



# Attention-deficit/hyperactivity disorder in adults: update on clinical presentation and care

Philip Asherson\*<sup>1</sup>, Iris Manor<sup>2</sup> & Michael Huss<sup>3</sup>

### Practice points

- Since the organizational demands of life grow more complex in adulthood, problems with inattention tend to cause more functional impairments than hyperactivity or impulsivity for most adults with attention-deficit/hyperactivity disorder (ADHD).
- Emotional lability consisting of volatile temper, irritability, anger and frustration is a commonly associated feature that is an independent source of impairment.
- In a significant subset of cases the burden of ADHD in adulthood is heavy, with symptoms leading to behavior problems and criminality, poor school and workplace performance, substance abuse, job loss, chronic financial stress, and disrupted personal/family relationships.
- The impact of ADHD on family life can be especially problematic, particularly because the condition tends to run in families.
- Diagnosis of ADHD in adults rests on a comprehensive assessment of developmental psychiatric history, current psychiatric status, and current mental state, preferably using a structured diagnostic instrument for ADHD. History should be corroborated by informants if possible.
- Adult ADHD may be difficult to recognize because of the very wide range of severity and impairments, and because it can resemble or coexist with other mental health disorders.
- Several changes have been made in DSM-5 that help to clarify the nature of ADHD and provide a more accurate reflection of the clinical presentation in adults. The criteria emphasise the evaluation of impairment in educational, occupational or social activities.
- Optimal treatment usually involves a multimodal approach that encompasses psychoeducation and targeted psychotherapeutic interventions.

<sup>1</sup>MRC Social Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, King's College & Maudsley Hospital, London, UK

<sup>2</sup>Attention Deficit Hyperactivity Disorder Unit, Geha Mental Health Center, Petah Tikva, Israel

<sup>3</sup>Department of Child & Adolescent Psychiatry, University of Mainz, Mainz, Germany

\*Author for correspondence: Tel.: +44 20 7848 0078; Fax: +44 20 7848 0866; philip.asherson@kcl.ac.uk

- Treatment can improve psychological functioning, self-confidence, personal/family relationships, professional/academic functioning, cognitive performance, concentration while driving, and quality of life, and may even reduce criminal behavior.
- Stimulants and non-stimulant treatment are generally safe and effective, and recent research suggests that the benefits are sustained over the long term.
- A potential drawback of stimulants is the possibility of worsening anxiety in patients with pre-existing anxiety disorders.
- The transition from pediatric to adolescent to adult medical services is often suboptimal and many adult ADHD patients are lost to follow-up.
- The key to transition from adolescent to adult mental health lies in providing stable therapeutic relationships, flexible dosing of medication, and good communication and support for future treatment plans.
- The success of long-term treatment depends on a carefully designed multimodal plan with regular review and adjustments as patients' needs change over the lifetime course of the illness.
- When drug therapy is indicated, current guidelines recommend stimulants as the first-line therapy. Drug treatments should be tailored to patients' educational, social and psychological needs.
- Awareness of the specific features and management challenges of ADHD in adolescents and adults can improve outcomes for patients, their families, and their communities.

## **KEYWORDS**

- adult • attention-deficit/hyperactivity disorder
- symptoms • diagnosis
- clinical presentation
- management • medical treatments

## **SUMMARY**

Attention-deficit/hyperactivity disorder (ADHD) is characterized by trait-like symptoms, with stable features frequently emerging in early childhood and persisting throughout adolescence and adulthood. The hallmarks are pervasive, developmentally inappropriate levels of inattention, hyperactivity and impulsivity leading to impairments in family life, social life, academic performance, and occupational functioning. Emotional lability is a commonly associated feature that is a further source of impairment. Diagnosis rests on a comprehensive assessment of developmental psychiatric history and current status, following DSM-5 guidelines on ADHD classification and diagnostic thresholds for adults. Medical and psychotherapeutic interventions can improve psychological functioning, self-confidence, personal/family relationships, professional/academic functioning, cognitive performance, driving safety, and quality of life, and may reduce criminal behavior. Future efforts should focus on supporting treatment adherence and smoothing transitions from pediatric to adolescent to adult medical services.

Over the past decade, understanding of attention-deficit/hyperactivity disorder (ADHD) in adults has advanced substantially. Significant changes in diagnosis and treatment are being driven by guidelines such as the UK National Institute for Health and Clinical Excellence recommendations [1] and revised diagnostic criteria in the Diagnostic and Statistical Manual Fifth Edition (DSM-5) [2]. A large body of evidence confirms the trait-like nature of the disorder, with stable features frequently emerging in early childhood and persisting throughout adolescence and adulthood [3]. Several studies

show that approximately two-thirds of children with ADHD continue to experience impairing levels of symptoms as adults [4,5]. Worldwide prevalence is approximately 5% in children [6] and 2–4% in adults. [4,5,7–16]. Despite this, many clinicians are unfamiliar with its onset, course, and presentation, and the availability of effective therapeutic options. Under-diagnosis and under-treatment are thought to be common in adults [12,17–20], although empirical data are lacking. Here we provide an overview of key findings in the current understanding of the diagnosis and its impact on clinical and psychosocial

impairments, and a summary of evidence-based treatments.

### Clinical presentation & diagnostic criteria

The hallmarks of ADHD are pervasive, developmentally inappropriate levels of inattentive, hyperactive and impulsive symptoms leading to impairments in multiple domains, including family life, social life, academic performance, and occupational functioning. Low self-esteem, emotional lability, and sleep problems are common [21]. According to DSM-5 diagnostic criteria, there are 18 symptoms divided into 9 for inattention and 9 for hyperactivity-impulsivity. The balance of symptoms may vary between individuals and also over time in the same individual, giving rise to predominantly inattentive, hyperactive-impulsive and combined clinical presentations of the two symptom domains. To meet the diagnostic criteria, individuals beyond the age of 17 years should have five or more symptoms in either domain. The symptoms must be maladaptive and inconsistent with the developmental level and reflect a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with function or development. Additional criteria include the requirement that several symptoms must have been present before the age of 12 years; symptoms must be present in two or more settings; and symptoms must interfere with or reduce the quality of social, educational and occupational functioning [2].

The core symptoms of hyperactivity and impulsivity tend to decline between childhood and young adulthood in both boys and girls, while inattention tends to persist [22]. Inattentive symptoms are worse on average in boys than in girls throughout childhood, adolescence, and young adulthood [22]. When high levels of hyperactivity and impulsivity do persist into adulthood, they may be particularly impairing and are often seen in high-risk patients such as those with addiction disorders [23]. In some cases the symptoms decline to sub-threshold levels, yet up to 50% of childhood cases may still be impaired by sub-threshold ADHD symptoms that have persisted from childhood [24].

Because the organizational demands of life grow more complex in adulthood, problems within the inattention domain tend to cause more functional impairments than hyperactivity or impulsivity for most adults with ADHD [14,20,25–28]. Inattention often presents as subjective complaints of a constant stream of

distracting, unfocused thoughts; forgetfulness, poor self-organization, and chronic lateness; difficulty in planning, initiating, and completing tasks; losing track of conversations; difficulty reading without losing track; and being easily distracted by external stimuli [12,14,18,20,26]. Hyperactivity and impulsivity in adults typically manifest as fidgeting; difficulty sitting still or relaxing; a persistent sense of restlessness; often feeling impatient; constantly needing to be doing something; intolerance for boredom or frustration; over-talkativeness or being too loud and boisterous; a tendency to interrupt or talk over people; and finding it difficult to wait one's turn without feeling irritable or angry. Associated features include avoiding mundane tasks and giving in to immediate temptations; a history of abruptly ending personal relationships or quitting jobs on an impulse; and attraction to thrill-seeking or high-risk activities (**Box 1**) [12,14,18,20,26,29]. Despite the overall decline in hyperactive and impulsive symptoms in adulthood, in clinical populations the majority show the combined presentation of ADHD, approximately one-third show predominantly inattentive symptoms, and less than 10% show predominantly hyperactive-impulsive symptoms [30]. Other surveys show a higher preponderance of the inattentive subtype in adults (approximately half to two-thirds) followed by the combined subtype (approximately one-third) [31,32]. There may be differences between European and US survey populations.

