Neglected Diseases

Packages of Care for Attention-Deficit Hyperactivity Disorder in Low- and Middle-Income Countries

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This is the last in a series of articles highlighting the delivery of "packages of care" for mental health disorders in low- and middleincome countries. Packages of care are combinations of treatments aimed at improving the recognition and management of conditions to achieve optimal outcomes.

Introduction

Attention-deficit hyperactivity disorder (AD/HD) is a chronic, pervasive developmental disorder that, although usually diagnosed in childhood, spans the preschool to adult years. The most recent version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) defines the disorder using the core features of age-inappropriate hyperactivity, impulsivity, and inattention (Box 1) [1]. The 10th edition of the International Classification of Diseases (ICD-10) provides operational criteria for the similar, but more severe and narrowly defined hyperkinetic disorder (HKD) [2]. We have used the term AD/HD throughout this paper because most of the published literature relates to the broader concept of AD/HD rather than to HKD.

A rapidly expanding body of literature from low- and middleincome countries (LMICs) largely refutes the notion that AD/HD is a "Western" concept, although cultural factors clearly influence illness perceptions and help-seeking behavior [3-7]. A systematic review and meta-regression analysis of 102 studies from all continents concluded that the worldwide pooled prevalence of AD/HD is 5.3%, and that the geographic variability between AD/HD prevalence estimates is best explained by the methodological characteristics of the studies [8].

A strong body of evidence from high-income countries (HICs) suggests that AD/HD is a neurobiological syndrome with complex genetic factors primarily implicated in its etiology. Although individual risk alleles identified by molecular genetic studies increase the risk of AD/HD only slightly, the mean estimate of total heritability is just under 80% [9]. A wide range of social determinants significantly influence the symptomotology of AD/ HD in HICs. These include low socioeconomic status, low parental education, family conflict, parental mental disorder, severe early deprivation, and institutional upbringing [9-11]. The involvement of these multiple determinants in the symptomatology of AD/HD is consistent with the hypothesis that AD/HD is an etiologically heterogeneous, final common pathway disorder that is influenced by genes, environment, and gene-environment interactions. Other nongenetic causes of AD/HD identified in HICs are factors that affect early brain development, such as perinatal stress, low birth weight, prenatal smoking and alcohol use, obstetric complications, head injury, epilepsy, and HIV/AIDS [9–11]. The mediating and moderating influence of these variables on the development of AD/HD amongst children in LMICs is less well researched and does not always match with that seen in HICs [11].

The Evidence on the Treatment of AD/HD

Detection

Accurate detection and diagnosis of AD/HD is crucial for the effective management of individuals with the disorder [12–14]. Two structured approaches are available to detect and diagnose AD/HD: clinical diagnostic interviews and rating scales (Table 1). The only clinical diagnostic interview that we are aware has been assessed in LMICs is the Diagnostic Interview Schedule for Children (DISC-IV) [15], which has been validated for use in China [16] and for Xhosa-speaking South Africans [17]. In China, the test-retest reliability of the AD/HD component was excellent for the version of the interview given to parents (k = 0.81) and poor for the version given to adolescents (k = 0.25). Similarly, for the South African Xhosa version of the DISC-IV the parent version resulted in substantial reliability (k = 0.56) whereas the youth version resulted in poor reliability (k = 0.23). Although systematic reviews have investigated the numerous rating scales developed to diagnose AD/HD in HICs [12-14], only a few scales have been developed for use in LMICs. In Brazil, the test-retest reliability of a scale for use by teachers based on DSM-III-R diagnostic criteria ranged from 0.56 to 0.70 [18], and the diagnostic performance of the Child Behavior Checklist Attention problem scale resulted in moderate areas under the curve (AUC = 0.78) [19].

Medication

The efficacy of pharmacological interventions for the treatment of AD/HD in HICs is well established (Table 1) [20-23]. Although there are few studies on medication for AD/ HD from LMICs, efficacy data from studies conducted in HICs are likely to be applicable to these settings. Pharmacologic agents used in the treatment of AD/HD include the psychostimulants (methylphenidate or amphetamine), atomoxetine,

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Abbreviations: AD/HD, attention-deficit hyperactivity disorder; DISC-IV, Diagnostic Interview Schedule for Children Version IV; DSM, Diagnostic and Statistical Manual of Mental Disorders; HIC, high-income country; HKD, hyperkinetic disorder; ICD-10, International Classification of Diseases 10th edition; LMICs, low- and middle-income countries; MTA, Multimodal Treatment Study of Children with AD/HD; TCA, tricyclic antidepressant

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Summary Points

- Attention-deficit/hyperactivity disorder (AD/HD) is a multidimensional disorder that, although commonest in childhood and adolescence, can be diagnosed across the age span. Worldwide prevalence is about 5%.
- An appropriate package of treatment for AD/HD in lowand middle-income countries (LMICs) should include screening of high-risk groups, psychoeducational interventions with caregivers, methylphenidate, and behavioral interventions.
- Strategies to facilitate the delivery of effective interventions in LMICs should increase demand for services, access to AD/HD interventions, and the capacity of health care teams, as well as improve recognition of AD/HD, develop community-based and practice-based programs, and address the impact of AD/HD on other health and social outcomes.
- Interventions to address AD/HD should be part of a more comprehensive package of services for mental disorders.

bupropion, tricyclic antidepressants (TCAs), and alpha-agonists [24,25]. The psychostimulants, which have been used clinically for more than 50 years, are supported by the most robust efficacy and safety data and are available as affordable generic immediate and sustained release formulations [25]. Methylphenidate has been established as an effective short-term treatment for school-age children and adults with AD/HD, and there are some data, albeit sparse, that support its efficacy in preschoolers [26,27]. The short-term efficacy of atomoxetine, a newer medication, is also supported by numerous large-scale clinical trials, although direct comparison studies with the psychostimulants have demonstrated greater treatment effect sizes for methylphenidate [28,29]. Also, the psychostimulants are less expensive than atomoxetine and more likely to be available in LMICs. Longer-term open label studies in HICs for methyphenidate and atomoxetine support the efficacy and safety of both these medications [30,31].

Before the introduction of atomoxetine, tricyclic antidepressants (TCAs) were a common alternative to the psychostimulants.

Box 1. DSM-IV-TR Criteria for Attention Deficit Hyperactivity Disorder and International Classification of Diseases 10 Criteria for Hyperkinetic Disorder

According to the DSM-IV-TR, to satisfy the criteria for AD/ HD, a patient must manifest six or more symptoms of inattention or hyperactivity-impulsivity that have persisted for at least six months "to a degree that is maladaptive and inconsistent with developmental level." Examples of symptoms of inattention include often having difficulty in sustaining attention in tasks or play activities, being easily distracted by extraneous stimuli, and often being forgetful in daily activities. Examples of symptoms of hyperactivityimpulsivity include often fidgeting with hands or feet or squirming in seat, often talking excessively, and often having difficulty awaiting turn. In addition, some of the symptoms causing impairment must have been present before the age of seven years, some impairment from the symptoms must be present in two or more settings, there "must be clear evidence of clinically significant impairment in social, academic, or occupational functioning," and the symptoms should "not occur exclusively in the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder and are not better accounted for by another mental disorder" [1].

According to the ICD-10, to satisfy the criteria for hyperkinetic disorder, a patient must demonstrate "abnormality of attention, activity and impulsivity at home, for the age and developmental level of the child," as evidenced at least three of a set of attention problems, plus at least three of a set of activity problems, plus at least three of a set of impulsivity problems. In addition, the patient must demonstrate "abnormality of attention at school or nursery (if applicable), for the age and developmental level of the child," as evidenced by at least two of a set of attention problems and at least three of a set of activity problems. Also, there must be "directly observed abnormality of attention or activity," which is "excessive for the child's age and developmental level." Finally, the child must not meet criteria for selected other conditions, onset must be before the age of seven years, the duration must be at least six months, and the IQ must be above 50 [2].

Table 1. The evidence in support of AD/HD treatment.

Intervention	Evidence from HICs	Evidence from LMICs
Screening and diagnosis	 Test-retest reliability of the Diagnostic Interview Schedule for Children (DISC-IV) [15] Systematic review of measures used to diagnose AD/HD in preschool children [14] Summary of evidence-based assessment of AD/HD [13] Ten-year review of rating scales for assessing AD/HD [12] 	Test-retest reliability of the Chinese [16] and Xhosa [17] version of the DISC-IV. Test-retest reliability of a scale developed for use by teachers to assess AD/HD in Brazilian schools [18] Assessment of the Child Behavior Checklist-Attention problem scale in Brazil [19]
Methylphenidate	Systematic reviews [20–23]	_
Behavioral therapy	Review of evidence-based psychosocial treatments for AD/HD [47] Meta-analyses of the efficacy of behavioral therapy for AD/HD [48]	_
Cognitive behavioral therapy	 Review of cognitive training for AD/HD children [50] Review of cognitive, cognitive behavioral, and neural-based Interventions [49] 	_
Family therapy	 Meta-analysis of parent involvement in treating AD/HD [52] Cochrane Review of family therapy for AD/HD [51] 	Evaluation of Parent Management Training in Iran [53] Evaluation of effectiveness of providing parents with training about attention enhancing tasks and child behavior in India [54]

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However, few studies have compared the efficacy of these two drug classes and the association of TCAs with troublesome side effects, potential cardiotoxicity, and the risk of death in the event of overdose has taken TCAs out of favor [21,24,25]. The evidence base for other medications in the treatment of AD/HD is

The most frequent troublesome side effects associated with the psychostimulant medications are reduced appetite, weight loss, and sleep difficulties [32,33]. Compared to the pyschostimulants, atomoxetine has less-pronounced effects on appetite and sleep but is more likely to be associated with gastrointestinal upset [34]. Both the pyschostimulants and atomoxetine may be associated with slight increases in heart rate and blood pressure. Finally, the psychostimulants are controlled substances and concerns exist regarding the risk of pyschostimulant misuse and drug diversion. However, there is no clear evidence that pyschostimulant-treated AD/HD children abuse prescribed medication when they are appropriately diagnosed and carefully monitored [35].

Children treated with medication require careful clinical monitoring for side effects, clinical response, adherence, treatment acceptability, and dose adjustment. Treating clinicians must have a proficient understanding of the pharmacokinetic and pharmacodynamic properties of these medications, the potential for adverse events, and strategies for addressing emergent side effects. Medication monitoring should include: a baseline assessment followed by regular assessment of symptoms, function, side effects, adherence, and the emergence of comorbid disorders or other medical conditions; measurement of height, weight, blood pressure, and pulse; and provision of psychoeducation that addresses emerging questions or concerns from the patient or family.

There is limited empirical evidence (all from HICs) to inform the duration of treatment with pharmacological agents in AD/ HD. Six- and eight-year follow-up data from the Multimodal Treatment Study of Children with AD/HD (MTA) failed to provide support for long-term medication treatment where care was provided in community settings without ongoing careful titration and monitoring [36]. Decisions about continuing or discontinuing medication should be individualized, with periodic discontinuations to assess need and benefit.

Finally, decisions regarding the use of pharmacological therapy should be informed by the level of impairment, symptom severity, availability of appropriately trained health personnel and support, accessibility to monitoring and follow-up services, acceptability to patient and the family, and cost. Pharmacologic treatment is not indicated if symptoms are mild, if there is minimal impairment or an unclear diagnosis, if there are inadequate services for close monitoring and follow-up, or if the use of medication is unacceptable to the patient or family.

Structured Psychotherapies

Two of the largest studies of psychotherapies for the treatment of AD/HD ever conducted are the New York-Montreal Study and the MTA study [37–41]. In the New York-Montreal Study, 103 children with AD/HD (ages 7–9), who did not have comorbid conduct or learning disorders and who had responded to methylphenidate were allocated randomly to three groups for two years: (1) methylphenidate treatment alone; (2) methylphenidate combined with multimodal psychosocial treatment that included parent training and counseling, academic assistance, psychotherapy, and social skills training; or (3) methylphenidate plus attention control treatment that excluded specific aspects of the psychosocial intervention. Individual assessments were conducted on outcome measures such as academic and emotional status [39] and symptomatic improvement [40]. This study found no significant difference between the combined-treatment groups and the medication-only group. In the MTA study, 579 children aged 7.0 to 9.9 years with AD/HD were randomly assigned to four treatment groups (medication, behavioral treatment, combined treatment, and community care) [38]. The authors concluded that after the 24-month follow-up, medication was superior over the other individual treatment options and that there was no significant difference between the combined treatment and medication-only [41]. However, further analysis of the data concluded that patients with AD/HD and either comorbid disorders [42-44] or psychosocial stressors [45,46] did benefit from adjunctive psychosocial interventions (parent training and behavioral interventions).

Several reviews have investigated whether psychosocial interventions are effective for treating children and adolescents with AD/HD (Table 1). A systematic literature review [47] and a metaanalysis that investigated 174 AD/HD treatment studies concluded that behavioral treatment is highly effective [48]. Reviews of cognitive-behavioral [49,50] and family therapy [51,52] interventions have yielded promising but inconclusive findings.

We were not able to locate any randomized controlled trials addressing the efficacy of structured psychotherapies for the treatment of AD/HD in LMICs. However, an Iranian study [53] reported that Parent Management Training (eight sessions, once a week for 1.5 hours) improved the behavior of 15 children with AD/HD and the general health of their parents. Similarly, an Indian study investigated the effectiveness of a program providing five training sessions to ten parents of boys aged 6-10 years with AD/HD. The training, which addressed attention-enhancing tasks and child behavior principles and techniques, had significant effects on the behavior of the children, and parent-reported study habits, pro-social behavior, and academic performance [54].

Delivery of Effective Interventions

Interventions to Increase Demand for Services

Similarly to the other disorders discussed in this series, stigma and a lack of awareness about mental health problems are important contributors to a relatively low demand for services for AD/HD in LMICs. In the case of AD/HD, however, the salience of these factors is magnified because AD/HD is most common among children and adolescents, an age group in which stigma and lack of awareness are particularly evident [55]. Among populations where stigma is high and knowledge levels low, efforts should be directed in the first instance to increasing general awareness and recognition of the disorder (Table 2). Once this goal has been achieved, attention may need to be focused on minority groups, inattentive type AD/HD, girls with AD/HD, and adult AD/HD. While specialists in mental health, education, and pediatrics should take a leading role in reducing stigma and increasing awareness, the potential contribution of communitybased advocacy groups should not be ignored. School is a particularly important setting for stigma reduction and information raising activities. While we were unable to locate any reports that evaluated awareness or recognition programs for AD/HD specifically, Hoven et al. [56] assessed children, parents, and teachers before and after an awareness program to determine changes in knowledge, attitudes, and understanding of mental health in nine countries including Azerbaijan, Brazil, China, Georgia, Russia, and Uganda. The authors reported a positive change in awareness in all the countries and an increased willingness to discuss emotional problems freely.

Table 2. Delivery treatments for AD/HD.

Step	How	By Whom	In What Settings
Increasing demand for services	 Develop and implement mental health literacy programs for the general public, government, non-government and private sectors focused on increasing awareness and understanding of common mental disorders and addressing the stigma associated with them. Develop and implement specific awareness programs for common child mental disorders specifically targeting the general public and community organizations that interface with children and adolescents. Target awareness programs to increase recognition of specific subgroups once services are available and accessible to the most prevalent groups. 	Child and adolescent mental health specialists Educational psychologists Community pediatricians Mental health advocacy groups	 Schools [56] Faith-based organizations Primary health care services Social development offices Traditional healing practices General practices Pediatric and psychiatric services
Increasing access to AD/HD interventions	 Create the necessary policy and legislative environment [57] Ensure access to methylphenidate and other medications Provide affordable and equitable services and referral pathways [9] Develop services in rural settings Encourage affordable local public transport to improve accessibility of services Provide selected interventions in school settings [58] Integrate child and adolescent mental health services with primary and traditional care systems For adolescents, provide interventions 'youth friendly' settings Offer incentives for child and adolescent mental health specialists to work outside of regional centers Establish shorter and more direct training pathways to registration as a sub-specialist 	 Child and adolescent mental health specialist teams Community pediatric teams General adult psychiatrists in regions without access to child and adolescent mental health services Primary mental health nurses Mental health advocacy groups Politicians Service planners and managers Pharmacists 	 Rural community clinics Village health teams General practice clinics Community pediatric services Schools Youth clubs and centers
Increasing the capacity of health care teams	 Provide training, supervision, liaison and consultation for all providers or potential providers of services for people with AD/HD [9,58] Strengthen formal links between services based in cities and those in rural areas, partly using tele-psychiatry if feasible [57] Establish shorter and more direct training pathways to registration as a sub-specialist 	 Child and adolescent mental health specialist teams Specialist and sub-specialist training institutions 	 Rural community clinics Village health teams General practice clinics Community pediatric services General adult psychiatric services
Improving recognition of AD/HD	 Increase capacity of health care teams Improve access to valid and reliable AD/HD rating instruments Improve access to psychometric testing to evaluate overall intelligence and exclude specific learning disorders 	Child and adolescent mental health specialist teams General adult psychiatrists in regions without access to child and adolescent mental health services Educational psychologists Community pediatricians	 Schools Primary health care services Social development offices Traditional healing practices General practices Community pediatric practices Institutional and alternative child care settings
Adapting AD/HD treatments to increase acceptability or reduce costs	 Integrate mental health services into the education and health care systems [57] Provide culturally acceptable and language-appropriate care [9] Reduce racial/ethnic disparities in access to child and adolescent mental health services Institute group psychotherapy interventions, including parent management training and social skills/anger management groups Increase access to less stigmatizing, longer-acting stimulant medications that do not need to be taken during school hours Develop nurse-led, specialist-supervised AD/HD clinics Consider motivational enhancement therapy for adolescents 	Child and adolescent mental health specialist teams Community paediatric teams Child psychiatric nurse specialists Primary mental health nurses and social workers Educators and school counsellors	 Schools Pre-schools Community clinics Community centers Youth clubs/centers General practice clinics Community pediatric services Child and adolescent mental health care services
Developing community- based programs	 Introduce classroom-based behavioral strategies Encourage caretakers to use behavioral techniques and improve communication between them and children with the disorder Persuade leaders of community-based programs to link people with the disorder with services that provide appropriate interventions Institute early childhood development programs 	Child and adolescent mental health specialist teams Community pediatric teams General adult psychiatrists in regions without access to child and adolescent mental health services Primary mental health nurses and social workers Educators and school counselors	Schools Pre-schools Community clinics Community centers General practice clinics Rural outreach teams and village health teams Community pediatric services Child and adolescent mental health services

Table 2. Cont.

Step	How	By Whom	In What Settings
Encouraging practice- based programs	Collaborative care	Specialists in mental health Non-professional health care workers	Primary health care settings
Addressing the impact of AD/HD on other health and social outcomes	 Deliver services for people with AD/HD together with services for other disorders Provide AD/HD services throughout the life span Provide interventions for specific problems that are associated with AD/HD, such as anger management, family conflict, scholastic deficiencies and substance misuse 	 Child and adolescent mental health specialist teams Community pediatric teams General adult psychiatrists in regions without access to child and adolescent mental health services Mental health service managers and planners 	All settings where AD/HD interventions are delivered

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Interventions to Increase Access to Interventions

Important elements of a strategy for increasing access include advocacy for the development of new, or the revision of existing, policy and legislative frameworks that ensure the promotion of mental health and the development of services that are accessible, affordable, appropriate, and acceptable to the children, families, and communities they are meant to serve (Table 2). Other important elements include ensuring that evidence-based, costeffective treatments are both accessible and consistently available and that appropriately trained, skilled, and experienced staff are available [57]. A crucial aspect of access to effective treatment for AD/HD is access to the psychostimulants and other pharmacological agents for which there is evidence of effectiveness. This may require that child and adolescent psychiatrists and pharmacists attend financial committees and other managerial structures to ensure that the appropriate psychopharmacological agents are available and affordable, that financing is sustainable, and that health and supply systems are reliable. Clearly, the inclusion of methylphenidate in national and transnational lists of essential drugs is crucial in facilitating such circumstances.

Interventions to Increase the Capacity of Health Care Teams

People with AD/HD may interface with health providers in many settings. Thus, a broad range of health care providers may be potential targets of capacity development activities. Depending on the context, providers may include child and adolescent mental health specialists, pediatricians, general psychiatrists, general medical service providers, and other nonphysician health providers, particularly those who work closely with children and adolescents. Opportunities for continual learning and support through mentorship, supervision, and continuing education should be built into capacity development initiatives. Training content should be tailored to the needs of target groups but should be based on an understanding of AD/HD as a chronic, pervasive disorder requiring a holistic, multisectoral approach to management and should be provided as part of a broader curriculum that addresses the comorbid mental health issues associated with AD/ HD. Ensuring that capacity development initiatives are accessible and available to target groups can be a challenge in any context, and how training is delivered may have to be tailored to best meet the needs of the recipients. General psychiatrists in rural areas might benefit from telepsychiatry to improve their prescribing practices, for example. Similarly, educators might benefit from continuing education seminars that focus on the identification of children with AD/HD and on classroom interventions, and pediatric primary health care nurses might benefit from supervised clinical practice followed by direct access to a nursing or medical specialist consultation.

Interventions to Improve Recognition of AD/HD

Strategies to improve recognition of AD/HD should be implemented only once access to services has been ensured and health care providers have sufficient capacity to respond to an increased demand for interventions. There are three aspects to improving recognition: (1) awareness of the risk factors for AD/ HD and the identification of persons at risk; (2) screening of persons at risk for ADHD; and (3) determination of a diagnosis of AD/HD. As mentioned above, there are many useful clinical instruments and rating scales for both screening and assessment of AD/HD. Depending on the context, informal health services, schools, faith-based organizations, and other community-based groups can be invaluable in the early recognition of risk factors for potential mental health problems including AD/HD. Where available, psychometric testing may also help to assess the extent to which low levels of intellectual functioning or deficits in academic skill contribute to the presentation. Clearly, such instruments, rating scales, and tests are most likely to produce optimum benefits when they are administered by people with the necessary skill, training, and facility in the language of the individuals who are being assessed.

Interventions to Adapt Treatments to Increase Acceptability or Reduce Costs

Both methylphenidate and amphetamine, the best-studied and most cost-effective medicines for AD/HD, are available in long-acting preparations that require once daily dosing. Such dosing is often preferable to multiple daily dosing, particularly for schoolaged children and adolescents, and should be made available where possible. Psychosocial interventions may be delivered in either individual or group format and may be offered in various settings including schools. Individual-level interventions, while having advantages over group-level interventions, are not always feasible because of the shortages of appropriately trained staff. While group-level interventions are implemented in many settings in both LMICs and HICs, there is a dearth of evaluations of such interventions, a gap that begs filling.

Integration of child and adolescent mental health services into the education and/or primary health care system can also increase the acceptability and affordability of AD/HD treatments [58].

There are numerous models for integrating mental health services into community and primary care that require the development of continuous care pathways linking different levels of the health system. One example is the development of nurse-led but specialist-supervised clinics. The strategy adopted will be highly dependent on the resources and infrastructure available in a particular setting.

Interventions to Develop Community-Based Programs

The establishment of community-based initiatives in partnership with formal health services allows the development of a continuous network of care and support for children with AD/HD and their families. Such care and support is essential to achieving and maintaining optimal functioning and ameliorating the disability associated with AD/HD. Schools, where most children spend most of their time, can be the cornerstone of such programs. Educators can be helped to implement classroom-based behavioral interventions such as token economy systems in which children are rewarded immediately for desirable behavior with tokens that can be exchanged later for a reward, or response cost systems in which a "fine" is imposed for bad behavior. Other interventions that could be introduced include increasing teacher-to-child classroom ratios and breaking the school day into brief academic assignments interspersed with brief periods of physical exercise [58]. Community-based organizations can also be used to deliver parenting interventions and support for families and caregivers, to provide gatekeeper functions and public mental health education, and to assist with accessing medications for which there is evidence of effectiveness.

Interventions to Encourage Practice-Based Programs

Collaborative care programs that are specific to a particular disorder (as opposed to more general strategies such as the integration of mental health care into the primary health care system) have been successfully implemented for depression [59]. Furthermore, there is evidence that with appropriate diagnostic and pharmacological training, both general practitioners and pediatricians can apply this intervention effectively in HICs for AD/HD [60,61]. However, we were not able to locate any studies in which practice-based programs to address AD/HD have been implemented and evaluated in LMICs.

Interventions to Address the Impact of AD/HD on Other Health and Social Outcomes

AD/HD is frequently comorbid with other mental health problems and is associated with a range of negative health and social outcomes. Thus, services for people with AD/HD should not be delivered in isolation from services for other disorders. Also, because most children with AD/HD will retain the diagnosis into adulthood or continue to be deleteriously affected by the symptoms associated with AD/HD, it is crucial that interventions

References

- American Psychiatric Association (APA) (2004) Diagnostic and Statistical Manual of Mental Disorders: Fourth Edition Text Revision (DSM-IV-TR). Washington DC: APA
- World Health Organization (WHO) (1992) The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva: WHO.
- Buitelaar JK, Barton J, Danckaerts M, Gillberg C, Hazell PL, et al. (2006) A comparison of North American versus non-North American AD/HD study populations. Europ Child Adolesc Psychiat 15: 177–181.
- Faraone S, Sergeant J, Gillberg C, Biderman J (2003) The worldwide prevalence of AD/HD: is it an American condition? World Psychiat 2: 104–113.
- Rohde LA, Szobot C, Polanczyk G, Schmitz M, Martins S, Tramontina S. (2005) Attention-deficit/hyperactivity disorder in a diverse culture: Do research

Table 3. Packages of care for AD/HD.

Low-Resource Settings	High-Resource Settings
Screening of high-risk groups	Screening of high-risk groups or routine screening with confirmation of diagnosis by a skilled clinician
Psychoeducational interventions with caregivers	Psychoeducational interventions with caregivers
Methylphenidate	Methylphenidate and other medication
Behavioral interventions	Behavioral interventions

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are not terminated in adolescence, as frequently occurs. By continuing to receive intervention, the probability of long-term adverse consequences of the disorder is reduced. Finally, it is important to offer interventions for selected specific problems that are associated with AD/HD, such as anger management, family conflict, scholastic deficiencies, and substance misuse.

Packages of Care for AD/HD in LMICs

AD/HD is a common developmental disorder that affects individuals throughout their lives and across all cultural contexts, and is associated with considerable social, psychological, and economic adversity. Recognition of the disorder can be improved by the use of screening instruments, some of which have been shown to have adequate psychometric properties in LMICs. Although there are few studies from LMICs that address the effectiveness of methylphenidate, the consistent and strong effects that have emerged from HICs suggest that this drug will be effective universally. In addition, although the evidence for structured psychotherapies is mixed, there is sufficient justification to include behavioral interventions in a package of care for AD/ HD in LMICs (Table 3). However, given that most people worldwide with AD/HD will not receive interventions from a mental health specialist such as a psychiatrist or psychologist, it is essential that efforts to deliver this package of care in LMICs are not dependent on such specialists. There are risks associated with such an approach. For example, the quality of the interventions may be less than would have been the case if they were delivered by specialists. However, such risks need to be weighed against the certainty that services will be less accessible if they are delivered by specialists. Finally, it is crucial that this package of care for AD/ HD form part of a more comprehensive package of services in which other disorders are also addressed.

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- and clinical findings support the notion of a cultural construct for the disorder? Biol Psychiat 57: 1436-1441.
- Canino G, Alegría M (2008) Psychiatric diagnosis is it universal or relative to culture? J Child Psychol Psychiatry 49: 237–50.
- Flisher AJ, Hatherill S, Dhansay Y, Swartz L. (2007) ADHD, Culture and the DSM-V (abstract). J Child Adolesc Mental Health 19: 173.
- Polanczyk G, De Lima MS, Horta BL, Biederman J, Rohde LA (2007) The worldwide prevalence of ADHD: A systematic review and metaregression analysis. Am J Psychiat 164: 942–948.
- Biederman J (2005) Attention-deficit/hyperactivity disorder: A selective overview. Biol Psychiatry 57: 1215–1220.
- Biederman J, Faraone SV (2005) Attention deficit hyperactivity disorder. Lancet 366: 237–248.

- 11. Patel V, Lund C, Hatherill S, Plagerson S, Corrigall J, et al. (in press) Social Determinants of Mental Disorders. In: Blas E, Sivasankara Kurup A, eds. Priority public health conditions: from learning to action on social determinants of health. Geneva: WHO.
- 12. Collett B, Ohan J, Myers K (2009) Ten-Year Review of Rating Scales. V: Scales Assesing Attention-Deficit/Hyperactivity Disorder. J Am Acad Child Adolsc Psychiat 42: 1015-1037
- 13. Pelham W, Fabiano G, Massetti G (2005) Evidence-Based Assessment of Attention Deficit Hyperactivity Disorder in Children and Adolescents. J Clin Child Adolesc Psychol 34: 449-476.
- 14. Smith K, Corkum P (2007) Systematic Review of Measures Used to Diagnose Attention-Deficit/Hyperactivity Disorder in Research on Preschool Children. Topics Early Child Spec Educ 27: 164.
- 15. Shaffer D, Fisher P, Lucas CP, Dulcan MK, Schwab-Stone ME (2000) NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): Description, differences from previous versions, and reliability of some common diagnoses. J Am Acad Child Adolesc Psychiatry 39: 28-38.
- 16. Leung PW, Lee CC, Tang CP, Hung SF, Kwong SL, et al. (2005) Test-retest reliability of the Chinese version of the Diagnostic Interview Schedule for Children-Version 4 (DISC-IV). J Child Psychol Psychiatry 46: 1135–1138.
- 17. Flisher AJ, Lund C, Sorsdahl K, Robertson B (2009) Test-Retest Reliability of the Xhosa Version of the Diagnostic Interview Schedule for Children (abstract). I Child Adolesc Mental Health 21: 88.
- 18. Brito G, Pinto R, Lins M (1995) A behavioral assessment scale for attention deficit disorder in Brazilian children based on DSM-IIIR criteria. J Abnorm Child Psychol 23: 509-520.
- 19. Lampert TL, Polanczyk G, Tramontina S, Mardini V, Rohde LA (2004) Diagnostic performance of the CBCL-Attention Problem Scale as a screening measure in a sample of Brazilian children with AD/HD. J Atten Disord 8:
- Vitiello B (2001) Methylphenidate in the treatment of children with attentiondeficit hyperactivity disorder. Can Med Assoc J 165: 1505-1506.
- 21. Banaschewski T, Coghill D, Santosh P, Zuddas A, Asherson P, et al. (2006) Long acting medications for the hyperkinetic disorders: a systematic review and European treatment guideline. Eur Child Adolesc Psychiatry 15: 476-495.
- 22. Karande S (2005) Attention deficit hyperactivity disorder a review for family physicians. Indian J Med Sci 59: 546-555.
- 23. Kratochvil CJ, Egger H, Greenhill LL, McGough JJ (2006) Pharmacological management of preschool ADHD. J Am Acad Child Adolesc Psychiatry 45:
- Taylor E, Döpfner M, Sergeant J, Asherson P, Banaschewski T, et al. (2004) A European clinical guidelines for hyperkinetic disorder - first upgrade. Eur Child Adolesc Psychiatry 13 (Suppl 1): 17-130.
- 25. American Academy of Child and Adolescent Psychiatry (2007) Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 46: 894-921
- 26. Greenhill LL, Kollins S, Abikoff H, McCracken J, Riddle M, et al. (2006) Efficacy and safety of immediate-release methylphenidate treatment for preschoolers with ADHD. J Am Acad Child Adolesc Psychiatry 45: 1284-1293.
- 27. Wigal T, Greenhill LL, Chuang S, McGough J, Vitiello B, et al. (2006) Safety and tolerability of methylphenidate in preschool children with ADHD. J Am Acad Child Adolesc Psychiatry 45: 1294-1303.
- 28. Michelson D, Allen AJ, Busner J, Casat C, Dunn D, et al. (2002) Once-daily atomoxetine treatment for children and adolescents with attention deficit hyperactivity disorder: a randomized, placebo-controlled study. Am J Psychiatry 159: 1896-1901.
- 29. Michelson D, Faries D, Wernicke J, Kelsey D, Kendrick F, et al. (2001) Atomoxetine in the treatment of children and adolescents with attention-deficit/ hyperactivity disorder: a randomized, placebo-controlled, dose-response study. Pediatrics 108: 1-9.
- 30. Wilens T, McBurnett K, Stein M, Lerner M, Spencer T, Wolraich M (2005) ADHD treatment with once daily OROS methylphenidate treatment: final results from a long term open-label study. J Am Acad Child Adolesc Psychiatry 44: 1015-1023.
- 31. Wilens T, Gao H, Thomason C, Gelowitz D, Kratochvil C, Newcorn J (2004) Longer term treatment with atomoxetine in adolescents with ADHD. Scientific Proceedings of the American Psychiatric Association, No. 578, New York, May.
- 32. MTA Cooperative Group (2004) National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: changes in effectiveness and growth after the end of treatment. Pediatrics 113: 762-769.
- Vitiello B, Severe JB, Greenhill LL, Arnold LE, Abikoff HB, et al. (2001) Methylphenidate dosage for children with ADHD over time under controlled conditions: lessons from the MTA. J Am Acad Child Adolesc Psychiatry 40: 188-196.
- 34. Greenhill LL, Newcorn JH, Gao H, Feldman PD (2007) Effect of two different methods of initiating atomoxetine on the adverse event profile of atomoxetine. Am Acad Child Adolesc Psychiatry 45: 566–572.
- Wilens TE, Faraone SV, Biederman J, Gunawardene S (2003) Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. Pediatrics 111: 179-185.
- Molina BS, Hinshaw SP, Swanson JM, Arnold LE, Vitiello B, et al. (2009) The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. J Am Acad Child Adolesc Psychiatry 48: 484-500.

- 37. Klein RG, Abikoff H, Hechtman L, Weiss G (2004) Design and rationale of controlled study of long-term methylphenidate and multimodal psychosocial treatment in children with ADHD. J Am Acad Child Adolesc Psychiatry 43:
- The MTA Cooperative Group (1999) A 14-month randomized clinical trial of treatment strategies for attention deficit/hyperactivity disorder (AD/HD). Arch Gen Psychiatry 56: 1073-1086.
- 39. Hechtman L, Abikoff H, Klein RG, Weiss G, Respitz C, et al. (2004) Academic achievement and emotional status of children with ADHD treated with longterm methylphenidate and multimodal psychosocial treatment. J Amer Acad Child Adolesc Psychiatry 43: 812-819.
- 40. Abikoff H, Hechtman L, Klein RG, Weiss G, Fleiss K, et al. (2004) Symptomatic improvement in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. J Amer Acad Child Adolesc Psychiatry 43: 802-811.
- 41. MTA Cooperative Group (2004) National Institute of Mental Health Multimodal Treatment Study of AD/HD Follow-up: 24-Month Outcomes of Treatment Strategies for Attention-Deficit/Hyperactivity Disorder. Pediatrics
- 42. Conners CK, Epstein JN, March JS, Angold A, Wells KC, et al. (2001) Multimodal treatment of ADHD in the MTA: An alternative outcome analysis. J Am Acad Child Adolesc Psychiatry 40: 159-167.
- 43. March JS, Swanson JM, Arnold LE, Hoza B, Conners CH, et al. (2000) Anxiety as a predictor and outcome variable in the multimodal treatment study of children with ADHD MTA. J Abnorm Child Psychol 28: 527-541.
- Jensen PS, Hinshaw SP, Swanson JM, Greenhill LL, Conners CK, et al. (2001) Findings from the NIMH Multimodal Treatment Study of ADHD MTA: implications and applications for primary care providers. J Dev Behav Pediatr 22: 60-73
- 45. Arnold LE, Elliot M, Sachs L, Bird H, Kraemer HC, et al. (2003) Effects of ethnicity on treatment attendance, stimulant response/dose, and 14-month outcome in ADHD. J Consult Clin Psychol 71: 713-727.
- 46. MTA Cooperative Group (1999) Moderators and mediators of treatment response for children with attention deficit hyperactivity disorder: the MTA Study. Arch Gen Psychiatry 56: 1088-1096.
- 47. Chronis A, Jones H, Raggi VL (2006) Evidence-based psychosocial treatments for children and adolescents with attention-deficit/hyperactivity disorder. Clin Psychol Review 26: 486-502.
- 48. Fabiano G, Pelham WE, Coles EK, Gnagy EM, Chronis-Tuscano A, et al. (2009) A meta-analysis of behavioural treatments for attention-deficit/hyperactivity disorder. Clin Psychol Rev 29: 129-140.
- Toplak ME, Connors L, Shuster J, Knezevic B, Parks S (2008) Review of cognitive, cognitive-behavioral, and neural-based interventions for Attention-Deficit/Hyperactivity Disorder (AD/HD). Clin Psychol Rev 28: 801-823.
- Abikoff H (1985) Efficacy of Cognitive Training Interventions in Hyperactive Children: A Critical Review. Clin Psychol Rev 5: 479-512.
- 51. Bjornstad GJ, Montgomery P (2009) Family therapy for attention-deficit disorder or attention-deficit/hyperactivity disorders in children and adolescents. Cochrane Database of Systematic Reviews. Art.No: CD005042. doi:10.1002/ 14651858.CD005042.pub2.
- Corcoran J, Dattalo P (2006) Parent Involvement in Treatment for AD/HD: A Meta-Analysis of the Published Studies. Res Soc Work Pract 16: 561-570.
- 53. Ghanizadeh A, Shahrivar FZ (2005) The Effect of Parent Management Training on Children with Attention Deficit Hyperactivity Disorder. J Child Adolesc Mental Health 17: 31-34.
- 54. Saugata B, Aniruddha D (1996) Parent training in children with attention deficit hyperactivity disorder: An integrated approach for greater effectiveness. Ind J Clin Psychol 23: 184–191.
- 55. Walker JS, Coleman D, Lee J, Squire PN, Friesen BJ (2008) Children's stigmatization of childhood depression and AD/HD: magnitude and demographic variation in a national sample. J Am Acad Child Adolesc Psychiatry 47: 912–920.
- 56. Hoven CW, Doan T, Musa GJ, Jaliashvili T, Duarte CS, et al. (2008) WPA Awarness Task Force. Worldwide child and adolescent mental health begins with awareness; a preliminary assessment in nine countries. Int Rev Psychiatry 20: 261-270.
- 57. Graeff-Martins AS, Flament MF, Fayyad J, Tyano S, Jensen P, et al. (2008) Diffusion of efficacious interventions for children and adolescents with mental health problems. J Child Psychol Psychiatry 49: 335-352.
- 58. Jitendra AK, Dupaul GJ, Someki F, Tresco KE (2008) Enhancing academic achievement for children with Attention-Deficit Hyperactivity Disorder: evidence from school-based intervention research. Dev Disabil Res Rev 14: 325-330
- 59. Patel V, Simon G, Chowdhary N, Kaaya S, Araya R (2009) Packages of Care for Depression in Low- and Middle-Income Countries. PLoS Med 6: e1000159. doi:10.1371/journal.pmed.1000159.
- 60. Rushton JL, Fant KE, Clark SJ (2004) Use of practice guidelines in the primary care of children with attention-deficit/hyperactivity disorder. Pediatrics 11: e23-28.
- Epstein JN, Rabiner D, Johnson DE, Fitzgerald DP, Chrisman A, et al. (2007) Improving attention-deficit/hyperactivity disorder treatment outcomes through use of a collaborative consultation treatment service by community-based pediatricians: A cluster randomized trial. Arch Pediatr Adolesc Med 161: 835-840.