
Psychiatrist
Department of Psychiatry & Mental Health
Hospital Sultanah Fatimah, Muar, Johor

Ms. Jacqueline Lai Mui Lan
Pharmacist
Institute of Paediatrics
Hospital Kuala Lumpur, Kuala Lumpur

Dr. Majmin Sheikh Hamzah
Family Medicine Specialist
Department of Family Medicine
Hospital Universiti Kebangsaan Malaysia
Kuala Lumpur

Dr. Norharlina Bahar
Psychiatrist
Department of Psychiatry & Mental Health
Hospital Kuala Lumpur, Kuala Lumpur

Ms. Permalatha Sundram
Head of Department & Occupational Therapist
Department of Medical Rehabilitation
Hospital Permai, Johor

Dr. Sheamini Sivasampu
Principal Assistant Director
Health Technology Assessment Section
Medical Development Division
Ministry of Health Malaysia, Putrajaya

Dr. Sheila Gopal Krishnan
Consultant Paediatrician
Department of Paediatrics
Hospital Ipoh, Ipoh

Dr. Sheila Marimuthu
Consultant Paediatrician
Institute of Paediatrics
Hospital Kuala Lumpur, Kuala Lumpur

Ms. Sin Lian Thye
Nursing Sister
Health Technology Assessment Section
Medical Development Division
Ministry of Health Malaysia, Putrajaya

Dr. Supiah Saad
Assistant Director
Department of Special Needs Education
(Jabatan Pendidikan Khas)
Ministry of Education, Putrajaya

Dr. Zil Falilah Mohd Said
Family Medicine Specialist
Kerteh Health Centre, Terengganu

REVIEW COMMITTEE

The draft guideline was reviewed by a panel of independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence supporting the recommendations in the guideline.

Chairman

Dato' Dr. Suarn Singh
Head of Services & Senior Consultant Psychiatrist
Hospital Bahagia, Perak

Members (alphabetical order)

Dr. Khoo Teik Beng
Consultant Paediatrician
Hospital Kuala Lumpur
Kuala Lumpur

Encik Shaharuddin Mohd Said
Persatuan Ibubapa Kanak – kanak Istimewa (GIAT)
Johor Bahru, Johor

Dr. Rose Peng
Consultant Child & Adolescent Psychiatrist
Ampang Puteri Hospital
Kuala Lumpur

Dr. Susan Tan
Consultant Child & Adolescent Psychiatrist
Department of Psychiatry
Hospital Universiti Kebangsaan Malaysia
Kuala Lumpur

Datin Dr. Rugayah Bakri
Head of Health Technology Assessment Section
Medical Development Division
Ministry of Health Malaysia, Putrajaya

Dr. Wong Swee Lan
Senior Consultant Paediatrician
Hospital Tuanku Jaafar
Negeri Sembilan

Dr. Sabariah Abdul Hamid
Principal Assistant Director
Mental Health Unit
Disease Control Division, Putrajaya

Dato' Dr. Zulkifli Ismail
Consultant Paediatrician
Selangor Medical Center
Selangor

EXTERNAL REVIEWERS (alphabetical order)

The draft guideline was also reviewed by a panel of external reviewers.

Dr. Alvin Ng Lai Oon
Clinical Psychologist
Faculty of Allied Health Sciences
Kuala Lumpur Campus
University Kebangsaan Malaysia, Kuala Lumpur

A/Prof Dr. Daniel Fung Shuen Sheng
Senior Consultant Psychiatrist and Head
Department of Child and Adolescent Psychiatry and Child Guidance Clinic
Institute of Mental Health, Woodbridge Hospital, Singapore

Dr. Kamarudin Ahmad
General Practitioner
Klinik Kamal
Johor Baharu

A/Prof Dr. Mary Marret
Lecturer and Consultant Pediatrician
Department of Paediatric
University of Malaya Medical Centre
Kuala Lumpur

A/Prof Dr. Mohd Jamil Yaacob
Head of Department and Consultant Psychiatrist
Hospital Universiti Sains Malaysia
Kubang Krian

Dr. Peter Birleson
Director, Integrated Mental Health Service
Adjunct Professor of Psychology, Deakin University
Clinical Associate Professor, University of Melbourne
Royal Children's Hospital, Australia

Dr. Teoh Hsien-Jin
Head, School of Health and Natural Sciences
Consultant Clinical Psychologist
Sunway University College, Selangor

SUMMARY OF RECOMMENDATIONS

RISK FACTORS

Parents and siblings of children and adolescents with ADHD should be screened for ADHD.	Grade C
Children who have a history of preterm birth, low birth weight and neonatal complications may benefit from assessment for ADHD.	Grade C
Pregnant mothers should be discouraged from smoking.	Grade A
Early recognition of maternal stress and subsequent intervention is encouraged.	Grade A
Television viewing in very young children (less than two years) should be discouraged.	Grade C
Children and adolescents should be discouraged from watching more than three hours of television per day.	Grade B

ASSESSMENT AND DIAGNOSIS

A comprehensive history from family members, teachers and patients should be obtained.	Grade C
Laboratory tests should **not** be routinely performed.	Grade C

SCREENING

The two screening questions for ADHD should be used routinely by teachers, parents and health-care providers.	Grade C

COMORBIDITIES

Children with ADHD should be evaluated for comorbidities (e.g. oppositional deficient disorder, conduct disorder, learning disorder) and referred to the psychiatrist or paediatrician for further management.	Grade C

MANAGEMENT OF ADHD

Management should be comprehensive and should include pharmocological methods and non-pharmocological methods.	Grade A
Treatment should be individualised and the preferences of the family should be taken into consideration.	Grade C
Preschoolers with ADHD should be referred to a child psychiatrist or paediatrician for further management.	Grade C

PHARMACOLOGICAL TREATMENT

Medication for school aged children and adolescents should be initiated by a psychiatrist OR a paediatrician.	Grade C
Initiation of medication should include medication counselling.	Grade B
Stimulants OR atomoxetine should be used.	Grade A
Long acting stimulants or atomoxetine should be considered due to convenience, adherence and stigma reduction.	Grade B
When stimulants or atomoxetine do not produce response or have serious side effects, TCAs or neuroleptics may be prescribed.	Grade B
If medication does not result in satisfactory treatment, a review of diagnosis and management should be considered.	Grade A
Medication for **preschoolers** should be initiated by a **child psychiatrist** OR a **paediatrician** familiar with the management of ADHD (in this group).	Grade C
If medication is required for preschoolers, methylphenidate may be prescribed in doses lower than those used in school aged children and titrated slowly.	Grade B
Children on stimulant medication should have their height and weight regularly monitored.	Grade A
'Drug holidays' may be offered in certain circumstances, e.g. to avoid the side effects of medication.	Grade C

NON-PHARMACOLOGICAL TREATMENT

Psycho-education should be provided to children and their families.	Grade B
Parental training should be offered by trained professionals as it improves symptoms in the patient and enhances coping mechanisms especially for the parents.	Grade B
Parental training should wherever possible be used in combination with medication therapy.	Grade A
Parents should be given advice on how to manage the behaviour of the child.	Grade C
A structured school based intervention programme should be made available.	Grade A
The child should be placed in a mainstream classroom with provision of teacher's aide.	Grade C
Dietary modifications should not be routinely recommended.	Grade C
Parents are encouraged to monitor the effects of specific food items on their child's behaviour and inform their doctor.	Grade C
Alternative interventions (e.g. homeopathy, EEG, biofeedback and neuro-feedback) are not recommended.	Grade C

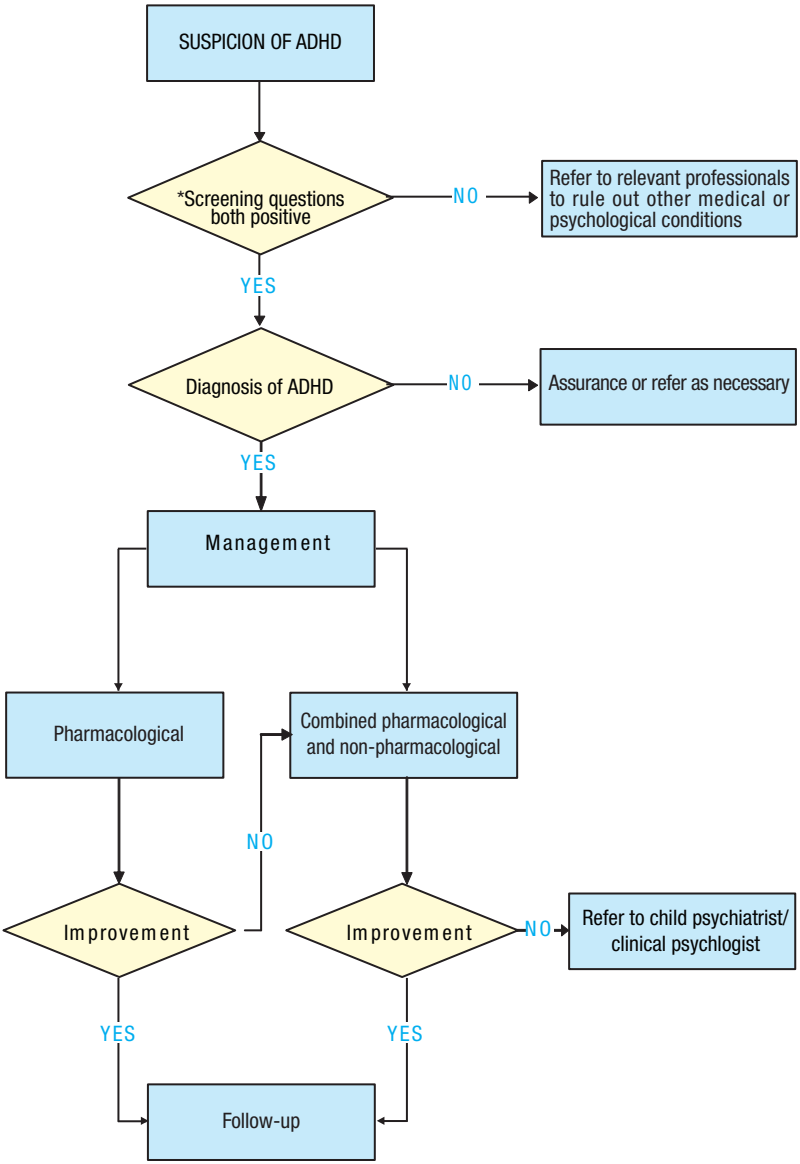
COMBINATION THERAPY

Either pharmacotherapy alone **OR** combination treatment (pharmacotherapy and non-pharmological treatment) should be offered.	Grade A

FOLLOW-UP

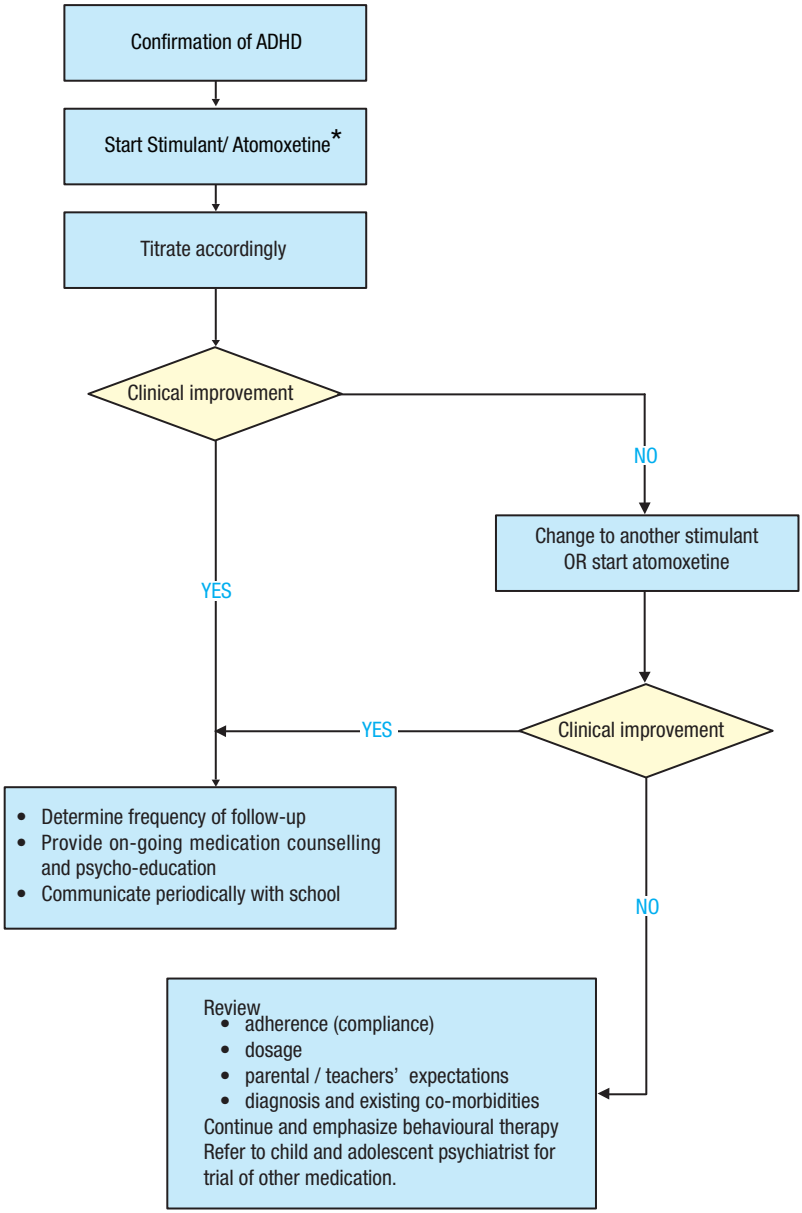
Children with ADHD should be regularly followed-up by their clinicians.	Grade A
The treatment of ADHD should continue as long as the symptoms persist. Cessation of medication may be considered after proper evaluation.	Grade A

ALGORITHM FOR MANAGEMENT OF ADHD



* The two screening questions are
  1. Is the child unable to pay attention?
  2. Is the child extremely active?

ALGORITHM FOR PHARMACOLOGICAL MANAGEMENT



*Psychiatrists OR paediatricians to initiate medication

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1. INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most frequently encountered childhood-onset neuro-behavioural disorders in primary care settings. It has defining features of inattention, over-activity and impulsivity. The core symptoms co-exist with other emotional, behavioural and learning disorders.[1, 2]

Often primary care physicians, paediatricians, psychiatrists, clinical psychologists and others are asked to evaluate and treat a child who has disruptive relationships with peers, defies parental discipline and does poorly in school. ADHD could account for some of these symptoms. Early recognition, assessment, and management of this condition can improve the educational and psychosocial difficulties faced by the child and adolescent.[1-3]

Screening for hyperactivity and inattention (the hallmark symptoms of ADHD) in a community survey amongst Malaysian children and adolescents between the ages of 5 – 15 years showed a prevalence rate of 3.9 %. It is more common in males compared to females.[3, 4]

2. RISK FACTORS

Several risk factors have been identified in the causation of ADHD. These factors may be biological or non-biological in nature. ADHD is three times more likely to occur in males[5, *Level 7*] and is more common in first born children.[6, *Level 8*]

Genetic factors are important in the causation of ADHD. Children with ADHD are two to eight times more likely to have a parent with ADHD.[7, *Level 7;* 8, *Level 7; 9, Level 9*] Mean heritability estimate of ADHD from twenty twin studies is 76%. There are at least seven genes that have been found to be significantly associated with ADHD i.e. DRD4, DRD5, DAT, DBH, 5-HTT, HTR1B, and SNAP-25.[9, *Level 9*]

Preterm birth is associated with more than twice the risk of developing ADHD,[10, *Level 1*; 11, *Level 7*] while children with low birth weight have two to three fold increased risk.[7, *Level 7*; 11, *Level 7*]

Children with ADHD have significantly higher rates of neonatal complications compared with their unaffected siblings.[12, *Level 7*]

A systematic review of 24 studies showed a greater risk of ADHD-related disorder among children whose mothers smoked during pregnancy. However, this same review showed inconclusive evidence for maternal alcohol use leading to ADHD in children and adolescents.[13, *Level 1*] Children whose mothers were exposed to poly-substance use (i.e. heroin, alcohol, tobacco, cannabis, amphetamines, benzodiazepines) during pregnancy had significantly elevated levels of impulsivity and attention problems.[14, *Level 7*] This is also seen in those exposed to lead and polychlorinated biphenyls (PCBs).[15, *Level 1; 16, Level 8*]

Maternal psychological stress during pregnancy contributes to ADHD symptoms in the offspring.[13, *Level 1*] Other studies demonstrated that single parent families, disadvantageous social factors and younger parental age were associated with increased risk of hyperkinetic disorder (HKD).[11, *Level 7*; *8, Level 7*] Offspring of fathers who had a substance use disorder had higher rates of childhood conduct disorder and ADHD.[17, *Level 7*]

In addition, children who suffered from traumatic brain injury and then developed ADHD were noted to have a direct correlation between severity of injury and ADHD symptoms.[18, *Level 4*]

Watching television at a young age (below 3 years) was associated with attentional problems at age 7 years.[19, *Level 6*] Children's exposure to television should be limited to not more than 1 to 2 hours of quality programming per day and television viewing for children younger than 2 years should be discouraged.[20, *Level 9*] A recent large cohort study showed both childhood and adolescent television viewing were associated with attention problems in adolescence especially those who watched more than 2-3 hours per day.[21, *Level 6*]

A meta-analysis of 23 randomised controlled trials,[22, *Level 1*] found that sugar does not affect the behaviour or cognitive performance of children. However, artificial food colouring may be related to neuro-behavioural toxicity in children who were already diagnosed to have hyperactivity.[23, *Level 1*] In the general population, artificial colours or a sodium benzoate preservative, or both in the diet resulted in hyperactivity in 3-year-olds and 8/9-year-olds.[24, *Level 2*]

RECOMMENDATION
Parents and siblings of children and adolescents with ADHD should be screened for ADHD. **(Grade C)**
Children who have a history of preterm birth, low birth weight and neonatal complications may benefit from assessment for ADHD. **(Grade C)**
Pregnant mothers should be discouraged from smoking. **(Grade A)**
Early recognition of maternal stress and subsequent intervention is encouraged. **(Grade A)**
Television viewing in very young children (less than two years) should be discouraged. **(Grade C)**
Children and adolescents should be discouraged from watching more than three hours of television per day. **(Grade B)**

3. ASSESSMENT AND DIAGNOSIS

Assessment involves obtaining information from parents, teachers and patients as well as conducting a thorough clinical examination.