Emotional lability consisting of volatile temper, irritability, anger, and frustration commonly co-occurs with ADHD and is an independent source of impairment [20,21,33]. Many adults with ADHD report swift changes from normal mood to other emotional states such as irritability and anger, often several times a day [20,21]. A recent carefully designed case-control study showed that adults with ADHD, in the absence of any comorbid mental health disorders, had significantly higher mean scores on self-ratings measuring rapid changes from normal mood to other emotional modalities (elation, depression, and anger) and negative emotions (feeling nervous, frustrated and upset) (**Figure 1**) [21]. Furthermore, the measure of negative emotions was an independent predictor of functional impairments in family life ( $p < 0.001$ ), schooling ( $p = 0.013$ ), life skills ( $p < 0.001$ ) and social interactions ( $p < 0.001$ ). The strong association between emotional lability and ADHD was not accounted for by sub-threshold psychopathologies. Individuals

**Box 1. Attention-deficit/hyperactivity disorder (ADHD) symptoms.**

**Inattention**

- Lack of attention to details, makes careless mistakes
- Difficulty sustaining attention
- Does not listen when spoken to directly
- Trouble completing or finishing job tasks
- Problems organizing tasks and activities
- Avoids or dislikes sustained mental effort
- Loses and misplaces things
- Easily distracted
- Forgetful in daily activities

**Hyperactivity**

- Fidgetiness (hands or feet) or squirming in seat
- Leaves seat when not supposed to
- Restless or overactive
- Difficulty engaging in leisure activities quietly
- Always ‘on the go’
- Talks excessively

**Impulsivity**

- Blurts out answers before questions have been completed
- Difficulty waiting in line or taking turns
- Interrupts or intrudes on others when they are working or busy

with ADHD had higher mean rates and instability of feeling angry, frustrated, and irritable that was only partially explained by excessive reactions to daily events. Similarly, Barkley and Fischer found that ‘emotional impulsivity’ in adults with ADHD contributed to multiple domains of impairment beyond that explained by core ADHD symptoms, including occupation, education, criminal behavior, driving, and financial outcomes [34]. These findings have led to alternative views on the relationship of emotional lability in ADHD, with the current consensus considering that emotional dysregulation reflects a separate but nevertheless highly correlated clinical domain [35].

**Burden of disorder**

Although many patients learn to adapt to or compensate for ADHD symptoms as they mature [11,28], the burden of the disorder is high in a substantial subset of cases. While we do not wish to suggest that all people with ADHD present with serious risks, there is increasing evidence that ADHD is linked to some of the most pressing issues in society, which is often overlooked.

Individuals with ADHD have an elevated risk of behavior problems and criminality, including conduct problems, arrests and incarcerations [5,12,19,36]. In one of the most striking studies in recent years, Swedish adults with ADHD were shown to have a markedly higher rate of criminal convictions than the general population over a 4-year period (36.6 vs 8.9% for men; 15.4 vs 2.2% for women) [37]. European and US studies suggest that up to half of the adult prison population had childhood ADHD, and 10% or more meet diagnostic criteria for ADHD as adults [38]. In an ongoing survey of more than 12,000 18- to 25-year-old male prisoners in southeast London by one of the authors, a conservative prevalence estimate for adult ADHD is 20% [ASHERSON P, UNPUBLISHED DATA]. Furthermore, prisoners with ADHD are eight-times more likely to be involved in aggressive incidents within prisons [38].

Academic achievement is also greatly impaired by ADHD. Compared with healthy controls, adults who were diagnosed with ADHD in childhood are significantly more likely to have been held back in school or suspended from high school, and significantly less likely to have graduated from high school or enrolled in college [39]. For many adults with ADHD, early behavioral problems combined with poor school and workplace performance, as well as ongoing symptoms, lead to job loss and chronic financial stress [4,5,14,19,36].

Long-term studies show that both substance abuse and nicotine dependence are significantly more common among adults with ADHD than among control subjects ( $p = 0.003$  and  $p < 0.001$ , respectively) [36]. In a longitudinal case-control study, lifetime rates of smoking dependence were 27% in men who had been diagnosed with ADHD in childhood, compared with 11% in control subjects ( $p = 0.02$ ) [40]. In adults, ADHD is also commonly seen among those with serious addiction disorders, with a 12% rate estimated in addiction clinics in southeast London [23] and 10% in a large international study of several addiction centers [41].

The attraction to high-risk activities seen in some cases not only endangers patients with ADHD, but can also put the safety of others at risk. Adults with ADHD are more likely to exhibit aggressive or careless driving, with the attendant risks and costs of accidents and injuries [19,25,42]. A survey of adults with ADHD and healthy controls revealed significantly higher rates of car accidents

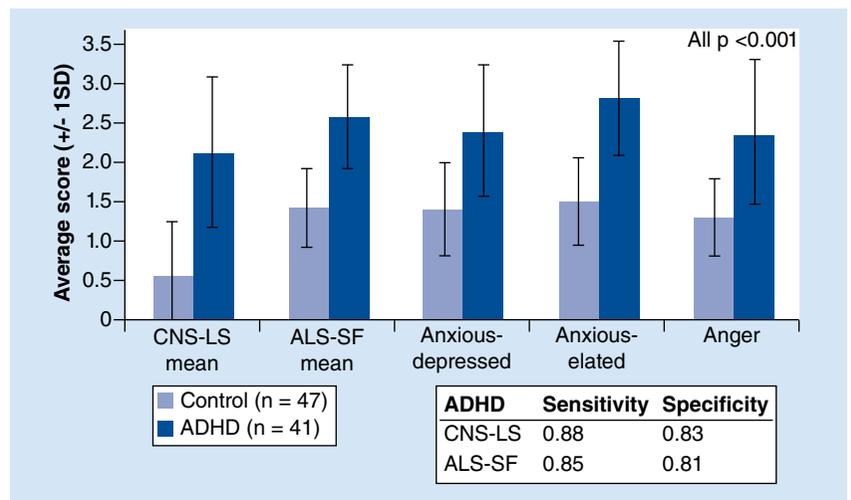
on the highway (35 vs 9%;  $p = 0.03$ ) and being rear-ended (50 vs 17%;  $p = 0.02$ ), as well as significantly higher scores on measures of driving errors and rule violations ( $p < 0.001$  for all) [42]. In one study of simulated driving conditions, the performance of sober adults with ADHD was comparable to that of healthy adults with a blood alcohol concentration considered to be legally impaired in the USA. Moreover, the impairments produced by alcohol were more severe in adults with ADHD than in healthy adults [43]. The real-world effects of ADHD were illustrated in a comparison of video recordings from routine on-road driving by young adults with and without ADHD. Those with ADHD were significantly more likely to have crashes, minor events, and g-force events (a measure of rapid changes in speed and direction) [44]. More recently, epidemiological data that linked together national driving accident and medical records showed that not only was ADHD strongly associated with serious accidents, but that medical treatments for ADHD reduced the risk by 58% in men (but not women) with ADHD [45].

A prospective study of psychosocial adversity in adults with childhood ADHD confirmed that the risks of overall mortality and accident-related mortality were almost doubled compared with control subjects (although the differences were not statistically significant). Mortality due to suicide was more than quadrupled in subjects with ADHD compared with controls ( $p = 0.032$ ) [46]. An epidemiologic survey of the adult outcomes of poor childhood self-control, a construct closely aligned to ADHD, found increased rates of poor physical health, financial problems, adult criminal convictions, and single-parent childrearing [47]. Further research is needed to clarify the extent to which the long-term health risks identified in this study are accounted for by the persistence of ADHD in adulthood.

