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by the Global ADHD Working
Group*

Global consensus on ADHD/HKD

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Introduction

Over the years, a wealth of evidence has been presented that confirms the validity of attention-deficit/hyperactivity disorder (ADHD) as a syndrome with important associated neurobiological aspects. It has also been clearly demonstrated that ADHD is a clinically impairing disorder with a broad-ranging and significant impact. Global clinical experience has led to the development of reliable diagnostic methodologies and effective treatments. Despite this, ADHD remains unrecognised,

■ **Abstract** A Global ADHD Working Group of experienced clinicians and researchers was gathered to review the latest evidence, discuss current best practice in the treatment of attention-deficit/hyperactivity disorder (ADHD), and make a statement based on consensus. The statement aims to re-affirm ADHD as a valid disorder that exists across different cultures, has a significant global impact, and should be diagnosed and effectively treated wherever it occurs.

ADHD is one of the most common neurobehavioural disorders of childhood and impacts on many aspects of development, including social, emotional and cognitive functioning, in the home and school environment. Although these findings are from developed countries, the impact in developing countries is likely to be similar.

There is strong supportive evidence for the validity of ADHD as a syndrome with neurobiological aspects, and complex genetic factors are primarily implicated in the aetiology. Accurate diagnosis and measurement of impairment is important to enable appropriate and successful management of symptoms. ADHD is a persistent condition that needs to be treated and monitored over time. The evidence supporting medication-based interventions (such as methylphenidate) is strong and consensus treatment algorithms to guide the multimodal treatment of ADHD, alone and in combination with common comorbidities, are suggested.

■ **Key words** consensus – ADHD – treatment

under-diagnosed and untreated in many countries, and regularly attracts public concern regarding its validity and impact.

To address this issue, a Global ADHD Working Group of experienced clinicians and researchers gathered to review the latest evidence, discuss current best practice in the treatment of ADHD, and make a statement based on consensus. The consensus statement aims to help foster and unify global opinion on the validity and impact of ADHD, and, more importantly, on its diagnosis and treatment. In line with these aims, the statement of this Working Group re-affirms that ADHD is a valid disorder

that exists across different cultures, has a significant global impact and should be diagnosed and effectively treated wherever it occurs.

Methods

The Global Working Group met on two separate occasions and consisted of an internationally recognised group of experts from nine countries spanning five continents (Australia, Brazil, France, Germany, South Korea, Mexico, Philippines, UK and USA).

The first meeting included a series of presentations on the validity and impact of ADHD, and general principles of diagnosis and treatment. All presentations were followed by an open discussion and general agreement on the wording of the consensus statement.

The second meeting focused on the development of treatment algorithms that would have an international relevance. To produce these algorithms the Global ADHD Working Group used reference materials gathered from guidelines previously developed for the treatment of ADHD, ADHD comorbid with disruptive behaviour disorder (DBD), and DBD without ADHD [10]. Based on consensus these were updated and extended to provide additional guidance for the treatment of ADHD with other comorbidities. The panel also reviewed and considered other national treatment algorithms in the development of this work [3, 12, 14] as well as treatment advances made during the intervening period.

Background

ADHD is one of the most common neurobehavioural disorders of childhood [4]. Prevalence rates vary from between 1–3% (diagnosed using ICD-10 criteria for hyperkinetic disorder (HKD), a more severe and stringently defined version of ADHD) to 4–8% (diagnosed using DSM-IV criteria). The lower prevalence rates still amount to a large population of children with pervasive ADHD, a significant proportion of whom are currently untreated [6]. ADHD impacts on many aspects of a child's development, including social, emotional and cognitive functioning, in both the home and school environment [2]. As such, all children with ADHD should be provided with appropriate assessment and treatment, to ensure their full and harmonious development. This is in line with the United Nations Convention on the Rights of the Child, which states that all children should be provided with the necessary medical assistance for the treatment of illness. Impairment persists in approximately two-thirds of children, who will continue to have problems into adolescence and adulthood. Long-term follow-up studies in North America and Europe have shown that untreated ADHD can lead to poor academic

achievement, low occupational status, increased risk of substance abuse and delinquency. Although the long-term impact in developing countries is not extensively studied, it seems to be similar.

Aetiology and pathophysiology

Family, adoption and twin studies support the conclusion that complex genetic factors are primarily implicated in the aetiology of ADHD. A wide range of studies of identical and fraternal twins converge on estimates of heritability of approximately 0.80, leading to the conclusion that the family environment is not the primary cause of ADHD [8]. The home environment, parental management and peer relationships can clearly influence the symptomatology of ADHD. Although single genes with major effects have not yet been identified, several candidate genes of small effect size have been identified such as DRD4, DRD5 and DAT1. Other factors affecting early brain development that may present as risk factors for the development of ADHD include maternal nicotine smoking and alcohol intake during pregnancy.