The clinical diagnostic evaluation in the section below is derived from. AACAP 2007, Cincinnati 2004, New Zealand 2001. [25, Level 9; 2, Level 9; 1, Level 9]

3.1 History

The clinical history should include the following:

- core symptoms of ADHD (inattention, hyperactivity and impulsivity) at home, in school and social settings
- age of onset
- duration of symptoms
- birth and developmental history
- family history of ADHD, substance abuse and maternal smoking
- family structure and dynamics, parenting styles and expectations
- past medical history (e.g. meningitis, traumatic brain injury, lead toxicity)
- school performance which includes behaviour, as well as strengths and weaknesses of learning (refer Appendix 1)
- the child's intelligence and when in doubt formal IQ assessment is to be considered
- functional impairment in family and peer relationships
- functioning and stressors in classrooms and at play
- independence in activities of daily living
- self-esteem
- disruptive and unsafe behaviours
- co-morbid psychiatric conditions including substance abuse and dependence
- medical/social conditions that mimic ADHD symptoms (e.g. conditions producing chronic sleep deprivation; obstructive sleep apnea; neuro-behavioural side effects of medications taken for other chronic conditions; physical; sexual and emotional abuse)

3.2 Clinical Examination

Mental status examination should focus on the following:

- General appearance and behaviour
- Activity level
- Speech and language
- Mood and affect
- Thought processes
- Social interaction
- Attention and concentration
- Intelligence

3.3 Physical Examination

A comprehensive physical examination (including vital signs and anthropometry-height and weight) should be performed to exclude physical conditions which mimic ADHD e.g. hyperthyroidism, anaemia, visual and auditory impairment, chronic adenoidal/ tonsillar hypertrophy and obstructive sleep apnoea.

3.4 Laboratory Studies

There is no diagnostic laboratory test for ADHD. Laboratory tests should only be performed if there is a clinical indication.

RECOMMENDATION
A comprehensive history from family members, teachers and patients should be obtained. **(Grade C)**
Laboratory tests should **not** be routinely performed. **(Grade C)**

3.5 Screening

The diagnosis of ADHD is made via a clinical interview. The routine use of screening instruments is not recommended. Furthermore, the screening instruments require translation as well as validation.

The following two questions may be used to screen for ADHD in the primary care setting or schools:

(1) "Is the child unable to pay attention?"

(2) "Is the child extremely active?"

If the answer is **"Yes"** to both questions, the child should be assessed for ADHD.

For these two questions**,** the reported sensitivity is 91% and specificity 82%. [26, *Level* 8] It is recommended that parents or teachers complete the checklist in Appendix 1 to assist clinicians in making an accurate diagnosis.

If rating scales are needed, specific scales should be used. Refer to Table 1 for details. It is important to note that the use of rating scales alone does not diagnose ADHD.

Table 1: Common behaviour rating scales used in screening

Name of scale
1.The Conners' Rating Scales-Revised (CRS-R)[25, *Level* 9] • Conners' Parent Rating Scale – Revised (CPRS) • Conners' Teacher Rating Scale – Revised (CTRS) • Conners' Wells Adolescent Self Report Scale
2. ADHD Rating Scale-IV ADHD RS-IV.[27, *Level* 9]
3. Vanderbilt ADHD Diagnostic Parent and Teacher Scales.[28, *Level* 9]
4. Brown ADD Rating Scales for Children, Adolescents and Adults.[29, *Level* 8]

Note: These rating scales are not validated in the Malaysian setting.

The actual number of children seen in clinical settings is much less than the actual prevalence of children with ADHD in the country.[30, *Level* 8] Children with ADHD are commonly undetected in schools hence disrupting their development and academic performance.

RECOMMENDATION

The two screening questions for ADHD should be used routinely by teachers, parents and health-care providers. **(Grade C)**

3.6 Diagnostic Criteria

The diagnosis of ADHD is made either by using criteria from the Diagnostic and Statistical Manual of Mental Disorders [DSM-IV-TR, 2000], (Appendix 2) **OR** 10th Revision of International Classification of Diseases [ICD- 10] (Appendix 3). DSM-IV-TR criteria include a broader group of children with combined or predominantly hyperactive-impulsive or predominantly inattentive presentations whereas ICD-10 criteria capture a narrower group that presents with both inattention and hyperactive-impulsive symptoms.

A diagnosis [DSM-IV-TR] is based on whether symptoms involve inattention **OR** hyperactivity–impulsivity, **OR** both. It is necessary that the symptoms:

- are present across different settings
- result in significant impairment and are present for at least six months
- began before seven years of age
- are not explained by other psychiatric disorders (i.e. pervasive developmental disorder, mood disorder)

4.0 DIFFERENTIAL DIAGNOSIS AND COMORBIDITIES

4.1 Differential Diagnosis

ADHD is often mistaken for other disorders. The differential diagnosis is listed in Table 2.

Table 2 : Differential diagnoses for ADHD

Psychiatric or developmental disorders • Oppositional defiant disorder (ODD) • Conduct disorder • Mental retardation / borderline intellectual functioning / traumatic brain injury • Autism and Asperger's syndrome • Anxiety disorders (including obsessive compulsive disorder) • Alcohol and substance abuse and dependence or withdrawal • Tic disorders (including Tourette's disorder) • Specific development disorder (e.g. speech, language and learning difficulties) • Mood disorder-bipolar disorder or agitated depression • Schizophrenia • Reactive attachment disorder • Personality disorders of adulthood emerging during adolescence (e.g. antisocial and borderline personality disorders)
Medical conditions • Medical / neurological primary diagnosis (e.g. hyperthyroidism and epilepsy) • Medication-related problems (e.g. anti-asthmatics, anticonvulsants, antihistamines, sympathomimetics and steroids)
Psychosocial problems • Child abuse • Divorce/ separation • Grief

Modified from New Zealand Ministry of Health, [1, *Level 9*]

4.2 Comorbidities

Studies have shown that ADHD children with comorbidities have significantly more difficulties,[31, *Level 8*] and a lower quality of life. [32, *Level 8* ; 33, *Level 8*] Hence these children need comprehensive assessment for comorbidities, as well as intensive and complex interventions.

76.2% of ADHD children [34, Level 8] have at least one comorbidity while 20% have at least two comorbidities. [33, Level 8]

Gender based studies have shown boys are more susceptible to conduct problems [32-36, Level 8] while girls have more depressive or anxiety disorders. [32,34,37-38, Level 8]

Almost 50% of ADHD patients will have oppositional defiant disorder (ODD). A large proportion of patients will have learning disorder. Refer to Table 3

Table 3: Prevalence of Comorbidities

Comorbid psychiatric disorders	Prevalence	Reference
Conduct disorder	19%; 15%; 18.6%	32, 33, 35, 36
Learning disorder	38.9%	33
ODD	34.4%; 46.7%; 41%	33, 34, 36
Anxiety disorder	23%; 33.3%; 33%; 23%	35-38
Bipolar disorder	14.3%; 13%; 14%	35-37
Depression	11%; 50%; 28%	33, 36, 37
Enuresis	30%; 19%	36, 37
Language disorder	20%	36
Tic disorder	10%, 12%	36, 37

Note: All the studies quoted above are cross sectional in nature.

RECOMMENDATION

Children with ADHD should be evaluated for comorbidities and referred to the psychiatrist or paediatrician. (Grade C)

5. MANAGEMENT OF ADHD

The goal of treating children and adolescents with ADHD is to improve symptoms, learning, social interactions and self-worth/self-esteem. [39 , Level 9]

A comprehensive treatment plan should be developed for each patient taking into consideration the family's preferences and concerns. The plan should include pharmacological and non-pharmacological treatment. When the selected management for a child with ADHD has not met target outcomes, clinicians should evaluate the original diagnosis, the dosages and adherence to medications as well as parental and teachers' expectations. [25, Level 1]

As ADHD is a chronic condition, children with ADHD and their families require a long term treatment program that is individualised, clinically based and with sufficient support for the child and family. [40, *Level* 9; 25, *Level* 1; 20, *Level* 9] In view of difficulties with diagnosis and special requirements of management, preschoolers with ADHD should be referred to a child psychiatrist or a paediatrician.

Children with ADHD are eligible for registration with the Ministry of Women, Family and Community Development using the "Borang pendaftaran dan cadangan penempatan kanak–kanak keperluan khas" (BPKK1 (Pindaan 2003). ADHD children requiring special education should be registered with the Education Department using the same forms. A copy of the completed form should be given to the school to accommodate the child's educational needs. Further information regarding strategies at school should also be provided by the healthcare professional.

RECOMMENDATION
Management should be comprehensive and should include pharmacological and non-pharmacological methods. **(Grade A)**
Treatment should be individualised and the preferences of the family should be taken into consideration. **(Grade C)**
Preschoolers with ADHD should be referred to a child psychiatrist or paediatrician. **(Grade C)**

5.1 Pharmacological Treatment

Pharmacological agents used include stimulants, non stimulants such as atomoxetine, anti-depressants, neuroleptics and others.

5.1.1 Stimulants

The main treatment for ADHD is stimulants which have been shown to be highly efficacious. [25,41, *Level* 1] The stimulant class of medications include Methylphenidate (MPH), detroamphetamine and mixed amphetamine salts. The mechanism of action of stimulants has been attributed to the binding of dopamine transporter and subsequent inhibition of dopamine reuptake resulting in increased levels of extra cellular dopamine.

MPH is the most commonly prescribed stimulant. Mixed amphetamine salts and dextroamphetamine have demonstrated equivalent efficacy to MPH. [42, Level 9;] Dextroamphetamine is also indicated for refractory hyperkinetic states [43, *Level* 1] and is said to have a longer duration of action compared to MPH, permitting less frequent doses. 80% of children who fail to respond to one stimulant may have a positive response to an alternative stimulant. [20, *Level* 9] However, dextroamphetamine and mixed amphetamine salts are not registered in Malaysia. Stimulants are divided into short-, intermediate, and long-acting forms (Refer table 4 and Appendix 4 and 5).

Table 4: Stimulant Medications

Generic name	Time to maximum effect	Duration of action
Methylphenidate Preparation:		
Short-acting: *Ritalin	2 hrs	3-5 hrs
Intermediate-acting: *Ritalin SR	3 hrs	3-8 hrs
Extended Release: *Concerta *Ritalin LA	4-7hrs 5 hrs	8-12 hrs 8-12 hrs
Amphetamine preparation:		
Short-acting (Immediate- Release) Dexedrine Adderall	1-4 hrs 3 hrs	9 hrs 6-8 hrs
Long- acting Dexedrine Spansule Adderall X	1-2 hrs 7hrs	8-10 hrs 12hrs

Adapted from Micromedex Healthcare series 2008

Notes: * Drugs available in Malaysia

There have been concerns regarding the association of sudden death and the use of stimulant medication in ADHD. [44, *Level* 9] However, sudden cardiac death in persons taking medication for ADHD is very rare and occurs at rates no higher than those in the general population of children and adolescents. The routine electrocardiogram (ECG) screening before beginning medication for ADHD treatment would not prevent sudden death. A careful history pertaining to the cardiovascular system e.g. hypertrophic obstructive cardiomyopathy, prolonged QT syndrome, arrhythmias and a family history of sudden death should be taken. [45, *Level 9*]

a. Short - acting (Immediate-release) stimulants

The short-acting stimulants have a short duration of action, providing clinical benefits for 3 to 5 hours after oral dosing.

(i) Short-term studies showed:

- Improvement in core ADHD symptoms at home, classroom and social situations in 65-75% of patients. [46, *Level* 1; 47, *Level* 9; 41, *Level* 1; 48, *Level* 9]
- Suppression of physical and non-physical aggression in ADHD children; improvement in their ability to follow rules and improve relationship with peers and family. [46, *Level* 1; 49, *Level* 9]
- There is also reduction in emotional lability and distractibility. [41, *Level* 1; 50, *Level* 6]
- Importance of treating children with ADHD beyond school hours to include evenings, weekends and vacations. [46, *Level* 1]

(ii) Long-term studies showed:

- Symptoms continue to improve after 2 years and beyond [50, *Level* 6; 51, *Level* 6]
- Improved reading achievement, decreased school absenteeism, and decreased grade retention in children. [52, *Level* 6]
- No improvement in antisocial behaviour or comorbid learning disability especially reading. [53, *Level* 4]
- Adverse effects may persist and the most common sustained side effect reported was appetite loss. [50, *Level* 6]
- Adolescents treated with stimulants had decreased risk for future substance abuse compared to those without treatment. [2, *Level* 9]

Difficulties with short-acting preparations [54, *Level* 9] include:

- Multiple doses (typically two or three) per day leading to poor compliance particularly with adolescents
- Children continuing to be disruptive and inattentive during the most unstructured times of the school day (e.g. lunch time, break time and travelling home)
- Schools often oppose administering medication
- Many children and adolescents worry about being ridiculed by peers and are unable, during the school day, to maintain privacy over their medication
- Some simply forget to take their medication unless reminded

b. Intermediate-acting stimulants

These stimulants are similar to short-acting stimulants except for the duration of action which is 5-8 hours. In Malaysia the only intermediate-acting stimulant is Ritalin® SR and this drug is also soon to be phased out in favour of long- acting stimulants.

Ritalin® SR is designed to exert an effect equivalent to two 10-mg tablets of immediate release MPH given 4 hours apart. However, the time course of Ritalin® SR appears to be variable, and individual responsiveness to the preparation may be highly variable. [55, *Level 4*]

c. Long-acting stimulants

The development of long-acting and extended release (ER) formulations permitting once-a-day administration is a major advancement, [55, *Level 4*] making it popular with both patients and clinicians. [56, *Level 3*] These long-acting formulations have begun to replace immediate-release formulations as the preferred therapy for patients with ADHD. [49, *Level 2*]

They are equally efficacious in children and adolescents [46, *Level 1*] and demonstrate similar safety, efficacy and side effects to short-acting stimulants. [57, *Level 3*]

The benefits of using the long- acting medications [40, *Level 9*; 55, *Level 4*] are:

- Once-a-day dosing improving compliance, eliminating the burden of medication administration by school personnel or other supervisory care providers
- Decreasing stigma associated with medication administration away from home
- Having benefits of the medication throughout the day
- Suitable for children who have severe rebound hyperactivity

The two available formulations are OROS MPH (Concerta) and Ritalin® LA. OROS MPH gradually releases methylphenidate over 10 to 12 hours [55, *Level 4*] which mimics the efficacy and side-effect profile of three times a day (TDS) MPH administration. [55, *Level 4*; 57, *Level 3*]

Ritalin® LA, is the extended-release methylphenidate formulation which allows 50% of the drug to be released immediately providing a rapid onset, and 50% to be released 4 hours after administration. This mimics the twice-daily administration of immediate-release methylphenidate and has safety and tolerability profiles consistent with the immediate-release formulations. [58, *Level 4*]

5.1.2 Prescribing Stimulants for Preschoolers

The use of stimulants in children younger than 6 years is considered off-label. There have been only a handful of studies looking at stimulant treatment in preschoolers. Amongst the stimulants, MPH is superior to placebo in efficacy. [59, *Level 3*; 60, *Level 7*] Many of these studies are limited by small sample size, approaches to diagnosis and have short duration of follow-up. The Preschool ADHD treatment study (PATS) showed MPH-IR produced significant reduction on ADHD symptom scales in preschoolers compared to placebo, although effect size was smaller than those cited for school age children. [61, *Level 2*]

The frequency of side effects appear to be higher among preschoolers compared to school-aged children. Some of the most commonly reported side effects were irritability, crying and increased emotional outbursts. [2,5 *Level 1*]

The data on long term safety of drugs used in preschoolers is limited. Therefore medication should be prescribed with caution and if used, lower doses and slower titration is recommended. [25, *Level 1*]

Both the AACAP [25, *Level 1*] and the American Academy of Pediatrics [20, *Level 9*] recommend beginning with some form of behavioural intervention, as it has been shown to be efficacious.

5.1.3 Non-Stimulants

The non-stimulant medications used in ADHD include atomoxetine, tricyclic antidepressants (TCAs), neuroleptics, bupropion, clonidine, guanfacine and modafinil. Only the first three drugs are available in Malaysia. The evidence for atomoxetine is stronger compared to other non-stimulants. [25, *Level 1*]

(a) Atomoxetine

Atomoxetine is a noradrenergic reuptake inhibitor that is superior to placebo. [62, *Level 2*; 63, *Level 2*] Atomoxetine has been shown to be effective for short [62, *Level 2*; 64, *Level 3*; 63, *Level 2*; 8, *Level 3*] and long term use. [65, *Level 2*] However MPH has a greater treatment effect than atomoxetine [65, *Level 2*] and the effect size was 0.62 for atomoxetine compared to long-acting MPH at 0.95. [66, *Level 1*]

Atomoxetine may have fewer side effects on appetite and sleep than stimulants but it may cause more nausea and sedation. [25, *Level 1*] Patients and parents should be warned of the risk of suicidal thinking which may occur during the first few months of treatment. [25, *Level 1*]

Atomoxetine may be considered or preferred for ADHD patients with an active substance abuse problem, those with severe side effects to stimulants, tics, Tourette's disorder, mood lability or comorbid anxiety. [25, *Level 1*; 43, *Level 1*]

(b) Tricyclic antidepressants (TCA)

Most of the studies on TCAs are before 1996. In one systematic review it was demonstrated that there was either moderate or robust response rates to TCAs e.g. imipramine, desipramine, amitriptyline, clomipramine, nortryptyline. [46, *Level* 1]

Some studies reported less consistent effects on cognition than on behaviour compared with the stimulants. [46, *Level* 1 ; 67, *Level* 3] One of the most common side effects is cardiac toxicity and therefore, cardiac evaluation is recommended when TCA's are being used.

(c) Neuroleptics

Neuroleptics used include haloperidol, chlorpromazine and risperidone. However these drugs are inferior to stimulants and are usually used in ADHD patients with comorbid mental retardation or autism. [46, *Level* 1 ; 68, *Level* 3 ; 69, *Level* 2] Risperidone, an atypical neuroleptic, has a better side effect profile than conventional neuroleptics and is well tolerated. [70, *Level* 1]

(d) Others

α-agonists like clonidine have also been used and studies conclude that it has a small to moderate effect size. [71, Level 1] Guanfacine has been shown to be superior to placebo in the treatment of ADHD and comorbidtic disorders. [72, Level 3]

There is limited evidence on the effectiveness of bupropion in the treatment of ADHD. [73, *Level* 3] Modafinil which has been more recently studied is effective compared to placebo. [61, *Level* 2; 74, *Level* 3] All the above drugs are not available in Malaysia.

RECOMMENDATION
Medication for **preschoolers** should be initiated by a child psychiatrist OR a paediatrician familiar with the management of ADHD in this goup. **(Grade C)**
Stimulants OR atomoxetine should be used. **(Grade A)**
Long acting stimulants or atomoxetine should be considered due to convenience, adherence and stigma reduction. **(Grade B)**
When stimulants or atomoxetine do not produce response or have serious side effects, TCAs or neuroleptics may be prescribed. **(Grade B)**
If medication does not result in satisfactory treatment, a review of diagnosis and management should be considered. **(Grade A)**

5.1.4 Medication Counselling

Health-care providers, parents, caregivers and patients should understand the need to comply with medication. There are various aspects that need to be reviewed including:

(i) Administration

Dosage, titration and side effects of medication are shown in Appendix 4. Although generally safe, stimulant medications do have side effects and some suggestions to manage these are provided in Appendix 6.

(ii) Side effects

Mild growth suppression over 2 years has been documented in children. However there is no height deficit when these children are followed up to adulthood. It is recommended that serial plotting of height and weight on growth charts should be considered once to twice a year. 'Drug holidays' or switching to another medication may be considered once a change in height or weight crosses two percentile lines on the growth chart. [25, *Level* 1]

(iii) Potential for abuse

There have been concerns of substance abuse with the use of stimulants. However studies have shown that stimulants do not contribute to risk for substance experimentation, use, dependence or abuse by the time adulthood is reached, and may in fact protect against later substance misuse. [75, *Level* 1, 76, *Level* 6]

(iv) Drug holidays

Drug holidays refer to periods when patients are allowed by their doctors to temporarily stop their medications. A common reason for drug holidays is to avoid side effects of medication (sleep delay, appetite suppression and perceived or real tolerance to therapy). [77, *Level* 8] Drug holidays should be tailored to the preferences and needs of the child and family.

Drug holidays' should be initiated in low stress times such as vacations. [25, *Level* 1] They should not be initiated at the beginning of the school year [25, *Level* 1] and around examination periods or during stressful situations.

Counselling points

- Importance of adherence
- Pharmacokinetics and pharmacodynamics of medications
- Management of adverse effects and monitoring of growth parameters
- Addressing fears and concerns of substance abuse and growth suppression
- Appropriate 'drug holidays'

RECOMMENDATION

- Initiation of medication should include medication counselling. **(Grade B)**
- Children on stimulant medication should have their height and weight regularly monitored. **(Grade A)**
- 'Drug holidays' may be offered in certain circumstances. **(Grade C)**

5.2. Non-Pharmacological Treatment

5.2.1 Psycho-education

Psycho-education is an established component in the treatment of ADHD. Although there is limited research on the effectiveness of psycho-education, many guidelines have recommended its usage. [2, *Level* 9; 78, *Level* 9; 25, *Level* 1]

Psycho-education

It involves educating the parent and child about the disorder by providing general advice to help improve the child's academic and behavioural functioning.

RECOMMENDATION

Psycho-education should be provided to children and their families. **(Grade B)**

5.2.2 Parent training and behavioural interventions

Parent training involves teaching parents behavioural approaches in the management of their children. This is to bring about positive behavioural change as well as provide opportunities to alter the child's environment.

Parent training has been shown to reduce parental stress and helps parents to cope better. It also improves compliance to medication and reduces severity of ADHD symptoms.[79, *Level* 8; 80, *Level* 4]

The most significant impact of parent training and behavioural intervention is the reduction of internalising symptoms and the improvement in academic performance. [81, *Level* 1; 82, *Level* 3] When combined with medication, it reduces disruptive behaviour and results in greater improvement in discipline.[83, *Level* 2; 82, *Level* 3]

Evidence shows that parent training programmes like Barkley Parent Training Programme, Forehand's Parent Training Programme, Positive Parenting Programme (Triple P)[84, Level 9; 85, Level 3] and Webster-Stratton [86, Level 3] have positive outcomes.

Parent training is best carried out by trained professionals.[87, Level 3] These interventions should also be imparted to other household members who are involved with the care of these children. Parents can be trained in individual sessions or in groups. However such established formal training programmes are lacking in Malaysia.

Trained professionals include psychiatrists especially child psychiatrists, clinical psychologists, occupational therapists, paediatricians, medical practitioners & teachers who have been trained in an established parenting programme.

The Development Group and the Review Committee recognises the lack of resources for formal parent training. there is a role in advising parents on how to deal with specific problems and difficult behaviours in their children. This advice on behavioural management is in Appendix 7.

Behavioural interventions involves working with parents to assist them in structuring an environment in which the child will have clear, firm, consistent and predictable limits, rules and consequences.[2, Level 9]

RECOMMENDATION

Parental training should be offered by trained professionals as it improves symptoms in the patient and enhances coping mechanisms especially for the parents. **(Grade B)**

Parental training should wherever possible be used in combination with medication therapy. **(Grade A)**

Parents should be given advice on how to manage the behaviour of the child. **(Grade C)**

5.2.3 School based intervention

School based interventions involve active participation of teachers. The outcome of these interventions is to improve academic, organisational and social skills. [88, Level 7] School based therapy includes self management intervention and token reinforcement (refer Appendix 8). At the present moment, there is no structured school based programme for ADHD under the Ministry of Education.

Children whose teachers were trained in a school based intervention training program showed improvement in their primary symptoms. [89, Level 3] Improvement in reading and mathematics was seen in children whose teachers had access to support and consultation. [88 , Level 2]

School based interventions are effective in reducing ADHD symptoms as well as improving academic and social outcomes when combined with pharmacological therapy. [90, Level 1]

Clinicians should assist the family in acquiring special provisions from the Education Department to help the child during examinations which includes

- Extra time for each paper
- Exam questions to be read out (reader)
- Special room with minimum distractions.
- Special devices e.g. computers.

RECOMMENDATION
A structured school based intervention programme should be made available. **(Grade A)**
The child should be placed in a mainstream classroom with provision of teacher's aide. **(Grade C)**

5.2.4 Occupational therapy

The goal of occupational therapy is to help master day to day skills, be engaged at school and at home by improving attention, controlling impulsivity and hyperactivity. [91, Level 9]

Different types of therapy have been tried on ADHD children and their families which include social skills training, [92, Level 7] [93, Level 8] weighted vest [94, Level 9], neurobio-feedback combined with training in meta-cognitive modalities. [95, Level 9] The evidence from these studies is poor. Other alternatives like sensory integration and exercise have not been extensively studied.

Although there is no strong evidence, occupational therapy has been noted to be beneficial in the management of ADHD. This includes improvement in activities of daily living and social functioning.

5.2.5 Diet intervention

Most studies looking at dietary modifications for ADHD were inconclusive. These include introduction of polyunsaturated fatty acids (PUFA's), [24, Level 2] mineral supplements, [96, Level 7; 97, Level 8] and reduction of sugars. [98, Level 9]

If parents suspect a particular food item causes increased symptoms of hyperactivity, attempts should be made to document this association. If behavioural changes are noted, the particular food item should be eliminated.

RECOMMENDATION
Dietary modifications should not be routinely recommended.**(Grade C)**
Parents are encouraged to monitor the effects of specific food items on their child's behaviour and inform their doctor.**(Grade C)**

5.2.6 Alternative interventions

Most of the studies conducted using Electroencephalography biofeedback (EEG biofeedback) or neuro-feedback failed to show sufficient evidence in the treatment of ADHD. [99, Level 6; 100, Level 7; 101, Level 7; 102, Level 7] Similarly there is lack of evidence for the usage of homeopathic treatment. [103, Level 8]

RECOMMENDATION
Alternative interventions are not recommended. **(Grade C)**

5.2.7 Support group

Peer support group for parents and patients should be offered to allow sharing of experiences and exchange of information. [1, Level 9]

5.3 Combination Therapy

A multidimensional model consists of several therapies done concurrently including pharmacological as well as behavioural treatment.

The Multimodal Treatment of ADHD Study (MTA) is a landmark study which included 579 children with ADHD. The modalities included in MTA were Medical Management, Intensive Behavioural Intervention (consists of parent training, school

based intervention and a summer treatment programme), a Combination Treatment (combination of medication and behavioural management), and a Community Treatment group. Patients on Medical Management and the Combination Treatment showed greater improvement compared to the other two modalities. [104, *Level* 2] Similar findings were obtained in another study involving 75 patients. [105, *Level 4*]

For the MTA subjects, follow-up at 24 months showed continued significant advantage of medical management alone and also combination treatment. [106 , *Level* 2] However, by the 36 month follow-up, the earlier advantage of having had 14 months of medication management was no longer apparent. [107, *Level* 6]

At present the intensive behavioural therapy model of the MTA study is not feasible in most areas of Malaysia due to lack of resources.

RECOMMENDATION

Either pharmacotherapy alone **OR** combination treatment (pharmacotherapy and non-pharmacological treatment) should be offered. **(Grade A)**

6. CRITERIA FOR REFERRAL

6.1 Referral from teacher/ primary care provider to paediatrician/ psychiatrist

Teachers and primary healthcare staff need to refer the child for medical attention if there is:

- Suspicion of ADHD
- Management difficulties

6.2 Referral from paediatrician / psychiatrist to child psychiatrist / clinical psychologist

Consult with or refer to Child and Adolescent Mental Health Professionals when:

- There is uncertainty about diagnosis
- Managing preschoolers
- There is a lack of response to treatment
- Prominent comorbidities exist (e.g. substance abuse)
- Severe side effects of medication are present

7. FOLLOW UP

It is recommended that the clinician provide periodic follow-up for the child and adolescent diagnosed with ADHD. This would include monitoring height, weight, blood pressure, pulse, emergence of comorbidity and medical conditions; [25, *Level* 1] monitoring target outcomes and adverse effects.

Frequency of follow-up visits during the months following diagnosis allows further exploration of issues identified in the initial assessment as well as education about ADHD. Frequency of follow-up visits should be individualised and dependent on response to management, medication and psychosocial interventions. [25, *Level* 1]

Intervals between visits may be increased when patients are:

- symptom free
- meeting desired outcome measures
- without serious side effects
- without significant academic difficulties

Adapted from Cincinnati Children's Hospital Medical Center – Evidence Based CPG on Outpatient Evaluation and Management of Attention Deficit/ hyperactivity Disorder. [2, *Level* 9]

Treatment of ADHD should continue as long as the symptoms persist and cause impairment. The decision to stop medication will depend on the child/ adolescent [25, *Level* 1]

- being symptom-free for at least 12 months while on medication, and
- not deteriorating, or have symptoms re-emerging when doses are missed or reduced
- Being able to concentrate while not on medication

RECOMMENDATION

Children with ADHD should be regularly followed-up by their clinicians. **(Grade A)**

The treatment of ADHD should continue as long as the symptoms persist. Cessation of medication may be considered after proper evaluation. **(Grade A)**

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REFERENCES

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APPENDIXES

☑ Checklist by Parents and Teachers

No.		Yes	No	Unsure
1	Does the child have difficulties paying attention?			
2	Is your child forgetful?			
3	Does the child often loses or misplaces things?			
4	Does the child have poor academic performance?			
5	Is the child easily distracted?			
6	Does the child have difficulty in focusing on a task?			
7	Does the child shift from task to task without completing any?			
8	Does the child often interrupt others?			
9	Does the child tend to blurt answers even before the question is completed?			
10	Does the child have difficulty waiting for his/her turn in school and / or social games?			
11	Does the child frequently do dangerous things?			
12	Does the child seem to be constantly on the move?			
13	Does the child have difficulty remaining in his/her seat; fidgeting excessively?			
14	Does the child have difficulty engaging in quiet activities?			

Other remarks

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Diagnostic criteria for ADHD based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision

A. Either (1) or (2):

(1) Inattention:

Six (or more) of the following symptoms of inattention have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

(a) Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities.

(b) Often has difficulty sustaining attention in tasks or play activities.

(c) Often does not seem to listen when spoken to directly.

(d) Often does not follow through on instructions and fails to finish school work, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions).

(e) Often has difficulty organizing tasks and activities.

(f) Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework).

(g) Often loses things necessary for tasks or activities (e.g. toys, school assignments, pencils, books, or tools).

(h) Is often easily distracted by extraneous stimuli.

(i) Is often forgetful in daily activities.

(2) Hyperactivity-impulsivity:

Six (or more) of the following symptoms of hyperactivity-impulsivity have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

Hyperactivity

(a) Often fidgets with hands or feet or squirms in seat.

(b) Often leaves seat in classroom or in other situations in which remaining seated is expected.

(c) Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness).

(d) Often has difficulty playing or engaging in leisure activities quietly.
(e) Is often "on the go" or often acts as if "driven by a motor".
(f) Often talks excessively.

Impulsivity

(g) Often blurts out answers before questions have been completed.
(h) Often has difficulty awaiting turn.
(i) Often interrupts or intrudes on others (e.g. butts into conversations or games).

B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before age 7 years.
C. Some impairment from the symptoms is present in two or more settings (e.g. at school [or work] and at home).
D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning.
E. The symptoms do not occur exclusively during the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder and are not better accounted for by another mental disorder (e.g. Mood Disorder, Anxiety Disorder, Dissociative Disorders, or a Personality Disorder).

Code based on type:

314.01 **Attention-Deficit/Hyperactivity Disorder**, **Combined Type:**
If both Criteria A1 and A2 are met for the past 6 months

314.00 **Attention-Deficit/Hyperactivity Disorder, Predominantly Inattentive Type:**
If Criterion A1 is met but Criterion A2 is not met for the past 6 months

314.01 **Attention-Deficit/Hyperactivity Disorder, Predominantly Hyperactive-Impulsive Type:**
If Criterion A2 is met but Criterion A1 is not met for the past 6 months

Coding note:
For individuals (especially adolescents and adults) who currently have symptoms that no longer meet full criteria, "In Partial Remission" should be specified.

ICD 10 CLASSIFICATION (World Health Organization 1992)

HYPERKINETIC DISORDERS

Note: The research diagnosis of hyperkinetic disorder requires the definite presence of abnormal levels of inattention and restlessness that are pervasive across situations and persistent over time that can be demonstrated by direct observation, and that are not caused by other disorders such as autism or affective disorders. Eventually, assessment instruments should develop to the point where it is possible to take a quantitative cut-off score on reliable valid and standardised measures of hyperactive behaviour in the home and classroom, corresponding to the 95th percentile on both measures. Such criteria would then replace G1 and G2 below.

G1. Demonstrable abnormality of attention, activity and impulsivity at home, for the age and developmental level of the child, as evidenced by (1), (2) and (3):

(1) at least three of the following attention problems:
- (a) short duration of spontaneous activities;
- (b) often leaving play activities unfinished;
- (c) over-frequent changes between activities;
- (d) undue lack of persistence at tasks set by adults;
- (e) unduly high distractibility during study e.g. homework or reading assignment;

(2) plus at least three of the following activity problems:
- (a) very often runs about or climbs excessively in situations where it is inappropriate; seems unable to remain still;
- (b) markedly excessive fidgeting & wriggling during spontaneous activities;
- (c) markedly excessive activity in situations expecting relative stillness (e.g. mealtimes, travel, visiting, church);
- (d) often leaves seat in classroom or other situations when remaining seated is expected;
- (e) often has difficulty playing quietly.

(3) plus at least one of the following impulsivity problems:
   (a) often has difficulty awaiting turns in games or group situations;
   (b) often interrupts or intrudes on others (e.g. butts in to others' conversations or games);
   (c) often blurts out answers to questions before questions have been completed.

G2. Demonstrable abnormality of attention and activity at school or nursery (if applicable), for the age and developmental level of the child, as evidenced by both (1) and (2):

(1) at least two of the following attention problems:
   (a) undue lack of persistence at tasks;
   (b) unduly high distractibility, i.e. often orienting towards extrinsic stimuli;
   (c) over-frequent changes between activities when choice is allowed;
   (d) excessively short duration of play activities;

(2) and by at least three of the following activity problems:
   (a) continuous (or almost continuous) and excessive motor restlessness (running, jumping, etc.) in situations allowing free activity;
   (b) markedly excessive fidgeting and wriggling in structured situations;
   (c) excessive levels of off-task activity during tasks;
   (d) unduly often out of seat when required to be sitting;
   (e) often has difficulty playing quietly.

G3. Directly observed abnormality of attention or activity. This must be excessive for the child's age and developmental level. The evidence may be any of the following:

1) direct observation of the criteria in G1 or G2 above, i.e. not solely the report of parent or teacher;
(2) observation of abnormal levels of motor activity, or off-task behaviour, or lack of persistence in activities, in a setting outside home or school (e.g. clinic or laboratory);
(3) significant impairment of performance on psychometric tests of attention.

G4. Does not meet criteria for pervasive developmental disorder (F84), mania (F30), depressive (F32) or anxiety disorder (F41).

G5. Onset before the age of seven years.

G6. Duration of at least six months.

G7. IQ above 50.

F90.0 Disturbance of activity and attention

The general criteria for hyperkinetic disorder (F90) must be met, but not those for conduct disorders (F91).

MEDICATIONS in ADHD

STIMULANTS

Drug / Types	Minimum Dose	Maximum Dose	Titration & Timing	Common Adverse Effects	Duration of Action	Comments
Methylphenidate • **Short- acting** - Ritalin (10mg)	8yrs (<25kg) start with 5mg BD >8yrs (>25kg) start with 10mg BD (Dosage range : 0.3-0.7 mg/kg/ dose) 3-5 years old : 2.5mg/day or 0.15mg/kg/day	Total daily dose not to exceed 60mg/day. Max per dose 20-30mg. 3-5 years old : 30mg/day or 1mg/kg/day	Increase by 2.5-5mg/dose (depending on weight) a.m. & noon; add 4 p.m. dose as needed.	Decreased appetite, insomnia, headaches, increased heart rate	3-5 hours	Discontinue if no response after 1 month and treatment suspended periodically to assess child's condition. Short acting often used for small children (<16kg).
• **Long-acting** - Ritalin LA Modified Release (20mg, 30mg, 40mg)	Children ≥6 yrs and adults: 20mg Once daily in a.m.	Total daily dose not to exceed 60mg/day.	May increase 10mg daily at wee,kly intervals.	As above	8-12 hours	No dosage adjustments required in renal / hepatic impaired patients.
- Ritalin SR (20mg)	20mg in a.m. only (consider for use in children tolerating 10mg/ dose a.m. and noon)	Total daily dose not to exceed 60mg/day.	Add 5mg-10mg in morning and/or at 4 p.m.	As above	3-8 hours	
- Concerta Extended Release (ER) 18mg, 36mg, 54mg)	Children ≥6 yrs and adults: 18mg once daily in the a.m.	Max. 72mg per day	Adjust doses every 1-2 weeks as needed and tolerated.	As above	12 hours	Concerta ER Tablet shells may appear in stool.

STIMULANTS

APPENDIX 4 (cont..)

Drug / Types	Minimum Dose	Maximum Dose	Titration & Timing	Common Adverse Effects	Duration of Action	Comments
Amphetamine • **Short acting** - Adderall (5mg, 7.5mg, 10mg, 12.5mg, 15mg, 20mg, 30mg)	3-5 yr old: 2.5mg once daily	Max dose 40mg/ day given in 1-3 divided doses. (>6yr: Max dose 60mg/day given in 1-3 divided doses)	Increase daily dose by 2.5mg at weekly intervals until optimal response achieved.	Decreased appetite, insomnia, gastrointestinal discomfort and emotional lability, cardiac abnormalities	3-5 hrs	
	≥6 yr-12 yr: 5mg once or twice daily. >12 yr and adults: 10mg once daily		Increase daily dose by 5mg at weekly intervals until optimal response achieved. Increase daily dose by 10mg at weekly intervals until optimal response achieved.			
- Dexedrine (5mg cap) - DextroStat (5mg, 10mg)	3-5 yr old: 2.5mg once daily ≥6 yr: 5mg once or twice daily.	Max dose 40mg/ day given in 1-3 divided doses	Increase daily dose by 2.5mg at weekly intervals until optimal response achieved. Increase daily dose by 5mg at weekly intervals until optimal response Achieved			
• **Long-acting** - Dexedrine Spansule (5mg, 10mg, 15mg)	≥6 yr: 5-10mg once or twice daily	Max. 40mg			8-12 hrs	
- Adderall XR (5mg, 10mg, 15mg, 20mg, 25mg, 30mg)	≥6 yr: 10mg once daily	Max. 30mg once daily	Increase daily dose by 5mg or 10mg at weekly intervals until optimal response achieved.			Adderall XR cap may be opened and sprinkled on soft foods.
- Lisdexamfetamine (30mg, 50mg, 70mg)	30mg once daily	Max. 70mg				

Note: Amphetamine-containing drugs are currently not available in Malaysia

NON STIMULANTS

APPENDIX 4 (cont..)

Drug / Types	Minimum Dose	Maximum Dose	Titration & Timing	Common Adverse Effects	Duration of Action	Comments
- Atomoxetine (10mg, 18mg, 25mg, 40mg, 60mg) (Strattera)	Children and adolescent ≤ 70kg: Initial dose 0.5mg/kg/day once daily Children and adolescent >70kg: Initial dose 40mg once daily	1.4mg/kg or 100mg, whichever is less 100mg/day	After 3 days of dosing increase to 1.2mg/kg/day. daily or divided into 2 doses, in morning and evening. After 3 days of dosing, increase to 80mg once daily or divided into 2 doses; in morning and evening.	Nausea, vomiting, abdominal pain, anorexia, dizziness, somnolence, skin rash, pruritus In adolescents- dysmenorrhoea, erectile dysfunction and ejaculatory dysfunction	May take several weeks for optimal effect	Renal failure: No adjustments. Hepatic failure : Moderate – 50% of normal dose Severe – 25% of normal dose
- Imipramine (10mg, 25mg) * Usually for older children and adolescent	0.5-1 mg/kg/day PO in 2-3 divided doses or 50mg/day	Not to exceed 5mg/kg/day or 200mg/day	Increase 1mg/kg/week up to 4mg/kg/day.	Cardiac conduction disturbances, dry mouth, urinary retention, headache	Onset of action: Peak effect usually after 2 weeks.	Renal failure: No adjustments.
- Amitryptiline hydrochloride	0.5-1mg/kg/day PO in 3 divided doses or 50mg/day.	Up to 3mg/kg/day for children 9-12 years old or 200mg/day.		Cardiac toxicity, dry mouth, constipation occasionally leading to paralytic ileus, urinary retention, blurred vision and disturbances in accommodation, increased intra-ocular pressure, and hyperthermia.	Onset of action: Peak effect usually after 2 weeks.	Use with caution in hepatic impairment. Non-dialyzable.
- Bupropion SR 150mg Tablet	3mg/kg/day up to 150mg/day.	250mg/day or 300mg-400mg for adolescents.	6-12 year old; gradually increase over 2 weeks to 6mg/kg/day up to 250mg/day in divided doses.	Sedation, constipation, dryness of mouth, may lower seizure threshold.	-	Max 150mg with hepatic disorder; avoid in severe hepatic cirrhosis. Renal impairment: Max 150mg daily.

HOW TO USE STIMULANT MEDICATION

Selecting the order of stimulants to be used

There are no clinical predictors to indicate which child will respond to which stimulant, thus the choice of stimulant is left to the physician and the parents. [108, *Level* 9] The decision should be based on the presence of other conditions such as epilepsy, adverse reactions, problems with compliance, drug diversion and misuse. [43 , *Level* 1]

MPH is usually the first choice, but dextroamphetamine may be preferred in children with epilepsy. [48 , *Level* 9]

Dose is usually not calculated based on body weight but on individual response, titrating upwards from an initial low dose and adjusting the dose in light of response. However, the dosage range based on the body weight may be a guide during titration. The aim is to find the best dose that achieves the highest efficacy with minimal side effects.

Titration is easiest with the short-acting forms and should begin with a low dose, the starting dose of stimulant is 5 mg for MPH (and 2.5 mg for DEX/AMP) and generally given in the morning after breakfast. The need for additional doses in the afternoon and evening can be determined upon response to treatment and child's schedule and behavior e.g. morning and afternoon school performance or activities.

Deciding on Minimum and Maximum Doses.

Increasing the dosage can be as frequent as **weekly,** until there is an adequate response or until unacceptable side effects are observed. The dose generally should be increased in weekly increments of 5-10 mg per dose for MPH.

Dosages and schedules must be individualized depending on target goals and must take into account child's age, home and school environment. [39, *Level* 9] Clinicians and family are advised to make their goals realistic and achievable. Spencer et al. [46, *Level* 1] suggested that adult-sized adolescents may need doses of MPH at a mean oral dose of 1.1 mg/kg/day to achieve an adequate response, but careful monitoring for side effects should be undertaken at such doses. Children weighing less than 25 kg generally should not receive single doses greater than 15 mg of MPH.

A second dose of a short acting medication given in the afternoon or evening will benefit children who have difficulty completing their homework. This also helps those children having difficulties in relationships with peers and family members.

There have been reports of inter-dose rebound, and increased hyperactivity/ impulsivity in the evening when the stimulant is no longer effective.

Clinicians may use long-acting forms as initial treatment with no need of titration from short-acting. [25, *Level* 1] Long-acting stimulants should be given as a single dose in the morning.

During titration, parent and teacher rating scales can be used to measure symptoms and side effects. Apart from target symptoms, monitoring should include recording of BP and pulse rate (at each dose adjustments and then every six months), height, weight on growth charts. Appearance of tics, depression and irritability, lack of spontaneity, withdrawal and rebound behaviour should also be assessed at every visit. [48, *Level* 9] It may take one to three months to establish the best dose and medication for the patient, thus they will need frequent follow-up. If 2 or more stimulants have been tried without success, then other medications may be considered. [20, *Level* 9]

Short-acting stimulants are often used as initial treatment in small children (<16 kg in weight), as there are no long-acting forms in a sufficiently low dose [25, *Level* 1] or in children who are vulnerable to side effects. [108, *Level* 9] Once the dose is established, patients are usually followed-up every 12-24 weeks.

Side Effects

Side effects are mostly due to the adrenergic activity and are dose dependent and can be managed by monitoring, adjusting the dose or timing, or changing the stimulant. Many of the side effects are transient and may resolve without treatment. It is prudent to monitor side effects and not to compromise the patient's health such that it may cause the patient and family to stop medication. [25, *Level* 1]

Early reports indicate that children with a history or family history of tics were at a greater risk of developing tic disorder when exposed to stimulants. Recent work has challenged these views; studies have reported that MPH effectively suppressed ADHD symptoms with only a weak effect on the frequency of tics. [46, *Level* 1] Children with co-morbid ADHD and tic disorders, on average, show a decline in tics when treated with stimulants. [25 , *Level* 1]

Concerns have been raised about possibility of growth suppression in patients with ADHD and treated with stimulants. Although stimulants routinely produce anorexia and weight loss, their effect on growth in height is less certain. [46, *Level* 1]

Controlled trials of stimulants do not support the widespread belief that stimulant medications induce aggression, mood lability and suicidal ideation. [25, *Level* 1] In fact reports suggest overall aggressive acts and antisocial behavior decline when ADHD patients are treated with stimulants.

Elevated heart rate and blood pressure have been observed in children undergoing therapy with stimulants. Children who receive too high a dose or who are overly sensitive may become over-focused or appear dull or overly restricted. [20, *Level* 1] Rarely, with high doses, do children experience psychotic reactions, mood disturbances, or hallucinations. [20 , *Level* 1]

APPENDIX 6

MANAGEMENT OF COMMON ADVERSE EFFECTS ASSOCIATED WITH STIMULANT USE

ADVERSE EFFECTS	MANAGEMENT
Anorexia, weight loss, stomach-ache	• Administer dose with/after meals • High calorie breakfast and snacks after school/bedtime • Limit stimulant to high priority needs • Consider dieticians referral for nutrition evaluation/ counselling • Give “drug holidays”
Insomnia	• Low stress “wind down time” after school • Administer dose earlier in day • Discontinue afternoon/evening dose • Change to short-acting preparation • Consider adjunctive medications (e.g. antidepressants)
Rebound irritability/moodiness (usually 4-5 hours after last dose)	• Overlap stimulant dosing • Step-down dosing • Try long-acting or combination short/long-acting preparations
Generalized irritability, dysphoria, agitation	• Assess timing of symptoms (e.g. peak withdrawal, what does this mean) • Consider co-morbid condition • Reduce dose or change to long-acting preparation • Consider alternative/adjunctive medication (e.g. another stimulant, antidepressant)
Tics (simple vocal, motor)	• Monitor if mild or infrequent • Weigh benefit-risk and discuss with parents • Consider alternative medication (e.g. atomoxetine) or adjunctive medication
Headache	• Assess timing • Reduce dose with gradual return to therapeutic dose • Try long-acting preparation • Consider alternative medication • If mild analgesics do not help, try different stimulant
Linear growth impairment	• Limit stimulant to high priority needs (e.g. try weekend/vacation drug “holidays”) If significant, consider alternative medication

ADVICE FOR BEHAVIOURAL MANAGEMENT

Adapted from University of Michigan [39, *Level* 9]

General

1. Schedule one on one time with your child every day to let her/him know how important he or she is to you. Even 10 to 15 minutes regularly will make a difference.
2. You are his best and most important teacher.
3. Be aware of and notice your child's strength areas and look for opportunities to praise him.
4. Be aware that children with ADHD benefit from more frequent feedback.
5. Remain calm and in control.
6. Model the behaviour you would like to see from your child.
7. Use schedules and routines.
8. Post lists and reminders for the routines in places they will be seen.
9. Discuss the behavioural goals with your child.
10. Discuss the behavioural target(s), expectation and the feedback with your child's other caretakers so she gets a consistent message.
11. Give directions one at a time.
12. Track your child's response.
13. Target one to three behaviours at a time for changing.
14. Use desired activities (television, video games) as privileges/rewards for success on behavioural targets.
15. All day is a long time for your child and you to work on behavioural goals. Therefore, consider focusing on the behaviour(s) for close tracking and feedback for an hour a day or around a regular routine.
16. Ensure regular mealtimes and good rest for your child and you.

Younger Children

1. Routines are very important.
2. Post pictures for the order of routines you'd like her to learn (e.g. the steps to get ready for bed).
3. Balance higher energy and quieter activities through the day.
4. Choose your battles – ignore minor misbehaviours.
5. Give choices but limit the number
6. Avoid high-risk situations and certain times of the day (shopping mall, grocery shopping on the way home)
7. Use and reinforce "rules" (e.g. keeping hands to self) immediately before venturing into a community setting.
8. Consider taking "practice trips" that will allow you to implement a consequence (leaving if the rules are not followed) without disturbing your planned and needed shopping trip.

School-age Child at Home

1. Invite peers one a time to reduce stimulation, encourage friendship and allow you to provide feedback about what went well.
2. Include homework time as a part of the family routine.
3. Organize a non-distracting place for homework.
4. Check your child's school bag everyday and help her organize the homework into doable portions.
5. Suggest brief breaks between the homework portions.
6. Use the activities your child enjoys as incentives for getting work done (homework and chores).
7. Help your child use a system (e.g. labelled folders for each subject) to get the homework back to school.
8. Many children benefit from work with a tutor, and a high school or college student might be a less-costly choice.
9. Use repetition (e.g. going over the spelling list).
10. Be aware of those long-term assignments. Post the information. Discuss a timeline and stick to it.
11. Communicate with your child's teacher about homework, grades, and behaviour.
12. If your child is struggling, consider requesting for special education

APPENDIX 8

SCHOOL BASED INTERVENTION

The following are suggestions for implementation of school based intervention programme.

- An orderly and predictable classroom
- Consistent rules and expectations
- Regular breaks
- Classroom should not be in noisy areas – near toilet, canteen, main road, school field
- Place the child near the teacher
- Give short and simple instructions
- Periodically check to see the child stays focused
- Teach the child time management and study skills
- Reduce the need for the children to copy assignments from the board. Instead use handouts and worksheets.
- Establish a daily communication book between school and home regarding targeted behaviors and learning tasks (e.g. homework)
- Allow extra time to complete tasks especially in tests and examinations
- Teach self monitoring and self reinforcement skills
- Praise and reward performance and good behaviour
- Refrain from using verbal or physical punishments
- Consider allowing computers or other digital devices to help the child in the learning process

Modified from The European Clinical Guidelines for hyperkinetic disorder- first update 2004, Dupaul GJ, et al., 1997, University of Michigan 2005 [78, *Level 9* ; 89, *Level* 1 ; 39, *Level 9*

LIST OF ABBREVIATIONS

AACAP	American Academy of Child and Adolescent Psychiatry
ADHD	Attention Deficit Hyperactivity Disorder
DEX/AMP	Dexamphetamine
DSM-IV-TR (2000)	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision
ECG	Electrocardiogram
EEG	Electroencephalography
ER	Extended release
HKD	Hyperkinetic disorder
ICD 10	10th Revision of International Classification of Diseases
MTA	Multimodal Treatment of ADHD Study
MPH	Methlyphenidate
NICE	National Institute of Clinical Excellence
ODD	Oppositional defiant disorder
PO	Oral
TCA	Tricyclic Antidepressants

ACKNOWLEDGEMENT

The committee for this guideline would like to express their gratitude and appreciation to the following for their contribution:

- Panel of external reviewers who reviewed the draft.
- Ms Rosnah Siran, Matron, Health Technology Assessment Section, Ministry of Health.
- Technical Advisory Committee for Clinical Practice Guidelines for their valuable input and feedback.

DISCLOSURE STATEMENT

The panel members have completed disclosure forms. (Details are available upon request from the CPG Secretariat)

SOURCES OF FUNDING

The development of the CPG on Management of Attention Deficit Hyperactivity was supported financially in its entirety by the Ministry of Health Malaysia and was developed without any involvement of the pharmaceutical industry.

LEVELS OF EVIDENCE SCALE

LEVEL	STRENGTH OF EVIDENCE	STUDY DESIGN
1	Good	Meta-analysis of RCT, Systematic review
2	Good	Large sample RCT
3	Good to Fair	Small sample RCT
4		Non-randomised controlled prospective trial
5	Fair	Non-randomised controlled prospective trial with historical control
6	Fair	Cohort studies
7	Poor	Case-control studies
8	Poor	Non-controlled clinical series, descriptive studies multi-centre
9	Poor	Expert committees, consensus, case reports, anecdotes

SOURCE: ADAPTED FROM THE CATALONIAN AGENCY FOR HEALTH TECHNOLOGY ASSESSMENT & RESEARCH, (CAHTAR) SPAIN

GRADES OF RECOMMENDATION

A	At least one meta analysis, systematic review, or RCT, or evidence rated as good and directly applicable to the target population
B	Evidence from well conducted clinical trials, directly applicable to the target population, and demonstrating overall consistency of results; or evidence extrapolated from meta analysis, systematic review, or RCT
C	Evidence from expert committee reports, or opinions and /or clinical experiences of respected authorities; indicates absence of directly applicable clinical studies of good quality

SOURCE: MODIFIED FROM THE SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK (SIGN)