Many adults with ADHD report difficulties forming and sustaining close personal relationships, and/or experience a diminished quality of life [14,19,25,48]. Teenage pregnancies are common among girls who had conduct problems and hyperactivity in childhood [49]. In a survey of young low-income women, ADHD symptoms were correlated with having risky sex partners (defined as male partners with HIV or AIDS, a history of using injected drugs, symptoms of a sexually transmitted infection, or having sex concurrently with another partner, or sex with another man). The lifetime adjusted odds ratio

(OR) for having risky sex partners was 1.23 ( $p < 0.0001$ ). Similarly, the adjusted OR for having had  $\geq 3$  sex partners in the last year was 1.15 ( $p < 0.05$ ). Mean ADHD symptoms score was significantly higher in those with a lifetime history of sexually transmitted disease than in those without (4.36 vs 3.70;  $p = 0.009$ ) [50]. The risk of sexually transmitted diseases is also significantly elevated in men with ADHD. A recent study found a rate of 15% in men with a history of childhood ADHD versus 7% in controls over a mean reporting period of 16.4 years ( $p = 0.03$ ) [51]. Interestingly, these departures from societal norms may confer an evolutionary advantage, since genetic risk factors for ADHD may be under positive selection, consistent with an increase in fecundity [52].

The impact of ADHD on family life can be especially problematic, particularly because ADHD tends to run in families [53,54]. Parents with ADHD are more likely to display maladaptive parenting techniques, negative parent-child interactions, and a poor response to behavioral parent training [55]. A recent case-control study showed that parents of children with ADHD not only had higher levels of ADHD symptoms but in addition more problems with depression than parents of matched control children, although the study was not designed to evaluate cause-and-effect relationships. Mothers were especially vulnerable to depression, while fathers frequently struggled with alcohol use [56].



**Figure 1. Emotional lability scores in adults with attention-deficit/hyperactivity disorder (ADHD) and matched controls.**

ALS-SF: Affective Lability Scale-Short Form; CNS-LS: Centre for Neurologic Study-Lability Scale.

Reproduced with permission from [21].

Parental ADHD may also be associated with more severe clinical presentation of ADHD in their children and higher levels of family conflict. In a survey of 570 children with ADHD, 29% of their parents met criteria for adult ADHD. Children whose mothers had adult ADHD showed significantly greater total ADHD severity ( $p = 0.044$ ) and inattention symptom severity ( $p = 0.048$ ) compared with children whose mothers did not have adult ADHD. They were also significantly more likely to have a diagnosis of conduct disorder ( $OR = 1.79$ ;  $p < 0.05$ ), and to have more severe conduct disorder symptoms ( $p = 0.04$ ). Similarly, conduct disorder was significantly more common ( $p = 0.029$ ) and the symptoms were significantly worse ( $p = 0.026$ ) in children whose fathers had adult ADHD. Significantly higher levels of conflict ( $p < 0.01$ ) and lower levels of cohesion ( $p = 0.02$ ) were reported by families in which the mother had ADHD symptoms [57]. One suggestion is that parental conflict, reflecting parental ADHD, is related to higher levels of ADHD symptoms in their children, although this study did not consider the causal directions of these associations [58]. In general, marital and family disruptions are not uncommon among adults with ADHD, and can then lead to a loss of much-needed support networks [5,25,36].

Experienced clinicians often recognize ADHD symptoms in the parents of their pediatric patients, as the rate of the disorder among parents and other first-degree relatives of child ADHD probands is approximately 20% [53,54,59]. Twin studies indicate that the familial risk stems largely from genetic effects acting across the lifespan with heritability estimated to be 70–80% for continuous trait measures of ADHD symptoms [12,60,61]. Although initial studies of self-rated ADHD in adults found lower heritabilities, higher estimates were found when parent or combined parent and self-ratings were used, or using concordance rates for clinically diagnosed cases of ADHD [61]. The existence of such strong genetic effects makes it difficult to know to what extent the behavioral problems that commonly accompany ADHD and the severity of individual ADHD cases are explained by genetic risks or the interplay between genetic and environmental factors.

#### • Causes of ADHD

The pathophysiology of ADHD is not yet well understood. As discussed above, ADHD tends

to aggregate in families and heritability is high throughout the lifespan, with little evidence for a role of shared environmental effects [62]. A key role for environmental effects is not however excluded by these findings, as there are likely to be gene-environment interactions, in which environmental risks for ADHD are moderated by individual genetic differences. One extreme environmental risk for ADHD appears to be severe early deprivation, demonstrated in follow-up studies of Romanian adoptees by Rutter and colleagues [63]. Other potential environmental risks were summarized by Banerjee [64] and include prenatal exposure to drugs and alcohol, maternal stress during pregnancy, preterm birth, low birth weight and severe childhood trauma [5,12,65,66]. Some associated environmental risks, such as maternal smoking during pregnancy, appear to have no direct effect on risk for ADHD. Once genetic effects have been controlled for, the association between smoking during pregnancy and offspring ADHD is no longer significant, suggesting that genetic effects that increase risk for ADHD are also associated with the risk for mothers smoking during pregnancy [67].

Currently there are a wide range of cognitive performance and neuroimaging changes associated with ADHD. However, it is not yet known which of these play a critical role in the pathways from genetic and environmental risks to expression of the clinical condition. Neurocognitive studies have identified several cognitive performance deficits, including slow and variable reaction times during vigilance tasks, impaired inhibitory control and impaired working memory – functions which are all improved by methylphenidate in children and adolescents [68]. Moreover, ADHD is associated with specific and general learning difficulties including a weak association with lower IQ and a stronger association with dyslexia [69].

Neuroimaging studies have identified various structural and functional abnormalities in the brains of patients with ADHD, including fronto-striatal dysfunction [12,70]; abnormal glucose metabolism in prefrontal and premotor areas of the frontal lobe [12]; smaller caudate, corpus callosum, cerebellum, right frontal areas, and anterior cingulate cortex [12,70,71]; and cortical thinning [12,70]. In adults, functional MRI shows hypoactivation in the frontoparietal system (involved in executive function) and hyperactivation in visual, dorsal attention, and default networks [72].

Functional MRI research in children with ADHD suggests that distractibility may be due to an inability to suppress activity in the default mode network in response to cognitively demanding situations [73]. Pivotal research using resting-state brain MRI has shown anomalies in developmentally dynamic functional connections in the default network in children with ADHD, suggesting possible maturation disturbances [74]. Both cortical control (executive functions) and nonexecutive processes are thought to be involved, such as cognitive energetic processes and/or changes of reward sensitivity [75].

### Diagnosis

Diagnosis of ADHD in adults rests on a comprehensive assessment of developmental psychiatric history, current psychiatric status, and current mental state, preferably using a structured diagnostic instrument for ADHD. Rating scales for past and present symptoms may be a helpful addition to provide a baseline for monitoring of treatment and provide an additional source of information on the number and type of symptoms. Adults should be asked about associated features such as emotional lability, sleep problems and comorbid disorders including specific learning difficulties such as dyslexia; full psychiatric history (including anxiety, depression, mood disorders, suicide attempts, eating disorders and forensic history); history of psychiatric and somatic treatments; and family history of psychiatric and neurologic problems (including signs of ADHD in their children) [12]. The symptoms must not occur exclusively during the course of schizophrenia or other psychiatric disorders. Medical conditions such as endocrine and metabolic disorders should also be considered. Patients presenting with chronic emotional/mood instability and/or angry outbursts should be screened for ADHD, and should not be assumed to have an affective disorder or a personality disorder until ADHD has been fully evaluated and other conditions included or excluded on the basis of a full diagnostic assessment.

Childhood onset of symptoms should be carefully evaluated as part of the developmental history. Whenever possible, the patient's recollections should be corroborated by informants (parents or older siblings) or by school records [20]. In cases when it is not possible to obtain a detailed account of childhood symptoms and behaviors, clinical judgment is needed to consider whether

the symptoms and impairments were likely to have been present during childhood. A clear history of impairment may not always be evident until the teenage or even young adult years, although symptoms of ADHD are expected to be seen before the age of 12 years. Observers such as siblings or spouses can also shed light on current symptoms that the patient may not recognize and give an alternative perspective on the degree of associated impairments.

Symptoms of ADHD should not be better accounted for by another disorder, and should be present throughout the lifespan, without fluctuating over time or reflecting changes from the normal premorbid state for that person [20]. Objective signs of the disorder may be noted during the interview or even in the waiting room, but will not be apparent in all patients. Concentration and performance are often highly variable across different contexts: attention may be well sustained for stimulating or interesting activities but very poor for routine or boring tasks [20]. Patients may need help to identify and properly attribute symptoms [18,65].

In some cases the condition may be difficult to recognize, particularly because of the very wide range of severity and impairment [18]. ADHD can also resemble or coexist with other mental health disorders, which can confound the differential diagnosis [8,9,12,17–19,26,29,76]. For example, symptoms such as physical and mental restlessness, poor concentration, impulsivity and sleep difficulties are seen in many other adult mental health disorders. For the Axis I disorders such as anxiety, depression and bipolar disorder, the distinction from ADHD is usually not difficult, because, unlike ADHD, symptoms of these disorders fluctuate over time and represent changes from the normal premorbid mental state for each individual. Furthermore, it is unusual for other disorders to generate the entire cluster of symptoms and behaviors that define ADHD, hence diagnostic specificity is improved by the correct application of the symptom thresholds. More difficult can be the distinction from personality disorders (particularly emotional unstable or borderline), since both ADHD and personality disorders reflect enduring traits that emerge in childhood and adolescence, and impulsivity and mood instability are common features of both disorders. In these cases the developmental history is particularly important, since in most cases characteristic features of ADHD are present from early childhood, and the adult

symptoms can be seen to reflect persistence of the same symptoms across the lifespan [20].

Overall, it is estimated that approximately 75% of adults presenting to clinical services with ADHD have at least one other clinical syndrome [12]. The US National Comorbidity Study showed significant ( $p < 0.05$ ) ORs of 3.0 or higher for any co-occurring mood disorders (including dysthymia and bipolar disorder), any anxiety disorders (including generalized anxiety disorder, post-traumatic stress disorder, panic disorder, agoraphobia and social phobia), and intermittent explosive disorder [8]. If these comorbid conditions are not identified and treated, the treatment of the ADHD may be ineffective and the patient may not improve. Even patients who do not meet the full criteria for psychiatric comorbidities show sub-threshold psychopathologies significantly more often than controls – particularly fatigue, sleep problems, irritability and worry [21]. Interestingly, in a 16-year follow-up study from child to adult ADHD, high levels of comorbidities were found across the lifespan, but at the 16-year follow-up most of the comorbidities were no longer present, yet individuals were still impaired by the persistence of ADHD symptoms [40].

Causal relationships between ADHD and comorbidities remain poorly understood. Some ‘comorbidities’ may be consequences of ADHD (e.g., dysphoria over personal and professional failures; avoiding shopping because of aversion to waiting in queues; fatigue because of effort required to concentrate on tasks; insomnia because of distractible thought processes and physical restlessness). It is, however, important to distinguish comorbid Axis I and II disorders that require independent treatment from symptoms or sequelae of ADHD, particularly bipolar disorder, anxiety disorders, major depression and severe personality disorder [12,20,26,29,65,66].

The diagnosis of ADHD is established when the symptoms are severe enough to result in significant impairment in at least two life domains (e.g., social, academic, or occupational function). In judging what degree of impairment is significant, clinicians should weigh the severity of the symptoms, the degree of dysfunction relative to the patient’s potential, and the personal distress felt by the patient and others [20]. Recognizing impairment can be more difficult in patients who are managing well, even though they still find symptoms to be troublesome and stressful.

#### • Diagnostic tools & instruments

The core of the diagnostic process is the clinical interview. Available instruments providing semi-structured interviews for ADHD include the Conners Adult ADHD Diagnostic Interview for DSM-IV (CAADID) [77] and the Diagnostic Interview for Adult ADHD (DIVA) [78]. One of these instruments should be used when evaluating ADHD in adults, with the clinician recording the presence or absence of symptoms based on examples of symptoms and behaviors elicited during the diagnostic interview. Both tools are based on DSM-IV criteria and only need very slight modification to conform to DSM-5 (discussed below). The DIVA has the advantages of being freely available, translated into multiple languages, and having an app version for ease of use. It is now increasingly being used, particularly in Europe. Both DIVA and CAADID systematically evaluate each of the 18 DSM symptoms that characterize ADHD in childhood and adulthood, as well as the additional criteria required for impairment and situational pervasiveness and age of symptom onset. The DIVA provides detailed examples for each symptom item based on daily life events, and includes a detailed section on impairment from the symptoms covering difficulties in work and education, relationships and family life, social contacts, free time and hobbies, self-confidence, and self-image. The diagnostic interviews are best completed in the presence of a family member or informant, particularly for childhood behavior.

Several rating scales and neuropsychologic measures have been developed for ADHD in adults, but are not sufficiently sensitive or specific to make the diagnosis without supporting evidence from the clinical interview. Rating scales are most useful for screening, establishing baselines, monitoring response to treatment, and long-term follow-up [20]. Widely used scales include the Conners Adult ADHD rating scale [77], and the World Health Organization Adult ADHD Self-Report Scale [79,80]. The Wender Utah Rating Scale can be used for retrospective assessment of childhood ADHD [81]. Other useful scales for both current and retrospective ADHD symptoms and impairments are published in a handbook by Russell Barkley [82]. The Weiss Functional Impairment Scale is a useful instrument that evaluates impairment across the domains of family, work, education, life skills, self-concept, social and risk behavior [83]. Quality of life can be evaluated using ADHD-specific

tools [84]. There are no neurocognitive or biological tests with adequate positive and negative predictive value [20], therefore they should not be used to establish the diagnosis [1,12].

The Sheehan Disability Scale (SDS) is a validated instrument in adults that assesses functional impairment in three domains: social, work, and family. It is self-administered by the patient and measures disruptions caused by emotional symptoms over the last month, using a ten point visual analog scale where 0 = not at all; 1–3 = mildly; 4–6 = moderately; 7–9 = markedly; and 10 = extremely. The total score ranges from 0 to 30. The scale is designed to identify primary care patients with functional impairment related to any mental health condition, not just ADHD [85]. Impairment scales specific to ADHD include the Weiss impairment scale [86]. Functional response to treatment can be documented using instruments such as the Clinical Global Impression – Improvement (CGI-I) scale, the SDS, or other instruments.

#### • DSM-IV versus DSM-5

In the development of DSM-5 criteria, several important changes were made that help to clarify the nature of ADHD and provide a more accurate reflection of the clinical presentation in adults. First, ADHD has been reclassified from a childhood disorder reflecting ‘disruptive behaviors’ to the new category of ‘neurodevelopmental disorders’. This not only recognizes the strong clinical association and overlapping genetic influences with neurodevelopmental disorders such as autism [87], but also the lifespan nature of the condition. Second, the diagnosis is now permitted in the presence of comorbid Autism Spectrum Disorder, further supporting the recommendation from clinical guidelines that ADHD should be treated in individuals with co-occurring autism [1]. Third, the age of onset criterion has been changed from some ‘symptoms and impairments’ before the age of 7 years, to several ‘symptoms’ but not necessarily impairment before the age of 12 years. This recognizes the difficulty in identifying or recalling symptoms in early childhood and that it may be easier to recognize ADHD symptoms among older children; and that, in some cases, individuals are less impaired during childhood because of the structure that parents and school can provide, so that impairments do not always become apparent until they leave home. Adults who meet full diagnostic criteria for ADHD

with onset of impairing symptoms prior to the age of 7 years have a similar profile of symptoms and impairments as adults who meet all the ADHD criteria except for the early childhood onset. This raises doubts about the validity of stringent age-of-onset criterion for adults when making retrospective diagnoses of ADHD [88]. Fourth, examples have been added to the diagnostic criteria to facilitate application across the lifespan. Fifth, the threshold for the number of symptoms has been dropped from six or more to five or more in the two symptom domains in patients over the age of 17 years. This reflects the observation that the overall symptom count tends to decline with age, and that persistence of five or more symptoms in either domain defines an impairing disorder in most adults. Finally, it is recognized that the clinical subtypes of ADHD are not developmentally stable and as a result they are now referred to as clinical presentations.

It is important to recognize that the DSM-5 diagnostic system is not intended to be a complete list of all ADHD symptoms, clinical features, and impairments. Like DSM-IV, its purpose is to provide criteria for establishing the diagnosis rather than a full clinical characterization of the disorder. However, the DSM-5 does include a section on supporting evidence such as symptoms of emotional lability; mild delays in language, motor or social development; and cognitive problems on tests of attention, executive function and memory. Most importantly, the DSM-5 emphasizes the evaluation of functional impairment, including interference with, or reduced quality of, social, academic and occupational functioning. This perspective is supported by the recent European Medicines Agency guidelines on ADHD research, which require that “two primary endpoints should be stipulated reflecting the symptomatic and the functional domain” [89]. These recommendations are in line with the core diagnostic criteria for ADHD, and what patients and physicians find important (i.e., daily functioning in addition to extreme levels of symptoms).

#### Treatment

Patients face growing academic, social, and occupational challenges as they mature from childhood to adolescence to adulthood, while at the same time they can lose support systems such as parents, schoolteachers, counselors and even medical treatment. Pharmacologic treatment yields benefits in many adults with ADHD

(Table 1) [20,90–100]. However, due to the demands and complexities of adult life, optimal treatment usually involves a multimodal approach that encompasses psychoeducation and targeted psychotherapeutic interventions [20,101].

In addition to reductions in ADHD symptoms, the benefits of targeted treatment include improvements in psychological functioning, self-confidence, personal/family relationships, professional/academic functioning, cognitive performance, concentration while driving and quality of life, as well as reductions in and criminal behavior [12,19,25,37,48]. Treatment has been shown to improve the driving performance of adolescent boys with ADHD in their own cars on the open road, particularly with respect to inattentive errors such as driving past a designated turn. In one study, improvement in driving performance from the first to the second test was positively correlated with medication dosage ( $r = 0.60$ ;  $p < 0.01$ ) [102]. Treatment has also been shown to significantly improve driving performance in adults with ADHD [103] and reduce the risk of accidents [45].

A further striking set of findings relates to reductions in criminal convictions. Using the Swedish national database, criminal convictions were recorded in over 25,000 adults with ADHD over a 4-year period, with an approximately six-fold higher rate of convictions in ADHD cases compared with controls [104]. Within individuals in the study, periods when ADHD medications were prescribed were associated with lower criminal conviction rates than periods when ADHD medications were not being used (Figure 2) [37]. No such effect was seen when a similar analysis was conducted with selective serotonin reuptake inhibitor antidepressant medications. The reduction in criminal convictions was observed in both men and women receiving ADHD drug treatments. Compared with untreated periods, the likelihood of a criminal conviction was 32% lower for men and 41% lower for women. The reduction in criminality was clearly not a long-term effect of medication, but was rather related to ongoing treatment with stimulants [37].

Based on currently available data, the UK National Institute for Health and Clinical Excellence guidelines recommend that drug therapy should be used as the first-line treatment for all adults meeting criteria for ADHD with either moderate or severe levels of impairment, unless they would prefer a psychological approach [1]. It should however be recognized that while this

is clearly the case for ADHD with severe impairment, there has been little research to investigate the potential benefits of psychological treatments without medication for those with mild to moderate impairment [2]. Stimulants (methylphenidate, dexamethylphenidate and amphetamines) are the first choice for ADHD drug treatment, although they are not all approved for adults worldwide [1,20]. In most European countries, methylphenidate is recommended as the first-line treatment, followed by either dexamphetamine, lisdexamphetamine or atomoxetine as second-line drug treatments. Average response rates in adults are in the order of 60% for short-term and 75% for long-term treatment with stimulants, but vary considerably across studies [27]. The average effect size is approximately  $d = 0.5$  [105]. Emotional dysregulation improves with stimulant treatment, to approximately the same degree as the core ADHD symptoms of inattention and hyperactivity-impulsivity [106,107]. Similar but slightly lower average effect sizes (approximately  $d = 0.4$ ) have been reported for the non-stimulant atomoxetine (discussed in more detail below) [108].

Adverse events are generally mild to moderate: the most common are dry mouth, insomnia, edginess, diminished appetite, weight loss, dysphoria, obsessiveness, tics and headaches [27]. Paradoxically, sleep may improve in some patients once the ADHD symptoms are under better control. Consistent increases in systolic and diastolic blood pressure (3–5 mmHg) and heart rate (5 bpm) are observed [27], although there is no evidence of an increased risk of serious cardiovascular events [109]. Nevertheless, cardiovascular status should be kept under constant review with pulse and blood pressure checks every 3–6 months, particularly in older patients where potential risks may be higher. A review of three studies of stimulants in adults found an increased risk for transient ischemic attack and sudden death/ventricular arrhythmia. However, the findings should be interpreted carefully due to differences in population, cardiovascular outcome selection/ascertainment and methodology [110].

The average effect size for methylphenidate in adults, around 0.4–0.5, is lower than that reported in studies of childhood ADHD [105,111]. There are a number of possible reasons. For example, methylphenidate sensitivity may be age-dependent. A recent animal study showed that developing prefrontal neurons were more responsive to methylphenidate than adult

**Table 1. Pharmacologic treatment of adult attention-deficit/hyperactivity disorder: recent randomized, double-blind, placebo-controlled trials.**

Author	Study treatments	Duration	Key efficacy results	Ref.
<b>Methylphenidate</b>				
Huss <i>et al.</i> (2014)	MPH-LA 40–80 mg/day (n = 542) or placebo (n = 180)	40 weeks	MPH significantly superior to placebo for response rate and symptom scales	[90]
Retz <i>et al.</i> (2012)	MPH extended release (n = 84) or placebo (n = 78)	8 weeks	MPH significantly superior to placebo for response rate and symptom scales	[95]
Rösler <i>et al.</i> (2009)	MPH extended release 10–60 mg/day (n = 241) or placebo (n = 118)	24 weeks	MPH significantly superior to placebo for response rate and symptom scales	[91]
Biederman <i>et al.</i> (2010)	OROS MPH (n = 109) or placebo (n = 114)	34 weeks	OROS MPH significantly superior to placebo for response rate	[96]
Ginsberg and Lindefors (2012)	OROS-MPH (n = 15) or placebo (n = 15)	5 weeks with 47-week open-label extension	OROS MPH significantly superior to placebo for response rate and symptom scales	[98]
<b>Dexmethylphenidate</b>				
Adler <i>et al.</i> (2009)	Dex-MPH extended release (d-MPH-ER) or placebo (total n = 170)	5 weeks with 6-month open-label extension	Improvement in symptoms in patients switched from placebo to d-MPH-ER and those maintained on d-MPH-ER	[99]
<b>Atomoxetine</b>				
Young <i>et al.</i> (2011)	Atomoxetine (n = 268) or placebo (n = 234)	24 weeks	Atomoxetine significantly superior to placebo for response rate and symptom scales	[97]
Adler <i>et al.</i> (2009)	Atomoxetine (n = 250) or placebo (n = 251)	6 months	Atomoxetine significantly superior to placebo for symptom scales	[93]
<b>Amphetamines</b>				
Wigal <i>et al.</i> (2010)	Lisdexamfetamine 30–70 mg/day and placebo (n = 142)	6 weeks	Lisdexamfetamine significantly superior to placebo for symptomatic and functional scales	[94]
Biederman <i>et al.</i> (2005)	MAS XR (total n = 223)	4 weeks with 24-month extension	Significant and sustained improvement from baseline with MAS XR	[100]

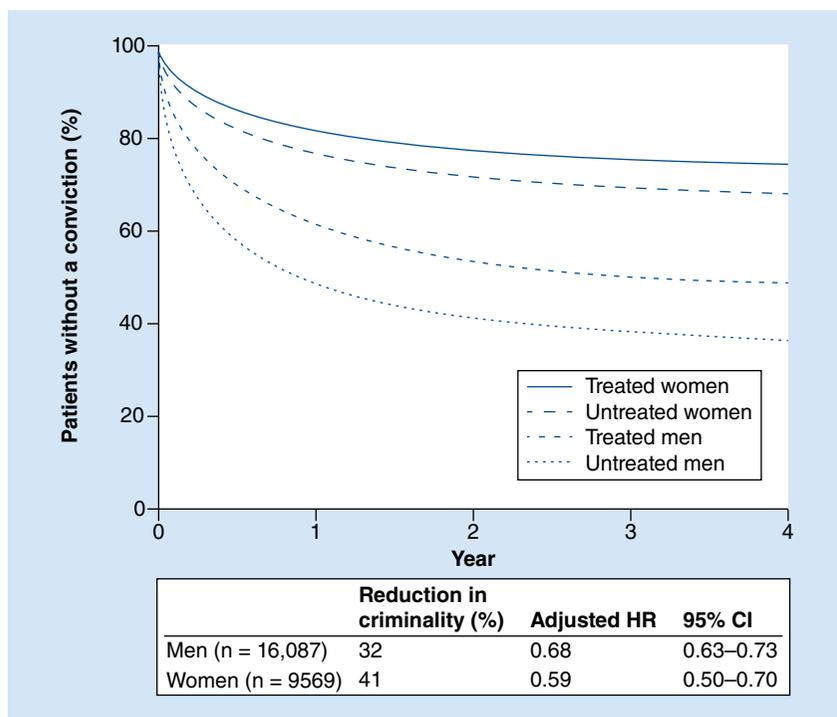
ADHD: Attention-deficit/hyperactivity disorder; MAS XR: Mixed amphetamine salts extended release; MPH: Methylphenidate; MPH-LA: Modified-release methylphenidate; OROS: Osmotic-release oral system.

prefrontal neurons [112]. Alternative explanations for the difference include dosages being lower on a mg/kg basis in adults [27,105]; compensatory upregulation of dopamine transporters in adults following long-term stimulant use [113]; a natural decline of dopamine transporters with age [114]; or the inherent subjectivity of self-evaluation in adult studies as opposed to observer reports typically used in pediatric studies [115,116]. A daily dose of 30–60 mg methylphenidate is sufficient for most adults, but there is a good deal of variability among individuals and higher doses (e.g., 90 mg or more) can be considered based on response and tolerability. Other stimulants are used in a similar way to methylphenidate, with daily doses of 15–60 mg of short-acting dexamfetamine and 30–70 mg of lisdexamfetamine being sufficient in most cases.

Until the last few years, little information was available on the long-term maintenance of effect

of any ADHD medication in adults. A systematic review of the indirect and direct effects of ADHD medications on long-term outcome in adults identified only five randomized controlled trials and ten open-label extension studies with a total follow-up of at least 24 weeks. All these studies found that medication was significantly more efficacious than placebo and the extension studies showed that the effect was maintained during the open-label follow-up period [117].

Recent research suggests that the efficacy and safety of once-daily modified-release methylphenidate (MPH-LA) are sustained for at least 40 weeks [90]. The study included three periods: a 9-week phase in which patients were randomized to MPH-LA 40, 60 or 80 mg/day or placebo; a 5-week phase in which patients were re-titrated to their individual optimal dose, and a 6-month, placebo-controlled withdrawal period. The trial was designed to meet the European Medicines



**Figure 2. Impact of attention-deficit/hyperactivity disorder (ADHD) treatment on rates of criminal convictions.**

Data taken from [37].

Agency requirements of co-primary endpoints for symptoms and functioning. Improvements from baseline in ADHD Rating Scale total score (Figure 3A) and SDS scale total score (Figure 3B) were significantly greater with each dose of MPH-LA than with placebo at the end of the first period. At the end of the third period, subjects receiving MPH-LA had a significantly lower treatment failure rate than those receiving placebo (21.4 vs 49.6%;  $p < 0.0001$ ). The safety results were consistent with the established safety profile for MPH-LA in children, and the safety profile in the long-term maintenance period was consistent with that reported in the short-term phase [90]. Similar to methylphenidate, a recent study of lisdexamfetamine also found a dramatic difference in the relapse rate between the active drug and placebo when patients showing a good treatment response were blindly switched to medication or placebo [118]. In general, the AE profile of stimulants in adults is similar to that in children. However, a potential drawback of stimulants is the possibility of worsening anxiety in patients with pre-existing anxiety disorders.

An alternative to the use of stimulants is the non-stimulant atomoxetine, a specific noradrenergic reuptake inhibitor that is now widely

licensed for adults in Europe and elsewhere, including first-time use in patients who were not treated for ADHD during childhood or adolescence. Notable reductions in ADHD symptoms and emotional dysregulation have been observed in short- and long-term studies in adults, with an average effect size around 0.4 [27,119,120]. The most common adverse events are dry mouth, insomnia, nausea, decreased appetite, constipation, sexual dysfunction in men, dizziness and sweating [27]. Its cardiovascular effects are similar to those of stimulants; hence, like stimulants, it should be used cautiously in adults with hypertension or other cardiovascular risk factors. Unlike the warning on the US label for children, no increased suicidality has been reported in adults. Atomoxetine may be especially helpful in patients with coexisting anxiety or tics. It has a very low abuse potential and is therefore particularly suitable for patients with coexisting substance abuse disorders. [27,121]. The usual treatment regimen is to start at a dose of 20 or 40 mg, then increase to a standard dose in most adults of either 80 or 100 mg. Unlike the stimulants, there is little immediate effect of atomoxetine, with effects developing over a period of 6 weeks or more.

Long-term adherence to prescribed ADHD medication tends to be poor for both adults and children [122]. Even patients who do continue medication may not use it as prescribed (e.g., only when they perceive or anticipate a need, rather than regularly). Forty percent or less of children and adolescents receiving drug treatment continue it as adults [123], and the percentages are much lower across most of Europe [12]. In the UK, for example, 12.77 of every 1000 15-year-old boys with ADHD received prescriptions for drug treatment in 2006, compared with just 0.64 of every 1000 21-year-old men [124]. The prevalence of prescribing of ADHD drugs to adult patients in the UK is much lower than the estimated prevalence of the condition [125,126], with similar findings in other countries such as Sweden [127] and even lower in many other European regions. The reasons are historical with a lack of awareness that ADHD persists beyond the childhood years. There is an absence of appropriate services for adults in Europe and continued skepticism or lack of experience among providers of adult mental healthcare. In adults, non-adherence may be due to clinician and patient failure to recognize and properly attribute ADHD symptoms [18,115]; improper use

of medications (inadequate dosage, side effects not explained, cost); the stigma of the condition; adverse events; concerns about long-term medication safety; and the negative impact of comorbidities on treatment persistence, response and self-regulation [29]. It is also the case that some patients with mild to moderate symptoms and impairments develop sufficient coping strategies to manage without medication.

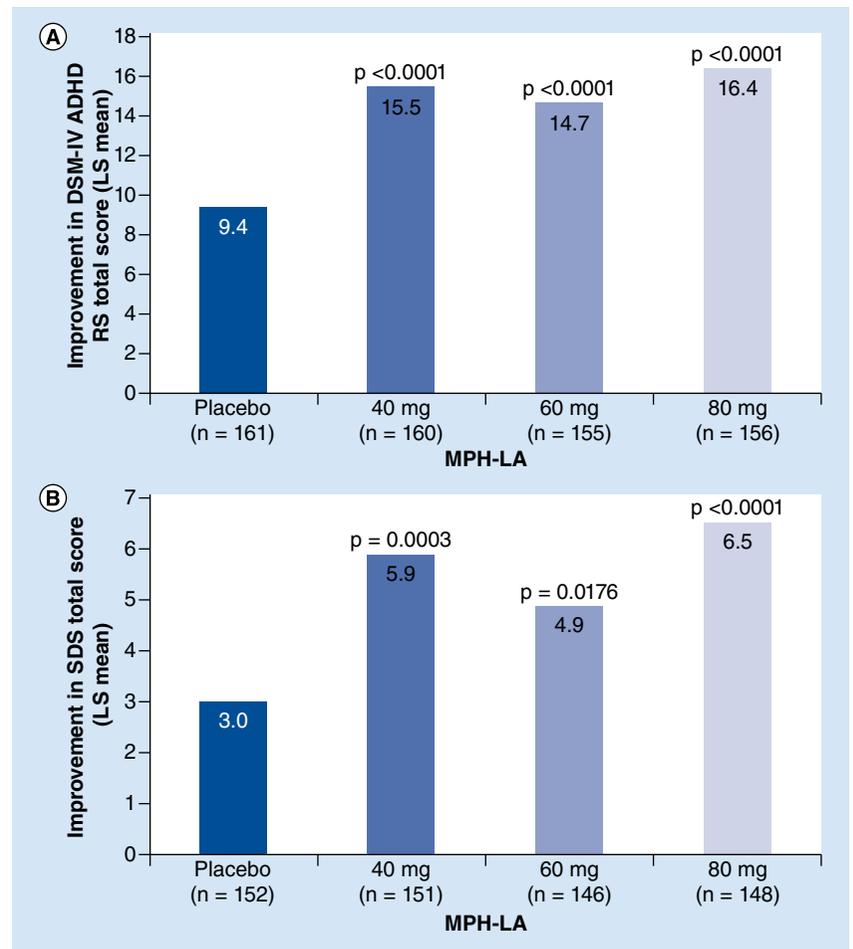
There is also the well-known general difficulty of retaining adolescents in medical treatment for many common conditions. This means that adolescents often drop out of care for both medical and mental health disorders, regardless of whether there is a continued need for it. Better services are therefore required to evaluate the continued need and provide appropriate support during the older adolescent and young adult years. Adherence to treatment plans can be encouraged through counseling, psychoeducation, reassurance and telephone follow-up. Adherence to medication is better with controlled-release formulations than with immediate-release formulations [128–130] and can be supported with the use of medication diaries. Long-acting preparations are especially useful for adults who become forgetful or disorganized when the first dose of immediate-release medication wears off [20].

### Psychotherapeutic & psychoeducation interventions

Response to drug treatment is variable, with many adult patients experiencing partial response or residual impairments, which underscores the need for multimodal care. Targeted psychotherapy and education form an essential part of such care. In particular, cognitive-behavioral therapy (CBT) has been shown to offer significant benefits, both alone [131–133] and in combination with drug treatment [131–137]. This structured approach typically includes practical advice on organizing and planning (such as calendars and checklists) and day-to-day problem-solving (weighing options, identifying solutions, and breaking down overwhelming tasks into steps). Patients may also be taught skills to reduce distractibility and procrastination, sustain motivation, and restructure their cognitive reactions to distressing or challenging situations [132,138]. Treatment can be administered in individual or group settings [136,137].

In a randomized, controlled study of 86 adults with persistent symptoms despite ADHD drug

therapy, a program of 12 CBT sessions produced significantly greater improvements on the clinician-rated CGI-I scale ( $p = 0.03$ ) and ADHD Rating Scale ( $p = 0.02$ ) as well as patient-rated ADHD symptoms ( $p < 0.001$ ) compared with a control intervention of relaxation therapy with education. Improvements were sustained for at least 12 months [138]. Similarly, a 12-week Meta-Cognitive Therapy (MCT) program to enhance time management, organization, and planning was shown to significantly improve inattentive symptoms in 88 adults compared with a control intervention that did not use cognitive-behavioral principles. The odds ratio for response in this randomized study was 5.41 favoring MCT. Surprisingly, even patients receiving apparently



**Figure 3. Improvement from baseline to 9 weeks in attention-deficit/hyperactivity disorder Rating Scale score and Sheehan Disability Scale score in adults receiving modified-release methylphenidate. (A) ADHD Rating Scale score. (B) SDS score.**

ADHD: Attention-deficit/hyperactivity disorder; MPH-LA: Modified-release methylphenidate; SDS: Sheehan Disability Scale.

Reproduced with kind permission from Springer Science+Business Media [90].

adequate doses of stimulants or atomoxetine did not differ from under-treated or untreated patients in baseline severity of ADHD symptoms or response to MCT, suggesting that MCT can be helpful even in unmedicated patients (though the investigators cautioned that the study entry criteria may have favored nonresponders or sub-optimal responders to medication) [132]. Similarly, responses were observed in both medicated and unmedicated adults in a study of structured group psychotherapy with skills training [131].

A randomized study of CBT in 25 unmedicated adults versus 23 adults receiving dextro-amphetamine showed robust improvements from baseline in both groups on the ADHD Rating Scale and the SDS. Investigators and patients were blinded to medication treatment. Within the framework of this small 20-week study, medication did not confer a statistically significant advantage over CBT alone, although trends toward better responses were observed with combination treatment [133].

Interventions that include both medication and CBT generally show medium to large effect sizes [134–136]. Considering the effect sizes across various studies of CBT interventions, it appears that targeted learning and practice of specific behavioral compensatory strategies may be critical success factors [136]. Overall there is a growing body of evidence for the effectiveness of CBT as an adjunct to medication. Furthermore, high placebo rates in recent studies of drug treatments suggest that psychological therapies are likely to be effective in at least a proportion of mild to moderate cases; however at this stage there are insufficient data to draw any firm conclusions.

A program of six therapeutic workshops including CBT and psychoeducation about ADHD has been shown to improve self-esteem, self-efficacy and knowledge about the condition in adults who were on stable ADHD medication compared with a waitlist control group [137].

Preliminary evidence suggests that modified mindfulness meditation techniques may also help adults with ADHD by alleviating some symptoms and improving executive function and emotional regulation [139,140]. The theory is that the attention control cultivated during mindfulness exercises will improve sustained attention and emotional regulation. This approach is unique among CBT interventions in that the goal is to change cognitive processing rather than develop skills to compensate for deficits [136]. Further larger scale

and adequately controlled studies are needed to clarify whether mindfulness training is an effective intervention.

---

### Transitioning medical & supportive treatment from pediatric to adult care settings

The transition from pediatric to adolescent to adult medical services is often suboptimal and many adult ADHD patients are lost to follow-up [12,17–19]. In some countries, patients must cross two boundaries: from pediatric to adolescent services, then from adolescent to adult services. In part this is due to patients and caregivers not anticipating or preparing for changing treatment needs, but it is also partially attributable to a lack of patient access to specialist care and logistical barriers to treatment (e.g., patients in the USA reaching adulthood may lose coverage under their parents' health insurance, or patients in Europe may lose access to ADHD medications that are only approved for children in their countries) [12,17–19].

Many cases of ADHD in adults continue to be unrecognized due to the variability of clinical presentation and healthcare providers' unfamiliarity with the finer points of diagnosis [20]. This is a particular concern for those with severe ADHD who may be misdiagnosed with conditions such as bipolar disorder or borderline personality disorder [141,142]. In addition, some adolescents and adults avoid medical evaluation due to a reluctance to accept the diagnosis and the need for treatment. The reasons for this are complex and are not specific to ADHD as a mental health problem. Some adults may fear change and resist leaving the 'comfort zone' of their current clinical status and compensatory mechanisms. Some may not fully perceive the impact that ADHD is having in their lives and/or the lives of their family. Some simply feel they are mentally or physically not themselves on medication. Patients who were diagnosed in childhood may have been told that their impairments will decline with age, and it can take time for them to understand that they have not 'outgrown' ADHD, that functioning does not always fully normalize, and that compensatory strategies can have their limitations [19].

The key to transition from adolescent to adult mental health lies in providing stable therapeutic relationships, flexible dosing of medication, and good communication and support for ongoing and future treatment plans. Teenage patients and

their families report that a positive transition from pediatric to adult mental health services is facilitated by continued parental support, and the caregiver's tenacity, empathy, listening skills, and practical advice [143]. Future priorities include better ADHD-specific training for clinicians in adult services, establishing effective services within adult mental health, and coordinating with primary care physicians to support adult mental health services [144].

---

### Conclusion

The symptoms of ADHD are known to persist from childhood into adulthood in many cases. The disorder displays consistent trait-like qualities over time that often lead to impairments throughout the adult years. Emotional lability (changeable emotional feelings, irritability, frustration and anger) appears to be a commonly associated feature of ADHD in adults, so much so that patients presenting with mood instability and anger outbursts should routinely be screened for ADHD. There is a need for collaboration among general/family practitioners, neurology/psychiatry specialists, and mental health-care professionals to better recognize this often chronic lifetime disorder and the associated functional impairments.

The transition from child to adult services is often problematic. The success of long-term treatment depends on a carefully designed multimodal plan with regular review and adjustments as patients' needs change over the lifetime course of the illness. When drug therapy is indicated, current treatment guidelines recommend stimulants as the first-line therapy [1]. Long-lasting and stable effects over 40 weeks have been demonstrated with MPH-LA in adults in placebo-controlled, double-blind research, and similar long term outcomes are expected for other ADHD medications. Drug treatments should always be offered within the context of a full review of educational, social, and psychological needs. Psychological support targeted to the specific problems that arise from ADHD should be available. Awareness of the specific features and management challenges of ADHD in adolescents and adults can improve outcomes for patients, their families and their communities.

---

### Future perspective

Looking into the future, we can see that the tide has turned, and despite a high level of unmet

needs that still exists for this patient group, there is a rapid increase in the recognition and treatment of ADHD in adults. More significantly, this is matched by advances in clinical management and the provision of much needed services in many regions of the world. Given the potential for any disorder to be over-diagnosed and treated (for example the rapid rise in prescriptions for antidepressants in primary care), due care must be taken to ensure that the diagnosis of ADHD is applied appropriately and treatments provided when they can best alleviate significant clinical and psychosocial impairments. However, the impairments to individuals and society from ADHD should not be underestimated. Most importantly, we need to move away from the current situation where many people who would benefit from treatment for ADHD are diagnosed with other common mental health disorders or told they do not have a real condition. Some of the most disadvantaged individuals in our society will benefit from the improved understanding of the condition, as well as those that struggle to cope with ADHD in everyday life at home and at work.

Part of the current problem is that, although ADHD is a common condition that is seen in the clinics of all primary and secondary care physicians, there remains a gap in understanding of the condition, how it presents, and what to expect from available treatments. This is as much a problem for psychologists as it is for psychiatrists and other health care professionals. Many newly developing services are set up as drug-only treatment centers, neglecting the importance of psychological treatments and a multimodal approach. That this will change is not in doubt however. As more clinicians start to treat ADHD in adults, the awareness and knowledge of the disorder are growing. In Europe, ADHD was largely ignored in children before the mid 1990s. Treatment for children began in specialist clinics, yet now almost all child and adolescents psychiatrists are well versed in clinical management of the disorder. Because of the high prevalence of the condition in adults as well as in children, the idea of multiple specialist clinics for ADHD is not a feasible long-term option, so we are confident that within 10 years most general adult mental health professionals, as well as primary care services, will be far more familiar with the condition and how best to help people with ADHD. Fortunately we have access to a range of effective treatments, making the

process of diagnosing and treating ADHD a fruitful and rewarding process for both patients and the health care profession.

### Financial & competing interests disclosure

Working on behalf of Kings College London, P Asherson was funded for consultancy with Lilly, Janssen, Shire and Novartis; and received grant funding for education or research from the same companies plus Vifor Pharma and GWPharma. He has spoken at events sponsored by Lilly, Janssen, Shire, Novartis and Vifor. I Manor has received funding from Teva Israel, Novartis Israel, Novartis Pharma AG, Janssen-Cilag, Enzymotec and Alcobra for research, lectures, consulting, and participation in Advisory Boards and workshops. M Huss has received funding from Lilly, Engelhardt, Janssen-Cilag, Lundbeck, Medice, Novartis,

Shire, Steiner-Arzneimittel, BMBF, BMFT, BfArM and the European Medicines Agency for research, lectures, consulting, and participation in Advisory Boards. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Medical writing assistance was provided by S Gilbert at ACUMED (NY, USA) and was funded by Novartis Pharmaceuticals Corporation.

### Open access

This work is licensed under the Creative Commons Attribution-NonCommercial 3.0 Unported License. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-nd/3.0>

### References

Papers of special note have been highlighted as:

- of interest
- of considerable interest

- 1 National Institute for Health and Clinical Excellence (NICE). Attention deficit hyperactivity disorder: the NICE guideline on diagnosis and management of ADHD in children, young people and adults. The British Psychological Society and the Royal College of Psychiatrists (2008). <http://guidance.nice.org.uk/cg72>
- 2 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (5th Edition)*. American Psychiatric Association, Arlington, VA, USA (2013).
- 3 Copeland WE, Adair CE, Smetanin P *et al*. Diagnostic transitions from childhood to adolescence to early adulthood. *J. Child Psychol. Psychiatry* 54(7), 791–799 (2013).
- 4 Faraone SV, Biederman J. What is the prevalence of adult ADHD? Results of a population screen of 966 adults. *J. Atten. Disord.* 9(2), 384–391 (2005).
- 5 Ebejer JL, Medland SE, van der Werf J *et al*. Attention deficit hyperactivity disorder in Australian adults: prevalence, persistence, conduct problems and disadvantage. *PLoS ONE* 7(10), e47404 (2012).
- 6 Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and meta-regression analysis. *Am. J. Psychiatry* 164(6), 942–948 (2007).
- 7 Kessler R, Adler L, Ames M *et al*. The prevalence and effects of adult attention deficit/hyperactivity disorder on work performance in a nationally representative sample of workers. *J. Occup. Environ. Med.* 47(6), 565–572 (2005).
- 8 Kessler R, Adler L, Barkley R *et al*. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. *Am. J. Psychiatry* 163(4), 716–723 (2006).
- 9 Fayyad J, De Graaf R, Kessler R *et al*. Cross-national prevalence and correlates of adult attention-deficit hyperactivity disorder. *Br. J. Psychiatry* 190, 402–409 (2007).
- 10 Montejano L, Sasane R, Hodgkins P *et al*. Adult ADHD: prevalence of diagnosis in a US population with employer health insurance. *Curr. Med. Res. Opin.* 27(Suppl. 2), 5–11 (2011).
- 11 Kooij JJ, Buitelaar JK, van den Oord EJ, Furer JW, Rijnders CA, Hodiadmont PP. Internal and external validity of attention-deficit hyperactivity disorder in a population-based sample of adults. *Psychol. Med.* 35(6), 817–827 (2005).
- 12 Kooij SJ, Bejerot S, Blackwell A *et al*. European consensus statement on diagnosis and treatment of adult ADHD: The European Network Adult ADHD. *BMC Psychiatry* 10, 67 (2010).
- Evidence-based expert guidelines on the recognition and management of attention-deficit hyperactivity disorder (ADHD) in adults.
- 13 Bitter I, Simon V, Bálint S, Mészáros A, Czobor P. How do different diagnostic criteria, age and gender affect the prevalence of attention deficit hyperactivity disorder in adults? An epidemiological study in a Hungarian community sample. *Eur. Arch. Psychiatry Clin. Neurosci.* 260(4), 287–296 (2010).
- 14 Das D, Cherbuin N, Butterworth P, Anstey KJ, Eastaerl S. A population-based study of attention deficit/hyperactivity disorder symptoms and associated impairment in middle-aged adults. *PLoS ONE* 7(2), e31500 (2012).
- 15 de Graaf R, Kessler R, Fayyad J *et al*. The prevalence and effects of adult attention-deficit/hyperactivity disorder (ADHD) on the performance of workers: results from the WHO World Mental Health Survey Initiative. *Occup. Environ. Med.* 65(12), 835–842 (2008).
- 16 Simon V, Czobor P, Bálint S, Mészáros A, Bitter I. Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. *Br. J. Psychiatry* 194(3), 204–211 (2009).
- 17 Retz W, Retz-Junginger P, Thome J *et al*. Pharmacological treatment of adult ADHD in Europe. Review. *World J. Biol. Psychiatry* 12(Suppl. 1), 89–94 (2011).
- 18 Goodman DW, Lasser RA, Babcock T, