CLINICAL PRACTICE GUIDELINES

2020

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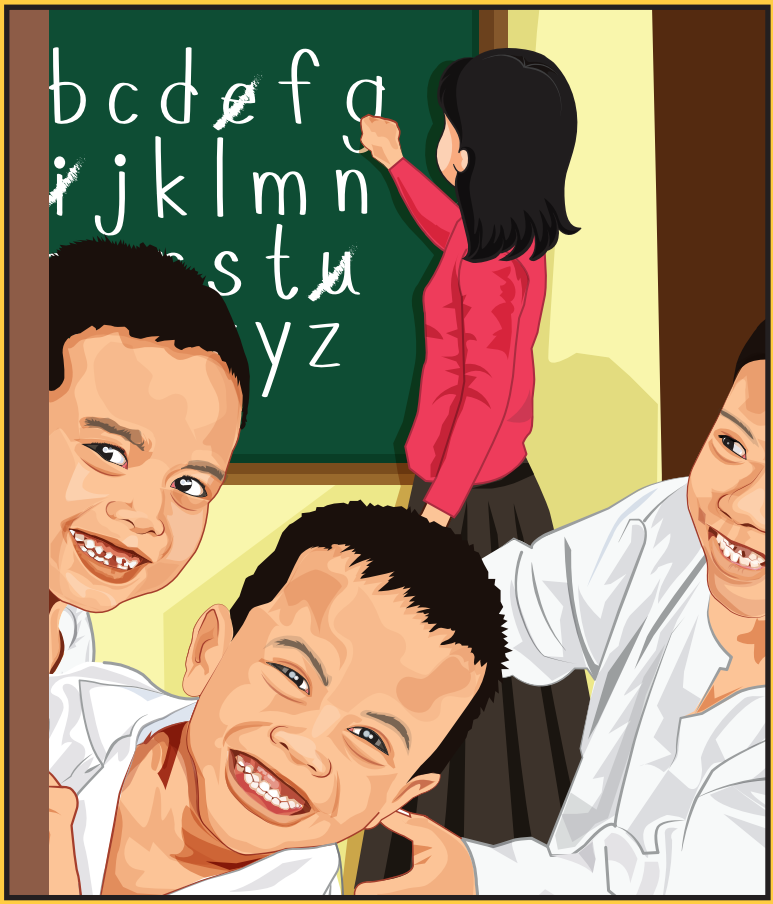
Management of Attention-Deficit/Hyperactivity Disorder in Children & Adolescents

(Second Edition)



Ministry of Health Malaysia

Malaysian Psychiatric Association

Malaysian Child and Adolescent Psychiatric Association

Academy of Medicine Malaysia

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STATEMENT OF INTENT

These clinical practice guidelines (CPG) are meant to be guides for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily guarantee the best outcome in every case. Every healthcare 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.

UPDATING THE CPG

These guidelines were issued in 2020 and will be reviewed in a minimum period of four years (2024) or sooner if new evidence becomes available. When it is due for updating, the Chairperson of the CPG or National Advisor of the related specialty will be informed about it. A discussion will be done on the need for a revision including the scope of the revised CPG. A multidisciplinary team will be formed, and the latest systematic review methodology used by MaHTAS will be employed.

Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions, corrections will be published in the web version of this document, which will be the definitive version at all time. This version can be found on the websites mentioned above.

TABLE OF CONTENTS

TABLE OF CONTENTS

LEVELS OF EVIDENCE

Level	Study design
I	Evidence from at least one properly randomised controlled trial
II-1	Evidence obtained from well-designed controlled trials without randomisation
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or group
II-3	Evidence from multiple time series with or without intervention; dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III	Opinions of respected authorities based on clinical experience; descriptive studies and case reports; or reports of expert committees

SOURCE: US / CANADIAN PREVENTIVE SERVICES TASK FORCE 2001

FORMULATION OF RECOMMENDATION

In line with new development in CPG methodology, the CPG Unit of MaHTAS is adapting **Grading Recommendations, Assessment, Development and Evaluation (GRADE)** in its work process. The quality of each retrieved evidence and its effect size are carefully assessed/reviewed by the CPG Development Group. In formulating the recommendations, overall balances of the following aspects are considered in determining the strength of the recommendations:-

- overall quality of evidence
- balance of benefits versus harms
- values and preferences
- resource implications
- equity, feasibility and acceptability

KEY RECOMMENDATIONS

The following are highlighted by the CPG Development Group as the key recommendations that answer the main questions addressed in the CPG and should be prioritised for implementation.

a. Assessment

- Information from parents/carers and teachers should be sought to increase accuracy of the attention-deficit/hyperactivity disorder (ADHD) assessment.
- Diagnosis of ADHD should be based on diagnostic criteria of Diagnostic and Statistical Manual of Mental Disorder Fifth Edition (DSM-5) or hyperkinetic disorders from International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10).
- Any child or adolescent presenting with academic difficulties, behavioural problems, mood disturbances, substance use or personality disorders should be evaluated for ADHD to prevent deleterious outcomes in adulthood.

b. Psychoeducation

- Psychoeducation should be offered in attention-deficit/hyperactivity disorder.

c. Non-pharmacological treatment

- Occupational therapy should be offered as an adjunct in attention-deficit/hyperactivity disorder (ADHD).
- The following therapies should be considered in ADHD:
  - organisational skills training
  - cognitive behavioural therapy-based interventions
- Parent training and behavioural intervention should be offered in ADHD.
- School-based interventions should be offered in ADHD.

d. Pharmacological treatment

- Methylphenidate should be offered to children aged ≥6 years and adolescents with attention-deficit/hyperactivity disorder (ADHD) if medication is indicated.

- If medication for ADHD is indicated in children <6 years old, it should be initiated by a child psychiatrist or a paediatrician with expertise in managing ADHD.

e. Combination treatment

- Combination treatment (pharmacological and non-pharmacological) should be considered in children ≥6 years of age and adolescents with attention-deficit/hyperactivity disorder when the symptoms persist and cause functional impairment.

f. Monitoring

- Healthcare providers should provide continued care and long-term monitoring to children and adolescents with attention-deficit/hyperactivity disorder.

GUIDELINES DEVELOPMENT AND OBJECTIVES

GUIDELINES DEVELOPMENT

The members of the Development Group (DG) for these Clinical Practice Guidelines (CPG) were from the Ministry of Health (MoH) and Ministry of Higher Education. There was active involvement of a multidisciplinary Review Committee (RC) during the process of the CPG development.

A systematic literature search was carried out using the following electronic databases: mainly Medline via Ovid and Cochrane Database of Systemic Reviews and others e.g. PubMed and Guidelines International Network (refer to **Appendix 1** for **Example of Search Strategy**). The search was limited to literature published on humans, "all child (0 to 18 years)" (in most searches), publication from year "2008 to Current" and English language. In addition, the reference lists of all retrieved literature and guidelines were searched and, experts in the field contacted to identify relevant studies. All searches were conducted from 19 Mac 2017 to 18 May 2018. Literature searches were repeated for all clinical questions at the end of the CPG development process allowing any relevant papers published before 21 January 2020 to be included. Future CPG updates will consider evidence published after this cut-off date. The details of the search strategy can be obtained upon request from the CPG Secretariat.

References were also made to other CPGs on attention-deficit/hyperactivity disorder (ADHD) e.g.:

- Canadian ADHD Practice Guidelines (CAP-Guidelines), 4.1 [Canadian ADHD Resource Alliance (CADDRA), 2020]
- Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents [American Academy of Pediatrics (AAP), 2019]
- Attention deficit hyperactivity disorder: diagnosis and management [National Institute for Health and Care Excellence (NICE), 2018]
- Management of attention deficit and hyperkinetic disorders in children and young people [Scottish Intercollegiate Guidelines Network (SIGN), 2009]

These CPGs were evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II prior to them being used as references.

A total of 14 clinical questions (CQ) were developed under different sections. Members of the DG were assigned individual questions within these sections (refer to **Appendix 2** for **Clinical Questions**). The DG members met 24 times throughout the development of these guidelines. All literature retrieved were appraised by at least two DG

members using Critical Appraisal Skill Programme checklist, presented in evidence tables and further discussed in each DG meetings. All statements and recommendations formulated after that were agreed upon by both the DG and RC. Where evidence was insufficient, the recommendations were made by consensus of the DG and RC. This CPG is based largely on the findings of systematic reviews, meta-analyses and clinical trials, with local practices taken into consideration.

The literature used in these guidelines were graded using the US/ Canadian Preventive Services Task Force Level of Evidence (2001), while the grading of recommendation was done using the principles of GRADE (refer to the preceding page). The writing of the CPG follows strictly the requirement of AGREE II.

On completion, the draft of the CPG was reviewed by external reviewers. It was also posted on the MoH Malaysia official website for feedback from any interested parties. The draft was finally presented to the Technical Advisory Committee for CPG, and the HTA and CPG Council MoH Malaysia for review and approval. Details on the CPG development methodology by MaHTAS can be obtained from Manual on Development and Implementation of Evidence-based Clinical Practice Guidelines published in 2015 (available at http://www.moh.gov.my/moh/resources/CPG_MANUAL_MAHTAS.pdf?mid=634).

OBJECTIVES

The objectives of the CPG are to provide evidence-based recommendations on the management of ADHD in the following aspects:

a. risk factors
b. assessment and diagnosis
c. treatment
d. referral and follow-up

CLINICAL QUESTIONS

Refer to **Appendix 2**.

TARGET POPULATION

1. Inclusion Criteria
Children and adolescents with ADHD (<18 years old)
In certain CQs, evidence is done on adults with ADHD

2. Exclusion Criteria
Management of other disorders with ADHD as co-morbidity is beyond the scope of this CPG.

TARGET GROUP/USERS

This document is intended to guide those involved in the management of ADHD at any healthcare level including:

i. doctors
ii. allied health professionals
iii. trainees and medical students
iv. patients and their advocates
v. professional societies

HEALTHCARE SETTINGS

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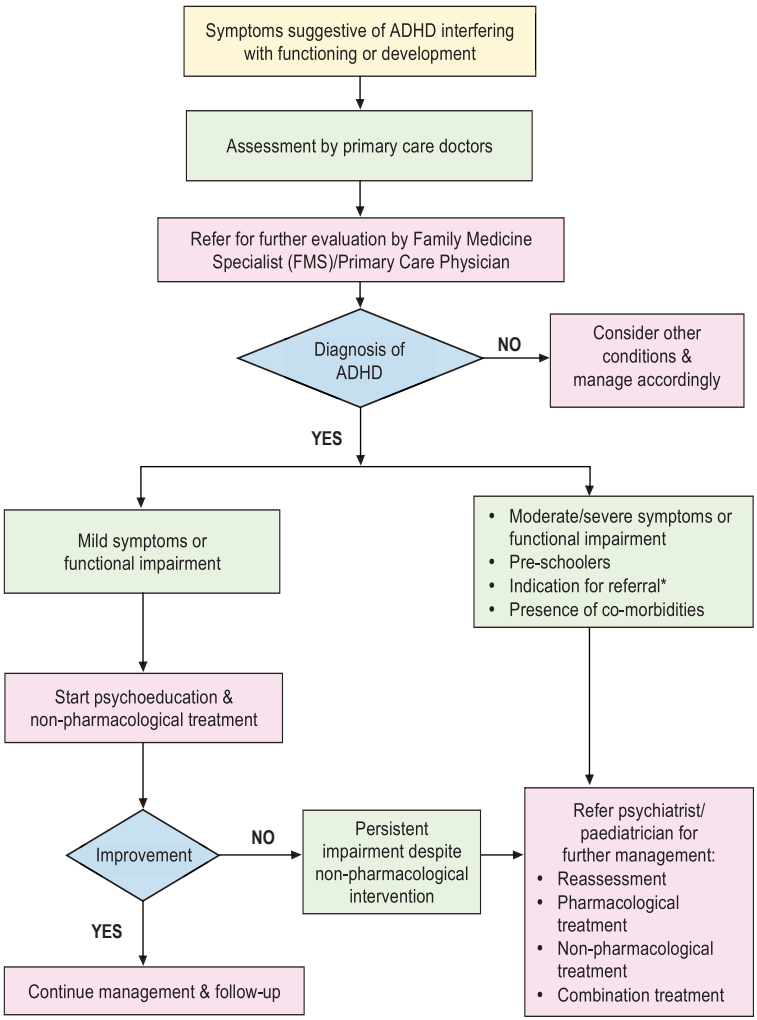
ALGORITHM: MANAGEMENT OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER (ADHD)



*Refer **Chapter 7** on **Referral**

1. INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders of childhood. It is defined as a persistent pattern of inattention and/or hyperactive and impulsive behaviour that is more frequent and severe than is typically seen in a child at a given developmental stage. It appears in childhood and often lasts into adulthood.

Children and adolescents with ADHD face significant problems in behavioural control, interpersonal relationships, academic performance and personal issues.[1, 2] They have worse health-related quality of life scores than the typically developing groups varying from a small to moderate degree in physical domains and a large degree in psychosocial domains.[3] Therefore, early recognition, assessment and management of this condition is very important in helping them and their parents to improve the educational and psychosocial difficulties.

Worldwide, the estimated prevalence of childhood ADHD is 5.29%.[4] In Malaysia, the estimated prevalence of ADHD range from 1.6% to 4.6%.[5, 6] Boys are three to four times more likely to be diagnosed with ADHD than girls.[6 - 8]

This CPG is a full review of the previous edition of guidelines on the management of ADHD published in 2008. It aims to reduce variation in practice and, address advancement in diagnosis and treatment of ADHD. In this edition, a new scope on adult ADHD and transition period into adulthood is addressed because of its growing significance in clinical practice.

2. RISK FACTORS

- ADHD has a multifactorial and complex aetiology which includes both biological and environmental factors.

a. Biological factors

- **Gender**
  - Males are associated with increased risk of ADHD (OR=3.05, 95% CI 2.34 to 3.98).[8, level II-2]
  - This is supported by a recent cohort study of more than 1.5 million individuals in Sweden showing the ADHD ratio between male and female of 3.7:1.[7, level II-2]
- **Genetics**
  - Genetics plays a role in the aetiology of ADHD with a heritability estimate of 76%.[9] The rate of ADHD in relatives of individuals with ADHD compared with the rate in relatives of individuals without ADHD is increased with increasing genetic relatedness:[7, level II-2]
    - monozygotic twins, HR=70.45, 95% CI 38.19 to 129.96
    - dizygotic twins, HR=8.44, 95% CI 5.87 to 12.14
    - full siblings, HR=8.27, 95% CI 7.86 to 8.70
    - maternal half-siblings, HR=2.86, 95% CI 2.61 to 3.13
    - paternal half-siblings, HR=2.31, 95% CI 2.07 to 2.58
    - full cousins, HR=2.24, 95% CI 2.11 to 2.38
    - half cousins, HR=1.47, 95% CI 1.35 to 1.61

b. Environmental factors

- **Pre-pregnancy maternal obesity**
  - Pre-pregnancy maternal obesity (BMI ≥30 kg/m^2) is associated with an increased risk of ADHD among children (HR=1.65, 95% CI 1.55 to 1.76). The risk is also increased in overweight women (BMI 25 - 29.9 kg/m^2) with HR of 1.27 (95% CI 1.17 to 1.37).[10, level II-2]
- **Prenatal factors**
  - **Hypertensive disorder in pregnancy (HDP)**
    In a meta-analysis, maternal HDP showed a small risk of ADHD in the offspring (OR=1.29, 95% CI 1.22 to 1.36).[11, level II-2]
  - **Maternal diabetes**
    A recent meta-analysis of six cohort studies demonstrated that maternal diabetes increased the risk for ADHD in offspring (RR=1.40, 95% CI 1.27 to 1.54), with gestational diabetes mellitus showing a higher risk (RR=2.00, 95% CI 1.42 to 2.81).[12, level II-2] However, significant publication bias would have overestimate the findings.
  - **Maternal psychosocial stress**
    Children born to mothers who experienced a major stressful event during pregnancy or reported a high level of perceived stress are more likely to have ADHD [OR of 1.45 (95% CI 1.06 to 1.99) and OR of 3.03 (95% CI 2.19 to 4.20) respectively].[13, level II-2]

- **Maternal cigarette, drug and alcohol use**
  - Maternal cigarette smoking and, drug and alcohol abuse are known to be associated with ADHD.[14]
  - Maternal smoking during pregnancy is associated with increased risk of ADHD in the offspring:[15, level II-2]
    - OR in cohort studies of 1.35, 95% CI 1.20 to 1.52
    - OR in case-control studies of 1.85, 95% CI 1.57 to 2.19
- **Maternal paracetamol use**
  A meta-analysis showed that maternal acetaminophen (paracetamol) use during pregnancy was associated with a small risk of ADHD in the offspring (RR=1.25, 95% CI 1.17 to 1.34). The duration of its use for ≥28 days prenatally showed a RR of 1.63, 95% CI 1.23 to 2.16.[16, level II-2] However the primary papers used in this meta-analysis has heterogenous methodology leading to possible misclassification bias.
- **Maternal antidepressants use**
  Antidepressants use during pregnancy was not associated with increased risk of ADHD (HR=1.2, 95% CI 1.0 to 1.4).[17, level II-2]
- **Maternal use of valproate**
  There is contradictory evidence on the association of maternal valproate use and ADHD.[18 - 19, level II-2]

- **Perinatal factors**
  - **Apgar score**
    A lower Apgar score is associated with a higher risk of ADHD in childhood compared with Apgar scores of 9 or 10 at 5 minutes.[20, level II-2]
    - Apgar scores of 1 to 4 (HR=1.75, 95% CI 1.15 to 2.11)
    - Apgar scores of 5 to 6 (HR=1.63, 95% CI 1.25 to 2.11)
  - **Preterm birth and low birth weight**
    Preterm birth is associated with more than twice the risk of developing ADHD, while children with low birth weight have two- to three-fold increased risk.[9]
- **Traumatic brain injury (TBI)**
  Children with TBI have higher risk of ADHD (HR=1.32, 95% CI 1.19 to 1.45).[21, level II-2]
- **Nutritional factors in children**
  - There is no association between sucrose consumption and the prevalence of ADHD among children.[22, level II-2]
  - To date there is no conclusive evidence that food dyes and food preservatives cause ADHD.
- **Screen-time**
  Preschool children with more than 2-hours of screen-time/day have an increased risk of ADHD (OR=7.7, 95%CI 1.6 to 38.1).[23, level II-2]
- **Others**
  Studies had shown that lead was associated with ADHD.[24, level II-2]

3. ASSESSMENT AND DIAGNOSIS

Children and adolescents presenting with core symptoms of inattention and/or hyperactivity and impulsivity should be evaluated for ADHD. The assessment and diagnosis of ADHD requires obtaining information from multiple informants, including parents and teachers, as well as conducting a clinical examination on the individual.

ADHD is commonly under-recognised in girls.[1] ADHD without hyperactivity (i.e. predominantly inattentive symptoms) is a diagnosis that needs to be considered in girls.[25]

A meta-analysis on diagnostic accuracy of ADHD using various rating scales revealed that either parents or teachers were able to identify ADHD with a sensitivity of 0.86. On the other hand, reports by both parents and teachers gave a specificity of 0.91.[26, level III]

3.1 Assessment

a. History

The clinical history should include the following:

- core symptoms of ADHD (inattention, hyperactivity and impulsivity) at home, in school and social settings and impact of the symptoms
- age of onset, duration and progression of symptoms
- perinatal history, birth and developmental history including development milestones, past medical history (e.g. meningitis, traumatic brain injury)
- behaviour in school and academic performance, as well as strengths, weaknesses and possible difficulties or stressors. Explore areas of learning difficulty, disciplinary issues, parenting concerns, bullies, peers' rejection, excessive punishment, school rejection and engagement in dangerous activities
- estimated level of intellectual functioning (via a detailed learning and adaptive functioning history)
- activities of daily living (ADL) functioning (self-care, play and leisure including screen-time, schoolwork and house chores)
- impact of difficulties and behaviour on the individual i.e. self-esteem, self-worth
- impact of child's difficulties and behaviour on family functioning and peer relationships
- restless, fidgety, disruptive and unsafe behaviours
- co-morbid psychiatric conditions including changes in mood, appetite, sleep and any substance use
- medical/social conditions that mimic ADHD symptoms (e.g. autism spectrum disorder (ASD), intellectual disability, conditions producing chronic sleep deprivation; obstructive sleep apnoea; neuro-behavioural side effects of medications taken for other chronic conditions; physical, sexual and emotional abuse)
- family structure and dynamics, parenting styles and expectations
- family history of ADHD, substance abuse and maternal smoking, parents' or carers' mental health e.g. maternal depression

b. Physical and Mental State Examination

A comprehensive physical examination (including vital signs, height and weight) should be performed to exclude physical conditions which mimic ADHD.[9]

Mental status examination should focus on the following:[9]

- general appearance and behaviour
- activity level and social interaction
- speech and language
- mood and affect
- thought process
- attention and concentration
- intelligence and academic skills

c. Rating scales

- Behavioural rating scales are useful adjuncts to the clinical interview in gathering more information about the individual. It should not be used as the sole criterion for clinical diagnosis of ADHD.[27, level III]
- Common behaviour rating scales used are:
  - Conners' Rating Scales (CRS)
  - Child Behavior Checklist (CBCL)
  - Vanderbilt ADHD Rating Scale
  - ADHD Rating Scale-5
  - Strengths and Difficulties Questionnaire (SDQ)
- These behavioural rating scales can be self-administered. However, they do not give a complete diagnosis of ADHD, and the scores should be interpreted with caution by trained healthcare providers.
- The evaluation of any child and adolescent for ADHD should consist of clinical interviews with the parents/caregivers and the patient by obtaining information about the patient's school or day care functioning, evaluating comorbid psychiatric disorders and reviewing the patient's medical, family and social histories.[2]

A meta-analysis showed that Conners' Abbreviated Symptom Questionnaire (ASQ), Child Behavior Checklist-Attention Problem (CBCL-AP) scale and Conners' Rating Scale–Revised (CRS-R) were effective rating scales to detect ADHD symptoms with sensitivity ranging from 0.75 to 0.83.[28, level III]

3.2 Diagnostic Criteria

- ADHD is diagnosed based on diagnostic criteria of Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (refer to **Appendix 3**) or hyperkinetic disorders from 10th Revision of the International Statistical Classification of Diseases and Related Health Problem (ICD-10) (refer to **Appendix 4**).

The core symptoms of ADHD are:[29; 30]
- inattention
- hyperactivity and impulsivity

In order to meet diagnostic criteria, the core symptoms should:[29; 30]
- be persistent
- be pervasive (present in two or more setting)
- have caused significant functional impairment
- not better accounted for by other mental disorders (e.g. pervasive developmental disorder, schizophrenia, other psychotic disorders, depression or anxiety)

The onset of symptoms should be before the age of five years for hyperkinetic disorder[30] or 12 years for ADHD.[29]

- Children and adolescents with signs and symptoms suggestive of ADHD should be referred for assessment and further management.

Recommendation 1
- Information from parents/carers and teachers should be sought to increase accuracy of the attention-deficit/hyperactivity disorder (ADHD) assessment.
- Diagnosis of ADHD should be based on diagnostic criteria of Diagnostic and Statistical Manual of Mental Disorder Fifth Edition (DSM-5) or hyperkinetic disorders from International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10).

3.3 Investigations

a. Laboratory tests

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

b. Other investigations

Electroencephalogram (EEG) and magnetic resonance imaging (MRI) are not indicated in the diagnosis of ADHD.

3.4 Co-morbidities

In children with ADHD:
- learning disorders, sleep disorders and oppositional defiant disorders (ODD) are common[31, level III]
- 31% have co-occurring ODD, 10% have conduct disorders (CD) while 3% have both ODD and CD[32, level II-2]
- 20% developed chronic tic disorder[33, level I]

In a meta-analysis of 18 cross-sectional studies, girls with ADHD showed higher risk of anxiety (OR=3.19, 95% CI 1.81 to 5.65) and depression (OR=4.21, 95% CI 2.08 to 8.51) compared with those

without ADHD.[34, level III] However, there was no mention on inclusion criteria and quality assessment in the meta-analysis.

A systematic review showed that ADHD in children and adolescents were significantly associated with allergic conditions e.g. allergic rhinitis, allergic conjunctivitis, atopic dermatitis and asthma.[35, level II-2]

- Children with ADHD should be evaluated for co-morbidities.

4. TREATMENT

As ADHD is a chronic condition, children and adolescents with ADHD and their families require long-term follow-up.

- The goal of treatment is to improve symptoms, functioning and learning. It also aims to increase the child's self-esteem and self-worth. The treatment includes psychoeducation, non-pharmacological and/or pharmacological approaches. In view of difficulties with diagnosis and special requirements of management, pre-schoolers (children below six years old) suspected of ADHD should be referred to a child psychiatrist or a paediatrician.

4.1 Psychoeducation

Psychoeducation should be provided to patients, parents, caregivers and teachers. In a systematic review, psychoeducation demonstrated positive outcomes in children and adolescents with ADHD with regards to:[36, level I]

- significant reduction of core ADHD symptoms
- excellent adherence to medical recommendations
- reduction in fears associated with medication usage (including side effects)
- improvements in academic achievements

Psychoeducation also improved maternal well-being.

Parents' perceptions of ADHD and treatment acceptability are the main barriers to medication adherence. An early structured psychoeducation programme provides a new approach in improving medication adherence and clinical symptoms in children with ADHD in the clinical setting.[37, level I]

- Psychoeducation should ideally contain the following:
  - a good patient-healthcare provider relationship
  - disorder-related information e.g. symptoms, potential causation/risk factors and negative effects in the life course
  - treatment-related information outlining pharmacological and non-pharmacological approaches, particularly regarding the effectiveness and adverse effects of medication
  - barriers to adherence and coping skills
  - parenting skills

Recommendation 2
- Psychoeducation should be offered in attention-deficit/hyperactivity disorder.

4.2 Non-Pharmacological Treatment

There are many non-pharmacological therapies available for individuals with ADHD. They differ in names and, have different techniques and strategies. However, they share a set of principles to achieve the same aims.

4.2.1 Occupational therapy

Occupational therapy is one of the supporting therapies in the management of ADHD. Therapeutic methods recommended include sensory motor activities, motor training, social skills training, cognitive interventions, behaviour intervention and play-based interventions. [38 - 39, level I]

A systematic review on the effectiveness of occupational therapy interventions for school-aged children with ADHD showed:[38, level I]

- cognitive interventions
  - cognitive orientation to daily occupational performance improved motor performance
  - family-centered intervention improved behavioural outcome and parental perception
- motor interventions
  - three-dimensional fine motor training significantly improved speed and consistent letter shapes in handwriting
  - Theraplay intervention significantly improved visual motor integration
- sensory interventions
  - weighted vests improved attention and on-task behaviour
  - stability balls improved in-seat and on-task behaviour
- play based interventions
  - Theraplay intervention reduced ADHD symptoms and, enhanced relationships and child's overall performance
  - play-based intervention improved playfulness and interpersonal empathy
  - parent-delivered intervention increased play skills
  - social skills training improved communication, interactions skills and improve process skills

In local settings, occupational therapy is a useful adjunct intervention in the management of ADHD.

4.2.2 Organisational skills training

Organisational skills deficits in children with ADHD are shown to impair academic performance and may be associated with psychosocial, occupational and economic difficulties later in life.[40, level I] These children frequently have problems dealing with school materials and completing school assignments on time.

In a meta-analysis of 12 RCTs, organisational skills training was more effective than control in improving organisational skills and the ratings of inattention and academic performance of children with ADHD:[40, level I]

- parent-reported organisational skills (Hedge's g=0.830, 95% CI 0.324 to 1.336)
- teacher-reported organisational skills (Hedge's g=0.539, 95% CI 0.169 to 0.909)
- parent-reported attention (Hedge's g=0.558, 95% CI 0.379 to 0.736)
- teacher-reported attention (Hedge's g=0.264, 95% CI 0.006 to 0.522)
- teacher-reported academic performance (Hedge's g=0.326, 95% CI 0.143 to 0.508)

4.2.3 Psychological intervention

a. Cognitive behavioural therapy-based interventions

Cognitive behavioural therapy-based intervention is one of the psychological interventions that has been proposed in the treatment of ADHD. A good meta-analysis showed modest effectiveness of cognitive behavioural therapy (CBT) in reducing externalising symptoms in children with ADHD (Cohen's d= -0.549, 95% CI -0.774 to -0.324).[41, level I]

In a cross-over RCT, an eight-month assessment showed CBT was effective for adolescents with ADHD who continued to exhibit persistent symptoms despite medications.[42, level I]

In another RCT, CBT group was significantly more effective than control group in reducing ADHD symptoms and severity, and decreasing functional impairment in adolescents who continued presenting with significant symptoms despite being on pharmacological treatment: [43, level I]

- self-rated ADHD symptoms (Cohen's d=7.5)
- parent-rated ADHD symptoms (Cohen's d=8.38)
- self-rated symptom severity (Cohen's d=3.75)
- clinician-rated symptom severity (Cohen's d=7.71)
- evaluator-rated functional impairment (Cohen's d=7.51)

CBT sessions include modules on psychoeducation, organisational/ planning skills, impulsivity and motivation management, and relapse

prevention.[42 - 43, level I] These sessions should be conducted by trained personnel.

b. Mindfulness-based intervention

Mindfulness-based intervention (MBI) is a promising strategy to reduce ADHD symptoms.

A meta-analysis demonstrated MBI was effective in children with ADHD in terms of:[44, level I]

- reduction in inattention (Hedges' g= -0.825, 95% CI -1.161 to -0.488)
- reduction in hyperactivity/impulsivity (Hedges' g= -0.676, 95% CI -0.975 to -0.377)

However, the above results must be interpreted with caution because of high heterogeneity across the studies (I^2=69.10 to 76.24%).

4.2.4 Assistive Technology

There is no strong evidence for assistive technology in ADHD. The use of fidget spinner is associated with only temporary decrease in gross motor activity (Cohen's d= -0.44, p<0.05). It worsens attentional functioning (Cohen's d=0.65, p<0.001).[45, level II-3]

Recommendation 3

- Occupational therapy should be offered as an adjunct in attention-deficit/hyperactivity disorder (ADHD).
- The following therapies should be considered in ADHD:
  - organisational skills training
  - cognitive behavioural therapy-based interventions

4.2.5 Family-based Intervention

Parent training and behavioural intervention

Parents often experience high level of stress in handling children with ADHD and their associated impairments. Stress may affect parenting effectiveness, quality of parent-child relationships and the child's functioning.

Adolescents with ADHD and their parents reported more parent-adolescent conflicts. Parents of adolescents with ADHD reported a greater intensity of anger in the parent-adolescent communication. They also reported having their own conflicts and mental health issues.[3, level III]

Parent training and behavioural interventions improve parenting skills [46, level I] and reduce parenting stress.[47, level I] Parent training assists parents to understand and support the child, cope with stressful situations and encourage appropriate behaviours. It helps parents to modify and shape their child's behaviour while improving the child's ability to regulate his or her behaviour.

In children with ADHD, parent training and behavioural interventions:

- reduce ADHD symptoms (SMD=0.61, 95% CI 0.40 to 0.83) for preschool children either with or without the child's involvement [48, level I]
- reduce oppositional behaviour,[49, level I] destructive behaviour and ADHD symptoms[46, level I]
- reduce anxiety and depression,[49, level I] as well as internalising behaviour[47, level I]
- increase self-control behaviour[49, level I]

Parent training and behavioural interventions may need to be done continuously for overall benefits to be sustained.[49, level I] The intervention can be done individually or in groups. Other caregivers involved in the care of the child are encouraged to take part in the training and intervention.

Parent training is also recommended by other guidelines in ADHD.[1; 14; 50] The positive effect of behavioural therapy persists while positive effect of medications cease when the medication is stopped.[2]

In view of the benefits of parent training, more local healthcare providers need to be trained to carry out the intervention. Refer **Appendix 5** on **Advice for Behavioural Management**.

Recommendation 4

- Parent training and behavioural intervention should be offered in attention-deficit/hyperactivity disorder.

4.2.6 School-based Intervention

School-based intervention is any strategy implemented in a classroom setting to improve the well-being of students. It reduces and prevents school-related difficulties. The intervention requires interdisciplinary coordination among healthcare providers and educational staff handling children with ADHD. Interventions may incorporate activities e.g. behavioural interventions and modifications to academic instructions.

A health technology assessment showed that school-based intervention led to improvement in both core ADHD symptoms and academic outcome:[51, level I]

i. average beneficial effect on core ADHD symptoms
   - neurocognitive assessment on inattention (Cohen's d=0.44, 95% CI 0.18 to 0.70) and hyperactivity/impulsivity (Cohen's d=0.33, 95% CI 0.13 to 0.53)
   - teacher-rated inattention assessed using various rating scales e.g. CRS, CRS-R, CBCL, ADHD-RS etc. (Cohen's d=0.60, 95% CI 0.14 to 1.06)

ii. small effect on externalising symptoms reported by teachers (Cohen's d=0.28, 95% CI 0.04 to 0.53)
iii. small effect on perceptions of school-related adjustment as assessed by teachers (Cohen's d=0.26, 95% CI 0.05 to 0.47)

A meta-analysis of 19 moderate quality RCTs showed that behavioural classroom programmes had small positive effects on teacher-rated disruptive behaviour (Cohen's d= -0.20, 95% CI -0.29 to -0.10) and classroom-observed on-task behaviour (Cohen's d=0.39, p<0.001).[52, level I]

National Institute for Health and Care Excellence (NICE) recommends that more education about ADHD be provided to trainee teachers. Teachers who have received training on ADHD and its management should provide behavioural interventions in the classroom to help children and young people with ADHD.[1]

American Academy of Pediatrics recommends that educational interventions and individualised instructional supports, including school environment, class placement, instructional placement and behavioural supports, are a necessary part of any treatment plan and they often include an Individualised Education Programme (IEP).[53]

Recommendation 5
- School-based interventions should be offered in attention-deficit/hyperactivity disorder.

Refer **Appendix 6** on **School-Based Intervention**.

4.2.7 Others

Neurofeedback (NF) consists of measuring brain waves and providing a feedback signal which teaches self-control of brain functions.[54] In a meta-analysis of 10 RCTs, NF was more effective than control in hyperactivity/impulsivity at six months follow-up (SMD=0.32, 95% CI 0.14 to 0.49) but not in inattention.[55, level I] However there was no report on quality assessment of primary papers. The Canadian ADHD Practice Guidelines concludes that there is insufficient data to recommend NF as a standard treatment for ADHD.[56]

- There is insufficient evidence to support the use of NF in the treatment of ADHD.

4.3 Pharmacological Treatment

- Medication should be offered to children aged ≥6 years and adolescents with attention-deficit/hyperactivity disorder:
  - if their ADHD symptoms are persistent and causing significant impairment in at least one domain despite behavioural and environmental interventions.[1]
  - along with evidence-based training interventions and/or behavioural interventions, if available.[53]

a. Stimulants/Non-stimulants

Methylphenidate (MPH) and atomoxetine (ATX) are indicated for ADHD in children six years and older.[57; 58, level III]

A Cochrane systematic review showed that MPH, compared with placebo, in children and adolescents with ADHD reduced:[59, level I]

- teacher-rated ADHD symptoms (SMD= -0.77, 95% CI -0.90 to -0.64)
- independent assessor-rated ADHD symptoms (SMD= -0.64, 95% CI -0.89 to -0.39)
- parent-rated ADHD symptoms (SMD= -0.66, 95% CI -0.82 to -0.51)

In a meta-analysis of 11 RCTs in children and adolescents with ADHD, symptom improvement was higher with MPH compared to ATX (RR=1.14, 95% CI 1.09 to 1.20). However, on the ADHD-RS, improvement was seen only in inattention (SMD= -0.13, 95% CI -0.25 to -0.01) and not in the total and hyperactivity/impulsivity domains.[60, level I]

In comparison with placebo, patients on MPH had more non-serious adverse events (RR=1.29, 95% CI 1.10 to 1.51).[59, level I] MPH had less drowsiness (RR=0.17, 95% CI 0.11 to 0.26), nausea (RR=0.49, 95% CI 0.29 to 0.85) and vomiting (RR=0.41, 95% CI 0.27 to 0.63) but more insomnia (RR=2.27, 95% CI 1.63 to 3.15) compared with ATX.[60, level I]

In both meta-analyses the primary papers were of moderate quality.

NICE recommends offering MPH (either short- or long-acting) as first-line pharmacological treatment for children aged ≥5 years and young people with ADHD. ATX can be offered in those who:[1]

- cannot tolerate MPH
- do not respond to separate 6-week trials of MPH, having considered alternative preparations and adequate doses

There is no current indication to perform an electrocardiogram (ECG) in a child prior to or during treatment using stimulants unless indicated

by history or physical examination.[1; 61, level III] Cardiac risk factors should be assessed, including child or adolescent's history of specific cardiac symptoms apart from family history of sudden death, cardiovascular symptoms, etc.[53]

Recommendation 6

- Methylphenidate should be offered to children aged ≥6 years and adolescents with attention-deficit/ hyperactivity disorder if medication is indicated*.
  - Atomoxetine may be used as an alternative.

*Refer yellow box above.

b. Others

In a good network meta-analysis of 133 double-blind RCTs on children and adolescents with ADHD, the following medications were superior to placebo in reducing ADHD core symptoms as rated by clinicians:[62, level I]

- amphetamines (SMD= -1.02, 95% CI -1.19 to -0.85)
- ATX (SMD= -0.56, 95% CI -0.66 to -0.45)
- bupropion (SMD= -0.96, 95% CI -1.69 to -0.22)
- clonidine (SMD= -0.71, 95% CI -1.17 to -0.24)
- guanfacine (SMD= -0.67, 95% CI -0.85 to -0.50)
- MPH (SMD= -0.78, 95% CI -0.93 to -0.62)
- modafinil (SMD= -0.62, 95% CI -0.84 to -0.41)

By contrast, in comparisons based on teachers' ratings, only MPH (SMD= -0.82, 95% CI -1.16 to -0.48) and modafinil (SMD= -0.76, 95% CI -1.15 to -0.37) were more efficacious than placebo.

In head to head comparisons, clinical ratings showed:[62, level I]

- amphetamines were superior to modafinil (SMD= -0.39, 95% CI -0.67 to -0.12), ATX (SMD= -0.46, 95% CI -0.65 to -0.27), and MPH (SMD= -0.24, 95% CI -0.44 to -0.05)
- ATX was inferior to MPH (SMD=0.22 95% CI 0.05 to 0.39)

With respect to tolerability, all study medications were inferior to placebo:[62, level I]

- amphetamines (OR=2.30, 95% CI 1.36 to 3.89)
- ATX (OR=2.30, 95% CI 1.36 to 3.89)
- bupropion (OR=1.51, 95% CI 0.17 to 13.27)
- clonidine (OR=4.52, 95% CI 0.75 to 27.03)
- guanfacine (OR=2.64, 95% CI 1.20 to 5.81)
- MPH (OR=1.44, 95% CI 0.90 to 2.31)
- modafinil (OR=1.34, 95% CI 0.57 to 3.18)

In head to head comparisons, MPH was more tolerable than ATX, amphetamines, guanfacine, clonidine and bupropion. However, the differences were not statistically significant.

In the MoH Medicines Formulary, only MPH and ATX are approved for use in the treatment of ADHD in children over six years.[57] Refer to **Appendix 7** on **Pharmacological Treatment of ADHD**.

c. Treatment for Pre-schoolers (Children below six years old)

There was no strong evidence retrieved for pre-schoolers with ADHD and the CPG DG acknowledges the concerns around the adverse effects of medication in this group.

NICE recommends not to offer medication to any child under five years without a second specialist opinion from an expert in managing ADHD in young children.[1]

In the previous Malaysian CPG, the recommendation was that medication for pre-schoolers should be initiated by a child psychiatrist or a paediatrician familiar with the management of ADHD in this group.[9]

Recommendation 7

- If medication for attention-deficit/hyperactivity disorder (ADHD) is indicated in children <6 years old, it should be initiated by a child psychiatrist or a paediatrician with expertise in managing ADHD.

4.4. Combination Treatment

Pharmacotherapy alone or in combination with non-pharmacological treatment can be offered in ADHD. The combination of pharmacotherapy and behavioural therapy in ADHD allows for the use of lower stimulant dosages, which may reduce risk of medication-related side effects.[2]

Recommendation 8

- Combination treatment (pharmacological and non-pharmacological) should be considered in children ≥6 years of age and adolescents with attention-deficit/hyperactivity disorder when the symptoms persist and cause functional impairment.

4.5. Dietary Modification

Dietary modification for ADHD is divided into elimination and supplementation diets. Elimination diet includes removal of artificial food colourants, additives, sugar, artificial sweeteners and Few Foods Diet (FFD). FFD is a diet that excludes all but a few food items for a certain duration. It normally includes two types of meat, two sources of carbohydrates, two vegetables, two fruits, oil and water. Supplementation diet involve addition of amino acids, essential fatty acids, vitamins and minerals.[63, level I]

The evidence for dietary modification in management of ADHD are mostly inconclusive.[63, level I]

NICE recommends not to advise elimination of artificial colouring, additives and dietary fatty acid supplementations. There is also no evidence of long-term effectiveness of FFD.[1]

In the previous Malaysian CPG on ADHD, the recommendation was that parents should monitor and document the association between a particular food item and hyperactive behaviour in children with ADHD. The particular food item should be avoided if it is clearly associated with behavioural changes.[9]

- There is insufficient evidence to recommend dietary modification in the treatment of ADHD.

5. TRADITIONAL AND COMPLEMENTARY MEDICATION

Traditional and complementary medication that were frequently studied in the management of ADHD include nutritional medicines (zinc, iron, omega-3, vitamin C and acetyl-L-carnitine) and herbal medicines [ginkgo, St. John's wort, French maritime pine bark and Ningdong granule (traditional Chinese herbal formula)]. There is no clear evidence for recommendation of these medications in treating ADHD.[64, level I]

A systematic review showed no evidence on the usefulness of medicinal cannabinoids for the treatment of ADHD in adults.[65, level I]

In a meta-analysis, physical exercise has a medium effect on ADHD functional outcomes (Hedge's g=0.627, 95% CI 0.273 to 0.982) with significant heterogeneity (I^2=78%).[66, level I] However, quality assessment of primary studies was not reported.

6. SPECIAL POPULATION

6.1. Transition to Adulthood

Transition is the period from adolescence to adulthood. It is important to continuously provide accessible and age-appropriate services in this period. A majority (60 - 85%) of children with ADHD will continue to meet the criteria for the disorder during their teenage and adult years.[2] However, ADHD treatment rates decline sharply from childhood through young adulthood.[67, level III] The decline in treatment is because:

- there is an interruption in management of the disorder when adolescent patients transit to adult health care services as there is no provision of transitional care for the patients[67, level III]
- of the belief that ADHD resolves during adolescence and young adulthood with minimal impact in functioning[68, level III]
- of the perception that adolescents with ADHD do not meet the diagnostic criteria and, therefore, do not require treatment[69, level III]
- the presentation is masked by the presence of comorbid psychiatric syndromes[68, level III]
- there is limited service availability[67, level III]
- clinicians are not well equipped to handle adults with ADHD[67, level III]
- the stigma and myths about ADHD and its treatment[68, level III]

Symptoms of ADHD in adolescence and adulthood:[68, level III]

- may change; hyperactivity and impulsivity becoming less evident, while inattention symptoms remain
- include prominent impairment in executive functioning
- are complicated by the presence of comorbid psychiatric symptoms
- are associated with continued clinical and psychosocial impairments

- Optimising services during childhood and transition to adult health care improves treatment and prognosis of individuals with ADHD.

Recommendation 9

- Children and adolescents with attention-deficit/hyperactivity disorder should continue to receive treatment throughout their lifespan.

6.2. Adults

Observational studies of childhood outcomes of ADHD suggested persistence of symptoms into adulthood. Inattention symptoms remained prominent, while symptoms of hyperactivity and impulsivity may persist, decline or change in their presentation.[70, level II-2] ADHD persistence rates from childhood to adulthood ranged from 40 - 50%.[71, level III]

a. Risk factors for persistence of ADHD into adulthood

A meta-analysis of 16 studies found that the risk factors for persistence of ADHD into adulthood were:[72, level II-2]

- severity of ADHD (OR=2.33, 95% CI 1.60 to 3.39)
- CD (OR=1.85, 95% CI 1.06 to 3.24)
- major depressive disorder (MDD) (OR=1.80, 95% CI 1.10 to 2.95)
- parental psychopathology
  - paternal anxiety-mood disorder (OR=2.40, 95% CI 1.10 to 5.50)
  - parental (mother or father) antisocial personality disorder (OR=2.20, 95% CI 1.20 to 4.20)

The same meta-analysis showed that factors not significantly associated with the persistence of ADHD into adulthood were gender, socioeconomic status at childhood, intelligence quotient (IQ), ODD, exposure to trauma and adversities e.g. single parent families.[72, level II-2]

b. Co-morbidities

In a small cross-sectional study on individuals aged 17 to 74 years old, adults with ADHD had significantly higher rates of DSM-IV Axis I (46.9%) and Axis II (27.31%) co-morbidities compared with non-ADHD adults.[73, level III]

Among adults with ADHD, those with ADHD-C (combined hyperactivity and inattention) had significantly higher rates of past and current MDD and anxiety disorders compared with ADHD-I (inattention). They also had significantly higher rates of past CD and antisocial personality disorder.[73, level III]

c. Outcome of childhood ADHD

Adults with childhood ADHD, compared with those without ADHD, had higher risk of:

- academic difficulties[74, level II-2]
  - grade retention (OR=3.64, 95% CI 2.39 to 5.56)
  - school suspension (OR=6.31, 95% CI 2.53 to 15.73)
  - increased use of education services (OR=6.37, 95% CI 2.58 to 15.73)
  - failure to finish high school (OR=3.70, 95% CI 1.96 to 6.99)
- psychiatric disorders[74, level II-2]
  - ODD (OR=7.05, 95% CI 2.63 to 18.85)
  - CD (OR=5.40, 95% CI 2.53 to 11.55)
  - antisocial disorder (OR=2.83, 95% CI 1.23 to 6.52)
  - depression (OR=2.31, 95% CI 1.45 to 3.70)
  - use of mental health services (OR=2.35, 95% CI 1.42 to 3.89)
- substance and alcohol use[75, level II-2]
  - lifetime nicotine use (OR=2.08, 95% CI 1.66 to 2.60)
  - lifetime marijuana use (OR=2.78, 95% CI 1.64 to 4.74)
  - nicotine abuse/dependence (OR=2.82, 95% CI 2.41 to 3.29)

  - alcohol use disorder (OR=1.74, 95% CI 1.38 to 2.20)
  - marijuana abuse/dependence (OR=1.58, 95% CI 1.16 to 2.14)
  - cocaine abuse/dependence (OR=2.05, 95% CI 1.38 to 3.04)
  - general illicit drug abuse/dependence (OR=2.64, 95% CI 1.77 to 3.94)
- legal issues[74, level II-2]
  - arrests (OR=2.43, 95% CI 1.62 to 3.65)
  - convictions (OR=2.01, 95% CI 1.25 to 3.24)
  - driving summons (OR=2.13, 95% CI 1.09 to 4.19)
  - vehicular-accidents-at-faults (OR=1.98, 95% CI 1.03 to 3.81)
- problems in other areas of life
  - social functioning[76, level II-2]
  - low self-esteem[76, level II-2]
  - less likely to stay married ($p<0.001$)[70, level II-2]
  - lower salary ($p<0.001$)[70, level II-2]
  - lower work functioning ($p<0.001$)[70, level II-2]
  - poorer social economic status ($p<0.001$)[70, level II-2]
  - obesity[76, level II-2]

Adults with ADHD who received treatment in childhood compared to those who did not, had higher academic attainment and employment, lower rates of lifetime occurrence of depression, anxiety and bipolar disorder.[77, level II-2] They also had better outcomes in driving, obesity, self-esteem, social functioning and drug use/addictive behaviour.[76, level II-2]

- In the management of adults with ADHD, the assessment and treatment of ADHD, co-morbidities and psychosocial complications are crucial.

Recommendation 10
- Any child or adolescent presenting with academic difficulties, behavioural problems, mood disturbances, substance use or personality disorders should be evaluated for attention-deficit/hyperactivity disorder to prevent deleterious outcomes in adulthood.

7. MANAGEMENT IN PRIMARY CARE

In primary care setting, diagnosis of ADHD can be confirmed by a Family Medicine Specialist (FMS)/Primary Care Physician. Patients can be managed in the primary care facility if the condition is mild. Patients with moderate to severe ADHD should be referred to a psychiatrist/ paediatrician for further management.

Table 1. Severity of ADHD based on DSM-5 Criteria

Severity	Features
Mild	Few, if any, symptoms in excess of those required to make the diagnosis are present, and symptoms result in no more than minor impairments in social or occupational functioning.
Moderate	Symptoms or functional impairment between "mild" and "severe" are present.
Severe	Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning.

Non-pharmacological treatment of ADHD can be initiated by FMS/ Primary Care Physician. They can provide psychoeducation and general advice on family- and school-based interventions. Patients can also be referred to an occupational therapist for further interventions.

8. REFERRAL

In view of no retrievable evidence on referral criteria for ADHD, the CPG development group proposes the following terms for referral.

- Patients with ADHD should be referred to the psychiatrist/ paediatrician when there is:
  - uncertainty of diagnosis
  - lack of response to non-pharmacological treatment
  - indication to start pharmacotherapy
  - severe side effects of medication
  - co-morbidities (e.g. substance abuse)
- All pre-schoolers (below six years of age) with suspicion of ADHD should be referred to the child psychiatrist or a paediatrician with expertise in managing ADHD for further management.

9. MONITORING AND FOLLOW-UP

Clinicians should provide regular follow-up for individuals with ADHD. During the follow-up, emphasise treatment adherence and, monitor the effectiveness and side effects of medication prescribed.[1]

The following should be monitored during follow-up:

- height and weight
- vital signs (especially heart rate and rhythm)
- loss of appetite
- rebound hyperactivity
- sleep
- worsening behaviour
- mood changes
- stimulant diversion (giving another person the medication meant for the individual, e.g. giving a friend or selling one's prescribed medication)

Refer to **Appendix 8** for further information.

In addition, for children aged 12 years and above, clinicians should assess for changes in mood and presence of risky behaviours e.g. intentional self-harm, substance use, suicidal and risky sexual behaviours. [2; 53]

If a child or adolescent's growth over time is significantly affected by medication (i.e. they have weight loss and/or have not met the height expected for their age) consider a planned break in treatment over school holidays to allow "catch-up" growth.[1]

If a patient with ADHD has been symptom free for at least one year, enquiries should be made on whether the patient and family still think the medication is beneficial. If the decision is made to discontinue the medication, it should be done at a low-stress time.[2]

Parents and adolescents with ADHD are encouraged to discuss any preferences to stop or change medication and to be involved in any decision about stopping treatment.[1] Medications should be resumed in the event of recurrence of symptoms or deterioration in functioning.

- Children with ADHD are eligible to get additional support e.g.:
  - registration for Orang Kurang Upaya (OKU) with District Social Welfare Office (Pejabat Kebajikan Masyarakat Daerah)
  - special needs education under District Education Office (Pejabat Pendidikan Daerah), including inclusive education in the mainstream setting
  - examination and classroom accommodation (e.g. extra time, reduced distraction)

Recommendation 11
- Healthcare providers should provide continued care and long-term monitoring to children and adolescents with attention-deficit/hyperactivity disorder.

10. IMPLEMENTING THE GUIDELINES

The management of ADHD should be guided by evidence-based approach in order to provide quality care to the patients. Several factors may affect the implementation of recommendations in the CPG.

10.1. Facilitating and Limiting Factors

Existing facilitators for application of the recommendations in the CPG include:
- wide dissemination of the CPG (soft- and hardcopies) to healthcare providers
- training and updates on ADHD
- public awareness campaigns related to mental health

Existing barriers for application of the recommendations of the CPG are:
- limited exposure and training among healthcare providers on management of ADHD
- variation in availability of expertise and access to service provision due to financial constraints
- lack of awareness among patients, families and educators on ADHD

10.2. Potential Resource Implications

In local scenario, children with ADHD are often missed. Adults and peers often consider the children as having behavioural problems, not listening and not putting in effort. They are often labelled, isolated, ignored or punished.

There are also negative/false perceptions regarding ADHD e.g.:
- it is not a medical illness
- the medications increase the risk of substance use
- the condition will disappear as the child gets older
- boys are usually hyperactive anyway
- only boys have ADHD

The CPG recommends early detection and referral, comprehensive assessment and treatment of the disorder. This requires increased awareness among parents, educators and healthcare providers to establish diagnosis and embark on intervention early. Collaboration with various experts and agencies is required to provide optimal

management e.g. psychological and behavioural intervention, parent and teachers training, and classroom accommodation.

Thus, the implementation of this CPG requires resources to provide:

- training of healthcare providers and educators
- assessment and intervention tools
- better access to pharmaco- and non-pharmacological therapy
- access to policy makers

The following is proposed as clinical audit indicator for quality management of ADHD:

- Percentage of newly diagnosed children and adolescents with ADHD offered parent training and behavioural intervention

$$= \frac{\text{Number of newly diagnosed children and adolescents with ADHD offered parent training and behavioural intervention in a period}}{\text{Number of newly diagnosed children and adolescents with ADHD in the same period}}$$

- Percentage of children ≥6 years diagnosed with ADHD prescribed methylphenidate (MPH) when indicated*

$$= \frac{\text{Number of children ≥6 years diagnosed with ADHD prescribed MPH in a period}}{\text{Number of children ≥6 years diagnosed with ADHD and indicated for MPH in the same period}}$$

*if their ADHD symptoms are persistent and causing significant impairment in at least one domain despite behavioural and environmental interventions.

Implementation strategies will be developed following the approval of the CPG by MoH which include launching of the CPG, Quick Reference and Training Module.

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Appendix 1

EXAMPLE OF SEARCH STRATEGY

Clinical Question: What are the safe and effective pharmacological treatments for ADHD? - Stimulants

1. ATTENTION DEFICIT DISORDER WITH HYPERACTIVITY/
2. (attention deficit adj2 disorder*).tw.
3. attention deficit disorder* with hyperactivity.tw.
4. ((attention deficit hyperactivity or attention deficit-hyperactivity) adj3 disorder*).tw.
5. (hyperkinetic adj1 syndrome*).tw.
6. adhd.tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. CENTRAL NERVOUS SYSTEM STIMULANTS/
9. (analeptic adj1 (agent* or drug*)).tw.
10. analeptic*.tw.
11. central nervous system stimulant*.tw.
12. METHYLPHENIDATE/
13. methylphenidate.tw.
14. (methylphenidate adj1 hydrochloride).tw.
15. ritalin.tw.
16. ritalin sr.tw.
17. ritalin-sr.tw.
18. concerta.tw.
19. ritalin LA.tw.
20. adderall.tw.
21. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22. 7 and 21
23. limit 22 to (english language and humans and yr=”2008 -Current” and “all child (0 to 18 years)”)

Appendix 2

CLINICAL QUESTIONS

1. **Risk Factors**
   - What are the risk factors for ADHD?
2. **Diagnosis**
   - What are the accurate screening instruments for ADHD?
   - What are the accurate diagnostic criteria and diagnostic instruments for ADHD?
   - What are the accurate supporting investigations for the diagnosis of ADHD?
   - What are the associated co-morbidities of ADHD?
3. **Treatment**
   - What are the safe and effective non-pharmacological treatments for ADHD?
     - Psychoeducation
     - Behavioural therapy
       - Individual
       - Family-based
       - School-based
     - Assistive technology
   - What are the safe and effective pharmacological treatments for ADHD?
     - Stimulants
     - Non-stimulants
     - Others
   - What are the appropriate assessments for pre-pharmacological treatment in ADHD?
   - What are the safe and effective pharmacological treatments for pre-schoolers with ADHD?
   - What are the safe and effective traditional and complementary medication in ADHD?
   - What are the safe and effective dietary modification in ADHD?
4. **Special populations**
   - What are the important issues to be addressed in ADHD in the following special population?
     - Transition to adulthood
     - Adults
5. **Referral**
   - What are the referral criteria of children with ADHD to the following services:
     - Primary care
     - Secondary/tertiary care
6. **Monitoring and follow-up**
   - What are the effective follow-up and monitoring practices in ADHD?
   - What is the safety and effectiveness of drug holiday in ADHD?

Appendix 3

DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDER FIFTH EDITION (DSM-5)

Attention-Deficit/Hyperactivity Disorder

Diagnostic Criteria

A. A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterised by (1) and/or (2):

1. **Inattention**: Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:
   Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.
   a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).
   b. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).
   c. Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).
   d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily side tracked).
   e. Often has difficulty organising tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganised work; has poor time management; fails to meet deadlines).
   f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).
   g. Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).
   h. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).

i. Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).

2. **Hyperactivity and impulsivity**: Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities: **Note**: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.
   a. Often fidgets with or taps hands or feet or squirms in seat.
   b. Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).
   c. Often runs about or climbs in situations where it is inappropriate. (**Note**: In adolescents or adults, may be limited to feeling restless.)
   d. Often unable to play or engage in leisure activities quietly.
   e. Is often "on the go," acting as if "driven by a motor" (e.g., is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).
   f. Often talks excessively.
   g. Often blurts out an answer before a question has been completed (e.g., completes people's sentences; cannot wait for turn in conversation).
   h. Often has difficulty waiting his or her turn (e.g., while waiting in line).
   i. Often interrupts or intrudes on others (e.g., butts into conversations, games, or activities; may start using other people's things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).

B. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years.
C. Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (e.g., at home, school, or work; with friends or relatives; in other activities).
D. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning.
E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety

disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

Specify whether:

314.01 (F90.2) Combined presentation: If both Criterion A1 (inattention) and Criterion A2 (hyperactivity-impulsivity) are met for the past 6 months.

314.00 (F90.0) Predominantly inattentive presentation: If Criterion A1 (inattention) is met but Criterion A2 (hyperactivity-impulsivity) is not met for the past 6 months.

314.01 (F90.1) Predominantly hyperactive/impulsive presentation: If Criterion A2 (hyperactivity-impulsivity) is met and Criterion A1 (inattention) is not met for the past 6 months.

Specify if:

in partial remission: When full criteria were previously met, fewer than the full criteria have been met for the past 6 months, and the symptoms still result in impairment in social, academic, or occupational functioning.

Specify current severity:

Mild: Few, if any, symptoms in excess of those required to make the diagnosis are present, and symptoms result in no more than minor impairments in social or occupational functioning.

Moderate: Symptoms or functional impairment between “mild” and “severe” are present.

Severe: Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning.

Source: American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. Arlington, VA: American Psychiatric Association, 2013

Appendix 4

INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND RELATED HEALTH PROBLEMS, 10TH REVISION (ICD-10)

F90 Hyperkinetic disorders

A group of disorders characterized by an early onset (usually in the first five years of life), lack of persistence in activities that require cognitive involvement, and a tendency to move from one activity to another without completing any one, together with disorganized, ill-regulated, and excessive activity. Several other abnormalities may be associated. Hyperkinetic children are often reckless and impulsive, prone to accidents, and find themselves in disciplinary trouble because of unthinking breaches of rules rather than deliberate defiance. Their relationships with adults are often socially disinhibited, with a lack of normal caution and reserve. They are unpopular with other children and may become isolated. Impairment of cognitive functions is common, and specific delays in motor and language development are disproportionately frequent. Secondary complications include dissocial behaviour and low self-esteem.

Excl.: anxiety disorders (F41.-)
mood [affective] disorders (F30-F39)
pervasive developmental disorders (F84.-)
schizophrenia (F20.-)

F90.0 Disturbance of activity and attention

Attention deficit:
- disorder with hyperactivity
- hyperactivity disorder
- syndrome with hyperactivity

Excl.: hyperkinetic disorder associated with conduct disorder (F90.1)

F90.1 Hyperkinetic conduct disorder
Hyperkinetic disorder associated with conduct disorder

F90.8 Other hyperkinetic disorders

F90.9 Hyperkinetic disorder, unspecified
Hyperkinetic reaction of childhood or adolescence NOS
Hyperkinetic syndrome NOS

Source: World Health Organisation. ICD-10 Classifications of Mental and Behavioural Disorder: Clinical Descriptions and Diagnostic Guidelines. Geneva. 2016. (Available at: https://icd.who.int/browse10/2016/en#/F90.0)

Appendix 5

ADVICE FOR BEHAVIOURAL MANAGEMENT

General advice for parents

1. Remain calm and in control.
2. Schedule one on one time, at least 10 to 15 minutes every day with your child to let him/her know how important he or she is to you.
3. Individuals with ADHD benefit from frequent feedback. Notice your child's strength and praise him/her regularly.
4. Model the behaviour you would like to see from your child.
5. Use schedules and routines.
6. Post lists and reminders for the routines in places they will be seen.
7. Discuss the behavioural goals with your child.
8. Discuss the behavioural target(s), expectation and feedback with your child's other caregivers so he/she gets a consistent message.
9. Target one to two behaviours that you want to change at one time.
10. Give directions one at a time and track your child's response.
11. Use desired activities (screen time/play) as privileges/rewards for success on behavioural targets.
12. Ensure regular mealtimes and good rest for your child and yourself.

Younger Children

1. Routines are very important. Balance higher energy and quieter activities throughout the day.
2. Use visual prompts in the order of routines you would like him/her to learn (e.g. steps to get ready for bed).
3. Choose your battles - ignore minor misbehaviours.
4. Give choices but limit the number.
5. Use and reinforce "rules" (e.g. keeping hands to self) immediately before venturing into a community setting.
6. Prepare your child before an outing (e.g. crowded areas, in the car)

School-age child at home

1. Include homework/study time as a part of the family routine in a venue free from distraction.
2. Check your child's school schedule every day and help him/her organise the homework into doable portions.
3. Help your child use a system (e.g. labelled folders for each subject) to get the homework back to school.
4. Plan brief breaks between the homework portions.
5. Use the activities your child enjoys as incentives for getting work done (homework and chores).
6. Consider getting one to one help for your child's schoolwork.
7. Help the child to be mindful of his/her deadlines.
8. Communicate with your child's teacher about homework, grades, and behaviour.

9. If your child is still struggling at school, consider working with the school and special education unit for inclusive assistance in the mainstream or in an integrated special education setting.
10. Invite peers one at a time to reduce stimulation and encourage appropriate social behaviours.

Adapted: Ministry of Health Malaysia (MoH). Management of Attention Deficit Hyperactivity Disorder in Children and Adolescents. Kuala Lumpur: MoH; 2008

Appendix 6

SCHOOL-BASED INTERVENTION

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

- Have consistent rules and expectations with predictable classroom settings e.g. use visual schedules in class.
- Allow regular breaks and incorporate movement during the breaks.
- Place the child near the teacher and away from distractions (e.g. windows and doors).
- Give short and simple instructions.
- Periodically check to see if the child stays focused.
- Teach the child time management and study skills (e.g. using timers).
- Reduce the need for the children to copy assignments from the board. Instead use handouts and worksheets.
- Establish a daily communication method between school and home regarding targeted behaviours and learning tasks (e.g. homework).
- Praise and reward performance and good behaviour (e.g. use reward chart).
- Refrain from using verbal or physical punishments.
- Consider allowing computers or other digital devices to help the child in the learning process.
- Establish "buddy system" in class to help the child adjust with schoolwork and socialisation.
- Work with school and education department for special measures that children with ADHD are eligible during tests and examination (e.g. extra time, separate exam room, reminder from invigilator to stay on task, etc).

Adapted: Ministry of Health Malaysia (MoH). Management of Attention Deficit Hyperactivity Disorder in Children and Adolescents. Kuala Lumpur: MoH; 2008

Appendix 7

PHARMACOLOGICAL TREATMENT OF ADHD

Drug	Minimum Dose	Maximum Dose	Titration and Timing	Duration of Action	Common Adverse Effects	Comments
Methylphenidate HCL 10 mg Immediate-release (IR) tablet	Children over six years and adolescents: Initial 5 mg 1 - 2 times daily	Total daily dose 60 mg/day (in 2 to 3 divided doses), not to exceed 2 mg/kg/day	Increase by 5 - 10 mg daily at weekly intervals	3 - 5 hours	Headache, insomnia, irritability, decreased appetite, xerostomia, nausea, increased heart rate	It is advisable to have a meal before taking the medication if patient develops loss of appetite as a side effect Avoid dosing late in the day because of risk of insomnia
Methylphenidate HCL 18 mg, 27 mg*, 36 mg Extended-release (ER) tablet	Children over six years and adolescents: 18 mg once daily	Total 72 mg once daily	Increase by 18 mg at weekly intervals Administer in the morning with or without food	8 - 12 hours		Conversion from IR to ER: • IR 5 mg 2 to 3 times daily: ER 18 mg once every morning • IR 10 mg 2 to 3 times daily: ER 36 mg once every morning • IR 15 mg 2 to 3 times daily: ER 54 mg once every morning • IR 20 mg 2 to 3 times daily: ER 72 mg once every morning
Methylphenidate HCl 20 mg, 30 mg*, 40 mg Long-acting (LA) capsule	Children over six years and adolescents: 20 mg once daily	Total 60 mg/day	May increase 10 mg daily at weekly intervals Administer in the morning with or without food For patients with swallowing difficulties, contents may be sprinkled on soft food	6 - 8 hours		Conversion from IR to LA: Use equivalent total daily dose administered once daily Refer to product insert for porcine/ bovine origin of gelatine capsule

Drug	Minimum Dose	Maximum Dose	Titration and Timing	Duration of Action	Common Adverse Effects	Comments
Atomoxetine HCl 10 mg, 18 mg, 25 mg, 40 mg, 60 mg capsule	Children over six years and adolescents: ≤70 kg: Initial dose 0.5 mg/kg/day once daily	1.4 mg/kg/day or 100 mg, whichever is less	Increase after minimum of three days to 1.2 mg/kg/day May administer as either a single daily dose or two evenly divided doses in the morning and late afternoon/early evening	Up to 24 hours	Headache, insomnia, drowsiness, hyperhidrosis, xerostomia, nausea, decreased appetite, abdominal pain, vomiting, constipation	Renal impairment: No dosage adjustment necessary Hepatic impairment: Mild: No dosage adjustment Moderate: Reduce to 50% of normal dose Severe: Reduce to 25% of normal dose
	Children over six years and Adolescents: >70 kg: Initial dose 40 mg once daily	100 mg/day	Increase after minimum of three days to 80 mg/day May administer as either a single daily dose or two evenly divided doses in the morning and late afternoon/early evening May increase to 100 mg/day in 2 - 4 additional weeks to achieve optimal response Take with or without food Swallow capsules whole Do not open capsules		In adolescents: erectile dysfunction, ejaculatory dysfunction, dysmenorrhoea	

*not listed in MoH Medicines Formulary

Source:

1. Ministry of Health Medicines Formulary (Updated April 2019)(Available at https://www.pharmacy.gov.my/v2/sites/default/files/document-upload/fukkm-bil.1.2019.pdf)
2. Wolters Kluwer Clinical Drug Information, Inc. UpToDate® [Mobile application software]
3. American Pharmacists Association. Drug Information Handbook with International Trade Names Index, 24th Edition. Lexi-Comp's Inc. Houston, 2015

Appendix 8

MANAGEMENT OF COMMON ADVERSE EFFECTS ASSOCIATED WITH STIMULANT USE IN ADHD

ADVERSE EFFECTS	MONITORING AND ADVICE
Decrease appetite and weight loss	• Ask about appetite regularly • Children ≤10 years old: measure weight every three months after starting treatment • Children >10 years old: measure weight at three and six months after starting treatment and, every six months thereafter or more often if concerns arise • Advise taking medication either with or after food, rather than before meals • Take additional meals early in the morning or late in the evening after medications effects have worn off • Take a planned break from treatment (drug holiday) • Change medication
Linear growth impairment	• Measure height every six months in children and adolescents • Consider drug holiday
Insomnia	• Monitor changes in sleep pattern (e.g. with a sleep diary) • Adjust medication accordingly
Palpitation (tachycardia)	• Monitor heart rate and blood pressure and, compare with the normal range for age before and after each dose change and every six months • ECG is not indicated unless there is clinical indication • If there is persistent tachycardia, reduce the dose and may refer to paediatrician or physician
Tics	• Consider if the tics are related to the stimulant (tics naturally wax and wane) • Observe and if it worsens may consider non-stimulant medications
Seizures	• Review ADHD medication and stop any medication that might be contributing to the seizures • After investigation and if ADHD medication is unlikely to cause the seizures, may cautiously reintroduce the medication or consider non-stimulant medications
Worsening behaviour	• Monitor the behaviour response to medication • If behaviour worsens, adjust medication and review diagnosis

Adapted:National Institute for Health and Clinical Excellence. Attention Deficit Hyperactivity Disorder: Diagnosis and Management (NG87). London, NICE, 2018

LIST OF ABBREVIATIONS

ADHD	attention-deficit/hyperactivity disorder
ADHD-C	ADHD, combined type
ADHD-I	ADHD, inattentive type
ADHD-RS	ADHD Rating Scale
ADL	activities of daily living
ASD	autism spectrum disorder
ASQ	Abbreviated Symptom Questionnaire
ATX	atomoxetine
CBCL	Child Behaviour Checklist
CBCL-AP	Child Behaviour Checklist - Attention Problem
CBT	cognitive behavioural therapy
CD	conduct disorder
CI	confidence interval
CPG	clinical practice guidelines
CQ(s)	clinical question(s)
CRS-R	Conners Rating Scale - Revised
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
ECG	electrocardiogram
EEG	electroencephalogram
e.g.	example
ER	extended release
FFD	few foods diet
FMS	Family Medicine Specialist
HCl	hydrochloride
HDP	hypertensive disorder in pregnancy
HR	hazard ratio
ICD-10	10th Revision of the International Statistical Classification of Diseases and Related Health Problem
IEP	Individualised Education Programme
IQ	intelligence quotient
IR	immediate release
kg	kilogramme
LA	long-acting
MBI	mindfulness-based intervention
MDD	major depressive disorder
mg	miligramme
MPH	methylphenidate
MRI	magnetic resonance imaging
NF	neurofeedback
NICE	National Institute for Health and Care Excellence
NOS	not otherwise specified
ODD	oppositional defiance disorder
OR	odds ratio
p	p-value
RCT(s)	randomised controlled trial(s)
RR	risk ratio
SDQ	Strengths and Difficulties Questionnaire
SMD	standardised mean difference
TBI	traumatic brain injury

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