Neuroimaging studies of brain anatomy provide converging lines of evidence that ADHD is associated with a global reduction in brain volume, and with particular abnormalities in the frontal and parietal cortex, basal ganglia and cerebellum. Studies of brain function using functional neuroimaging, electrophysiological and neuropsychological techniques have demonstrated altered patterns of neuronal function for individuals with ADHD compared to subjects without ADHD. Neurochemical investigations, studies in animal models and the effectiveness of particular medications suggest that abnormalities in dopaminergic and noradrenergic brain circuits are specifically implicated in ADHD. Considered together, these findings provide strong supportive evidence for the validity of ADHD as a syndrome with important neurobiological aspects (or bases).

Diagnosis

Accurate diagnosis of children with ADHD and measurement of impairment is important to enable appropriate and successful management of symptoms [5]. Clinical diagnosis is based on symptomatology and to date no biological markers exist. The current criteria for diagnosing HKD are included in the World Health Organization International Classification of Diseases (ICD-10) [15] and the criteria for ADHD are included in the American Psychiatric Association Diagnostic and Statistical Manual (DSM-IV) [4]. The behavioural symptomatology that forms the basis for diagnosis is similar in both systems. The main differences relate to the con-

comitance of the three domains (inattention, overactivity and impulsivity), exclusion of comorbidity and degree of pervasiveness. ICD-10 criteria require a full set of symptoms in all three domains (inattention, overactivity and impulsivity), both at home and in the school environment; thus a diagnosis of HKD is most congruent with a DSM-IV diagnosis of combined type ADHD without the presence of comorbidity. Patients with ADHD whose symptoms do not present in all three domains, such as girls, older adolescents and adults, are likely to present with predominantly inattentive type, which is not included in ICD-10 as a separate category. ICD-10 criteria also make special provision for a combined diagnosis category if a conduct disorder is present, and use the presence or absence of a conduct disorder as the basis for the main subdivision of HKD. As ADHD is a highly comorbid condition, a differential diagnosis recognising the possibility of coexisting conditions is important. It should be noted, however, that ICD-10 criteria do not recommend a diagnosis of HKD in the presence of internalising disorders such as anxiety and depression.

Treatment approach

For those diagnosed with ADHD, a management programme should be established that recognises ADHD as a chronic condition that needs to be treated and monitored over time [3]. Children should have access to treatments with evidence of proven benefit, delivered by appropriately trained professionals who are qualified in the diagnosis and treatment of mental health disorders in their country. Complex cases should be treated by experts or consultants who can provide more specialist advice. Educating the parents and the child by providing knowledge about the disorder and how it can affect learning, behaviour, self-esteem, social skills and functioning within the family will enable the parents to work with the clinician to develop the most effective management plan for their child. It is important to recognise parents who may also have a diagnosis of ADHD, as parental ADHD can significantly impact on treatment. Discussion of desired improvement with the child, parents, school teacher and the treating clinician, and setting target outcomes for treatment can provide a guide to managing the disorder.

The Multimodal Treatment Study of Children with ADHD (MTA study) [11] is one of the largest studies performed to date on the treatment of children with ADHD. This study has provided support for medication-based intervention (primarily methylphenidate) in a substantial group of children diagnosed as having ADHD. Behavioural interventions were found to be particularly effective in treating non-ADHD symptom domains, such as problems in parent-child relationships,

poor academic achievement, social skills difficulties and anxiety symptoms. Re-analysis of this study was performed recently to investigate the impact of the ICD-10 classification system on interventions. This study showed that 25% of children diagnosed with ADHD using DSM-IV criteria, and included in the original study, would have been diagnosed with HKD using the ICD-10 criteria [13]. The study supports the recommendation that medication should be the first line of treatment for children diagnosed with HKD in combination with other effective interventions as appropriate. Although comorbid symptoms may alter response to pharmacotherapy, a combined approach (pharmacotherapy and psychotherapy) is recommended for children with ADHD/HKD and comorbidities such as anxiety, conduct disorder and oppositional defiant disorder [1].

Treatment algorithms for ADHD and associated comorbidities

These consensus treatment algorithms are designed to guide the multimodal treatment of ADHD alone, and in combination with common comorbidities such as depression, conduct disorder and tics.

While previous guidelines suggested that patients with comorbid ADHD should be referred immediately to a specialist, differences in the global availability of specialists mean that this is not always practical. These guidelines provide practical suggestions and are intended to help clinical judgement where the treatment of ADHD and associated comorbidities is managed by professionals who, in their different countries, are qualified to make comprehensive mental health assessments, whether individually or as part of a team. The guidelines have been designed to have global relevance.

General principles of treatment

■ Differential diagnosis

An accurate diagnosis is crucial for the treatment of ADHD, and treatment should never begin before a diagnosis has been confirmed. Treatment of ADHD varies according to the presence of comorbidity and is yet further complicated by determining which of the concurrent conditions should form the primary diagnosis and should therefore be treated first.

For each of the algorithms presented here, a differential diagnosis is an essential first step. These algorithms are designed to be used where ADHD is the primary diagnosis. If other psychiatric conditions are primary, these conditions should be treated first using guidelines appropriate for those conditions.

■ How should target behaviours be monitored?

Treatment response can be monitored using a range of validated rating scales [12]. It is helpful to establish a quantitative baseline value that can be used to judge improvement. Whichever scale is chosen, it is important to use the same rating scale at baseline and subsequent monitoring visits. It is preferable to collect ratings from multiple sources, such as parents and teachers, as well as the child, and to use the same raters at each assessment to avoid inter-rater variance.

Establishing whether symptoms and impairments have resolved is largely a matter of clinical judgement and careful history taking. While sufficient response to treatment can only be defined as a significant decrease in symptoms (e.g. > 50% reduction in symptoms), a more appropriate definition of response would be an absolute reduction in symptoms to close to normal. This minimises the risk of patients with severe symptoms receiving sub-optimal treatment.

For patients who respond to treatment, medication should be reviewed at least 2–3 times a year to assess ADHD symptoms, monitor medication compliance and review adverse events, although regular medication visits at monthly intervals is preferred practice supported by findings from the MTA study [11]. Treatment should then continue for at least a year before a trial off medication is considered, although this is based on clinical experience, as there is little evidence to guide this decision.

Algorithm 1: ADHD without comorbidity¹

This treatment algorithm is suggested for cases of ADHD without comorbidity; however it is also considered appropriate for cases of ADHD comorbid with oppositional defiant disorder (ODD) where aggression and disruptive behaviours are not problematic.

a) Before treatment begins it is important to screen for at least the major comorbidities associated with ADHD

Common comorbidities associated with ADHD include ODD, conduct disorder (CD), anxiety disorder and depression. Many children with ADHD also have tic disorders and Tourette's syndrome. Learning disability (mental retardation) should also be considered as there is a need to ensure that a global deficit in functioning is not mistaken for a specific attention deficit. Screening for comorbidities is essential as comorbid conditions can affect treatment choice and can influence

the efficacy of treatment options. Clinical assessment to consider the co-occurrence of other conditions should form part of any evaluation for ADHD, and family adversity, neglect and abuse should also be considered.

b) Adolescents, in particular, should be involved in psychoeducation. Appropriate language and information should be used to encourage their active and knowledgeable participation

Following a diagnosis of ADHD, education of the patient, their families and teachers is an essential part of treatment and should be included at every stage. For the individual, education should include an appropriate explanation of the symptoms of ADHD. Age-appropriate information should involve the individual in treatment choices, progress and monitoring. It is important that educational strategies recognise the cognitive level of the child and parent. As well as discussing associated impairments, the strengths of the individual should also be discussed. Adolescents in particular should feel involved in their own treatment options and should be educated about self-observation and management. This can help aid treatment compliance.

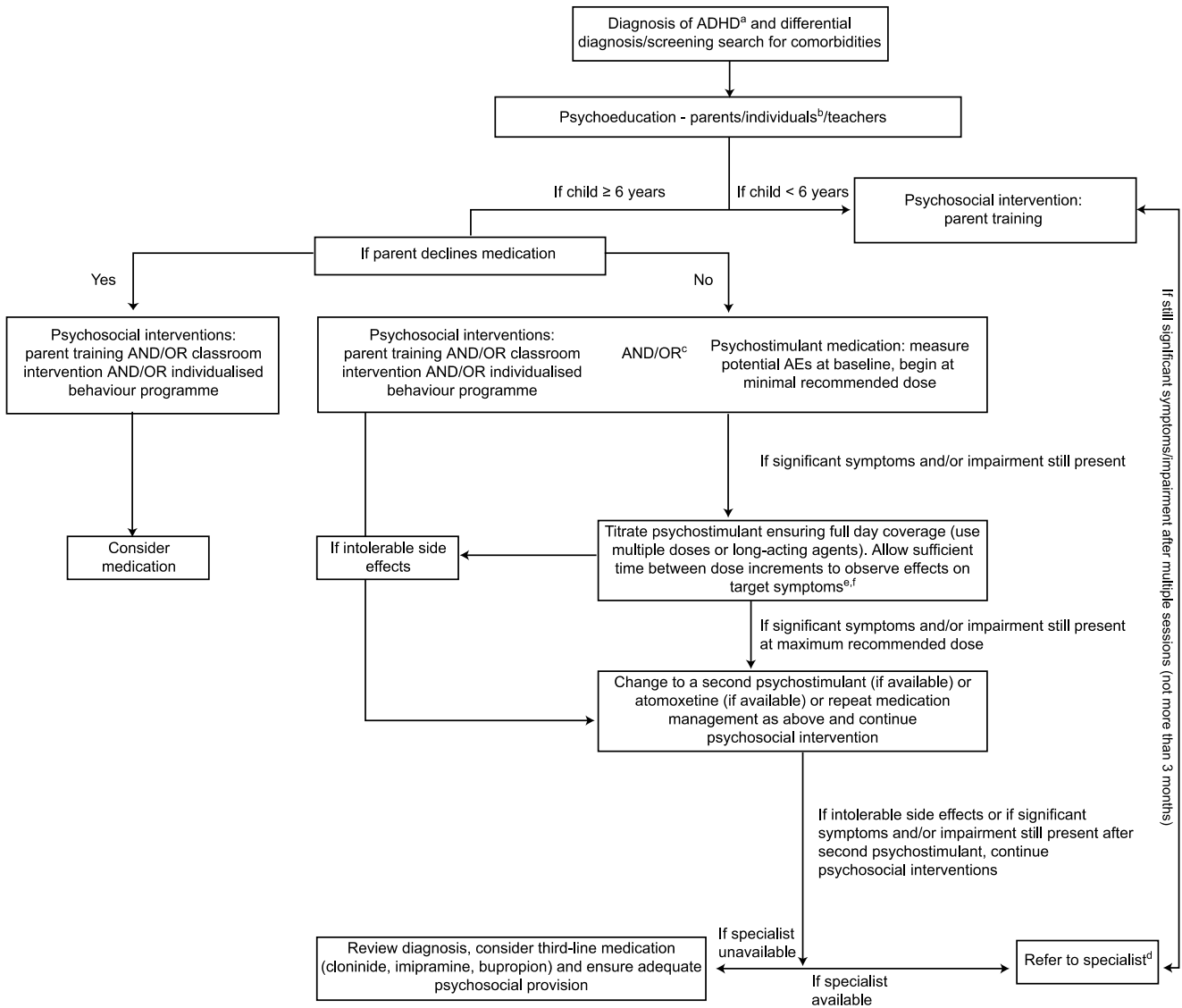
c) Medication guidelines and entry points for treatment

The decision of whether to use medication alone, behavioural therapy alone, or a multimodal approach should be based on the severity of symptoms and the diagnostic criteria used to make a diagnosis. Children with pure hyperkinetic disorder will have severe symptoms of inattention, hyperactivity and impulsivity and will require medication as their primary therapy. However, behavioural therapy can be useful if HKD is comorbid with ODD/CD. For less impairing symptoms, evidence suggests that behavioural therapy can be beneficial and may be tried first. A trial of medication is then indicated if impairment remains. The algorithm below provides a guide for entry points for treatment.

d) Children under 6 years who do not respond to psychosocial interventions should be referred to a specialist. The diagnosis should be reviewed and stressors and comorbidities identified

Specialist referral should be sought when psychosocial interventions have not been successful in managing a child under 6 years of age. The specialist should carefully evaluate the original diagnosis and consider stressors and the presence of comorbidities. If a diagnosis of

¹ Developed from Kutcher et al. (2004) Eur Neuropsychopharmacol



Algorithm 1 ADHD without comorbidity. The superscripts refer to the sections marked with lower case letters from a) to m)

ADHD is confirmed, medication should be considered with specialist management.

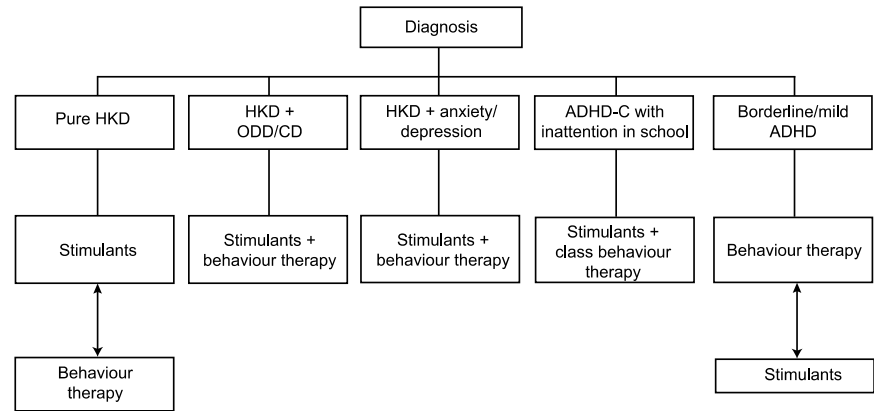
e) If considering doses above the equivalent of 0.7 mg/kg/dose methylphenidate (for prepubertal children; in adolescents equivalent to methylphenidate 25 mg/dose) then consider referral to specialist (see Table1)

Individuals requiring treatment with two or more medications should also be referred to a specialist.

Table 1 Dose conversion table

Medication	Equivalent dose at which patient should be referred to a specialist
Methylphenidate	0.7 mg/kg/dose or 60 mg/day
Dextroamphetamine	0.4 mg/kg/dose or 30 mg/day
Imipramine	1 mg/kg/day (option to refer all patients on imipramine to specialist)
Clonidine	Up to 0.05 mg tid for children < 45 kg Up to 0.1 mg tid for children > 45 kg
Bupropion	All patients on bupropion should be under specialist care
Atomoxetine	1.2 mg/kg

Individuals requiring treatment with two or more medications should also be referred to a specialist

Fig. 1 Guide for entry points for treatment

f) Inquire specifically about adverse events. Monitoring with blood tests is not routinely necessary

Monitoring of adverse events should include specific questioning using a checklist such as the one shown in Table 2.

Algorithm 2: ADHD and conduct disorder (including ODD with severe aggressive symptoms/outbursts)²

g) When ADHD is comorbid with conduct disorder, ADHD should be considered the primary diagnosis providing the patient does not pose a significant risk to themselves or others

In cases of ADHD and conduct disorder it is recommended that ADHD is treated first because conduct disorder is often secondary to this condition. Stimulant medications, as well as producing improvements in the core symptoms of ADHD, have also been shown to benefit oppositional symptoms, and the antisocial behaviour commonly associated with conduct disorder.

Table 2 Stimulant drug side effect rating scale [5] rated on a 10-point scale from 0 = absent to 9 = serious

Insomnia or trouble sleeping	Drowsiness
Nightmares	Sadness/unhappiness
Stares a lot or daydreams	Prone to crying
Talks less with others	Anxiousness
Uninterested in others	Bites fingernails
Decreased appetite	Euphoric/unusually happy
Irritable	Dizziness
Stomach aches	Tics or nervous movements
Headaches	

² Developed from Kutcher et al. (2004) Eur Neuropsychopharmacol

h) A multimodal approach to treatment should be adopted

Psychosocial interventions have been shown to be effective in the treatment of conduct disorder and should be included as first-line therapy for ADHD and conduct disorder.

Algorithm 3: ADHD and major depressive disorder (MDD)³

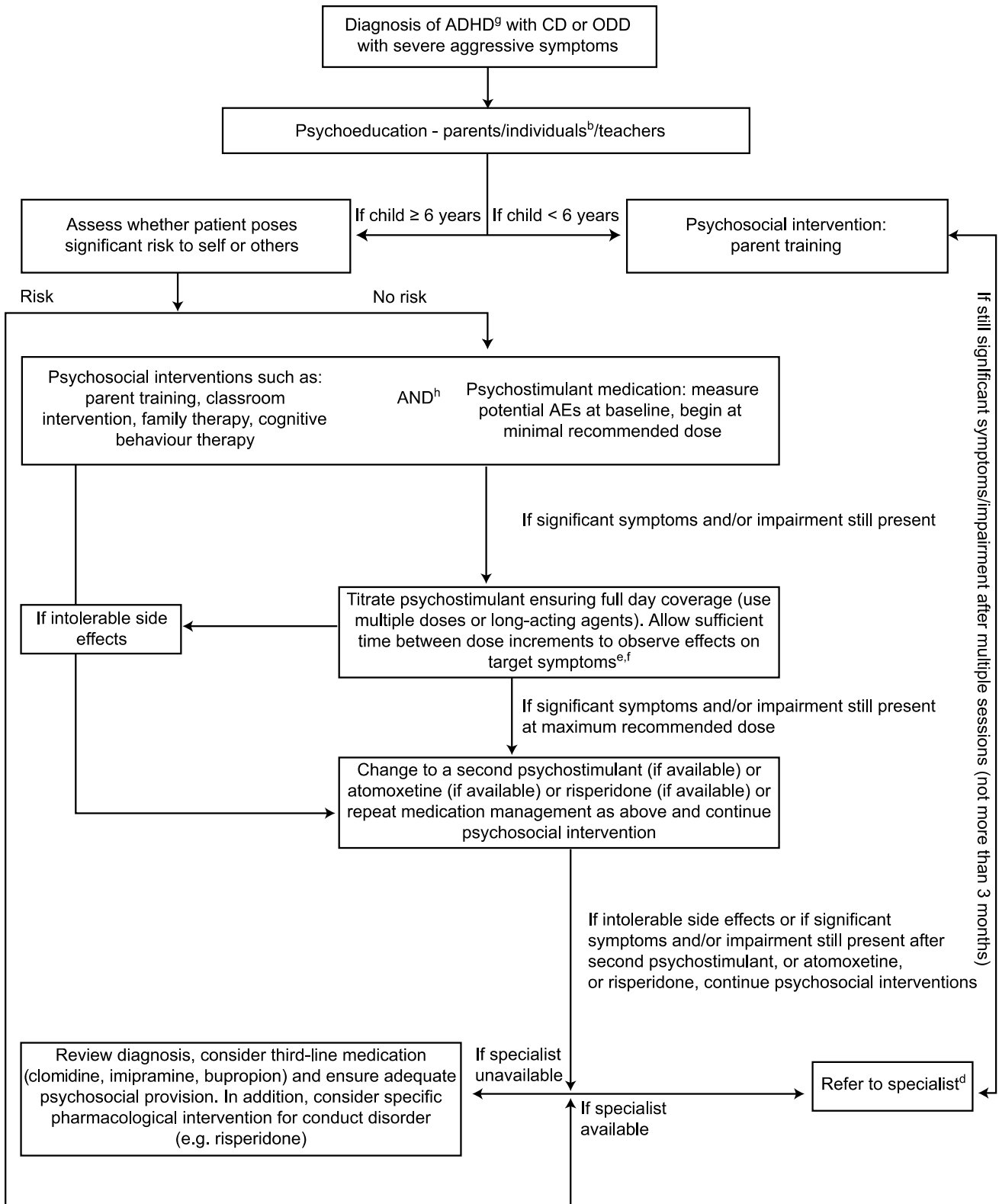
i) Treatment must be prioritised

MDD should be the focus of treatment for patients where MDD is the primary disorder or where MDD is characterised by very severe symptoms. In cases where MDD is secondary to ADHD, a stimulant trial should be performed first. As stimulants have a rapid onset of action, this can be accomplished quickly. ADHD patients with comorbid depression may also experience improvement in depressive symptoms related to improvements in academic, behavioural and social problems occurring with stimulant treatment.

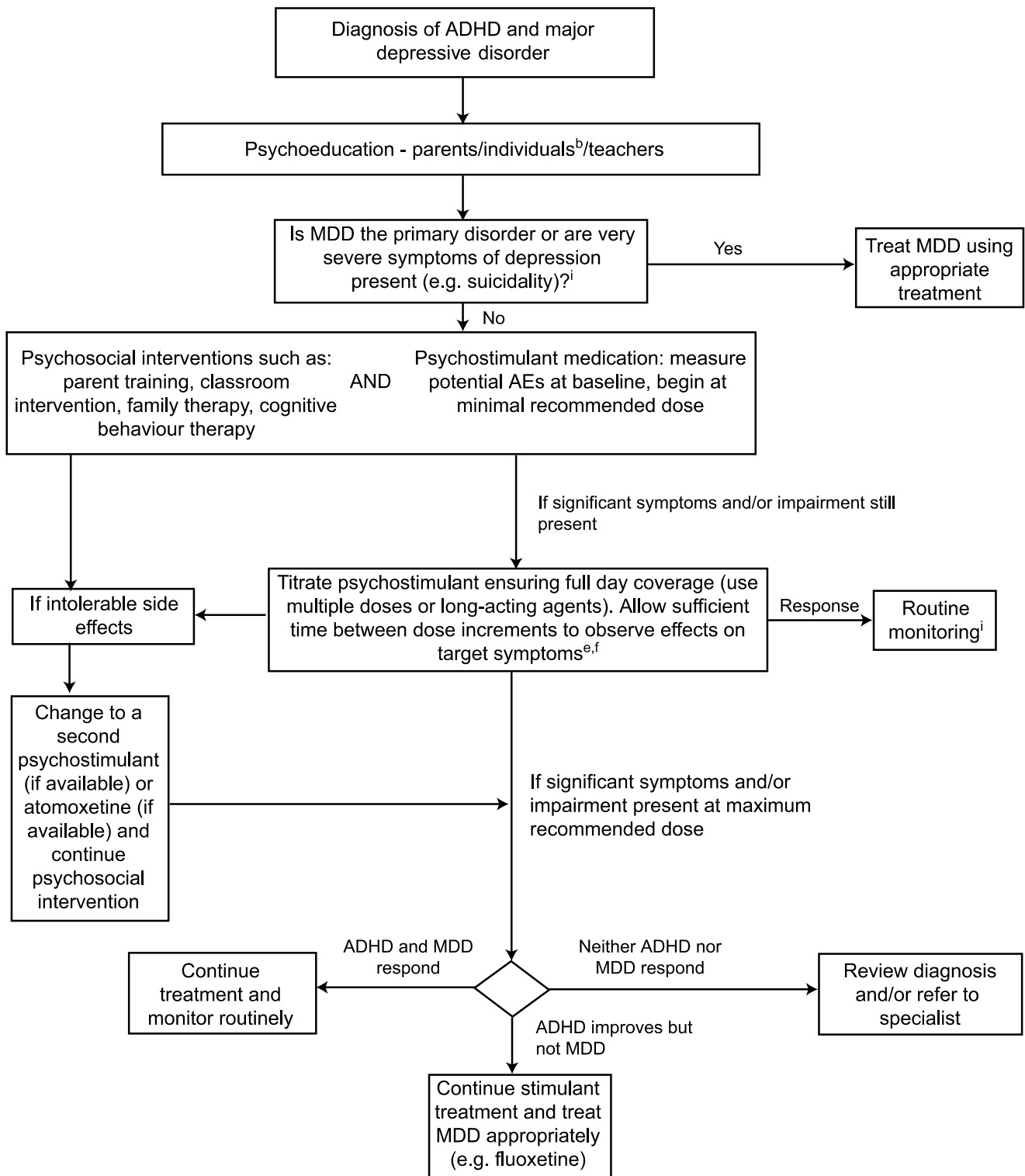
j) Following treatment response

Routine monitoring should include assessment for depressive symptoms as depression sometimes arises in the course of long-term ADHD treatment. If significant symptoms of depression arise during treatment, addition of an antidepressant may be helpful although treatment with two or more medications should usually require specialist referral [10].

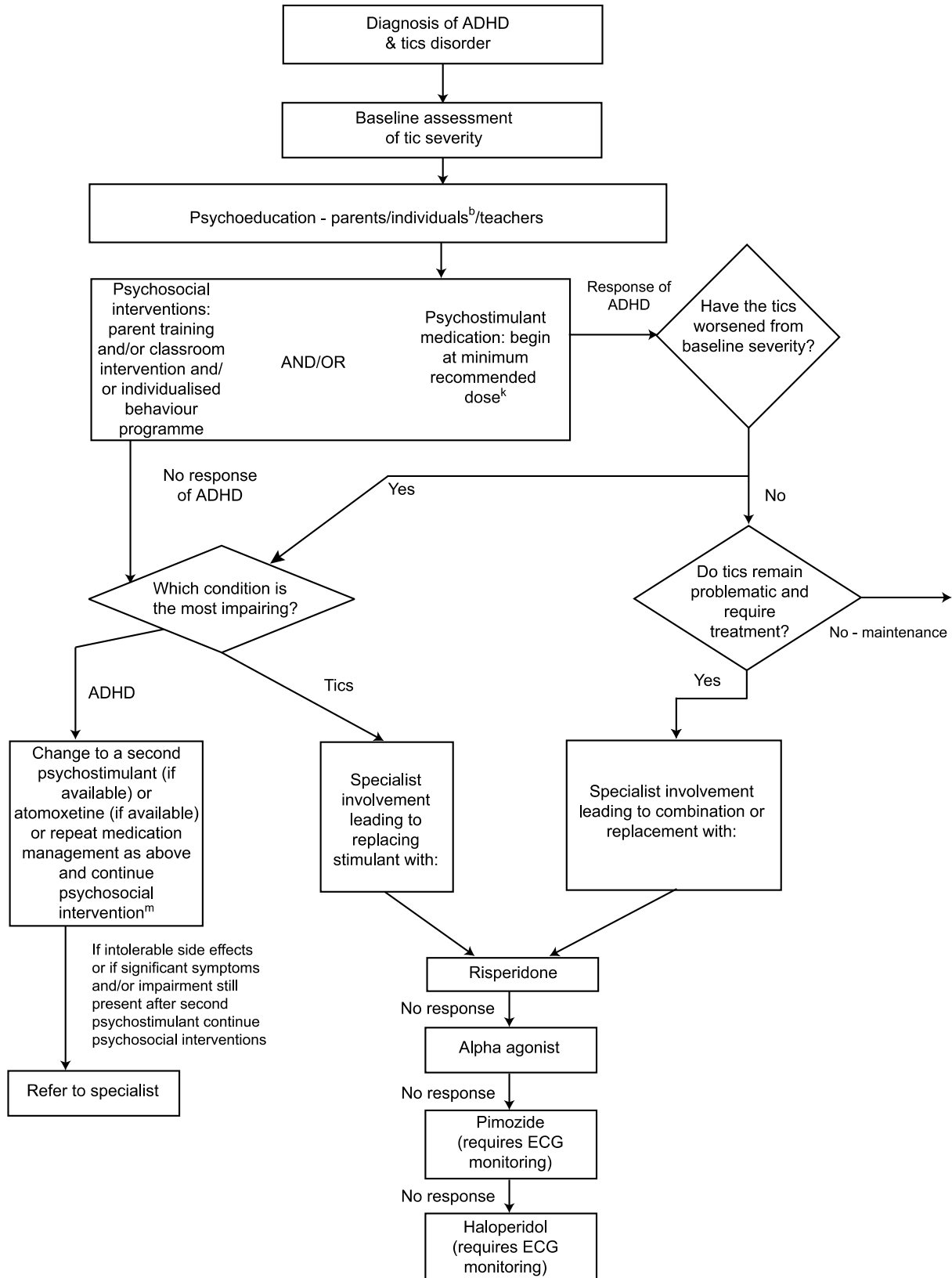
³ Developed from Kutcher et al. (2004) Eur Neuropsychopharmacol and Pliszka et al. (2000) J Am Acad Child Adolesc Psychiatry



Algorithm 2 ADHD and conduct disorder. The superscripts refer to the sections in the text marked with lower case letters from a) to m)



Algorithm 3 ADHD and major depressive disorder (MDD). The superscripts refer to the sections in the text marked with lower case letters from a) to m)



Algorithm 4 ADHD and the disorder. The superscripts refer to section in the text marked with lower case letters from a) to m)

Algorithm 4: ADHD and tic disorder⁴**k) Stimulants are an effective treatment in children with ADHD and tic disorders**

Stimulant medications can be given in children with ADHD and tics and are not necessarily contraindicated. Stimulant treatment is highly effective for the treatment of ADHD and recent research indicates that the incidence of tics does not increase significantly in most patients when treated with stimulants [7].

l) Patient preference should be considered when choosing a treatment plan

While many individuals with ADHD and comorbid tic disorder seek treatment for ADHD, tics are rarely seen as the primary reason for treatment, and often patients do not seek treatment for tics. Thus, when treating individuals with both disorders it is important to consider how impairing the tics are, and the treatment choice of the individual. When severe tics are more problematic than ADHD, treatment of tics should be prioritised.

m) Use clinical judgement to assess whether a second stimulant should be tried or whether to progress to a non-stimulant alternative

Following insufficient response to a stimulant or intolerable adverse events, clinical judgement should be used to determine whether a second stimulant should be tried based on the individual reaction to treatment and the child's age.

Treatments with no proven benefit

General play therapy, social skills training, occupational therapy, ergot alkaloids, biofeedback and acupuncture have no evidence of proven efficacy in ADHD and are not recommended. Cognitive behavioural therapy used in isolation has also been shown to be ineffective to treat ADHD and is not recommended by the panel [9].

Conclusions

While it is hoped that these algorithms will provide practical suggestions for the management of ADHD and associated comorbidities at a global level, the Global ADHD Working Group is aware that the practical implementation of algorithms can prove challenging. Members of the working group would be pleased to receive comments regarding the integration of these algorithms into clinical practice.

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⁴ Developed from Kutcher et al. (2004) *Eur Neuropsychopharmacol* and Pliszka et al. *J Am Acad Child Adolesc Psychiatry*

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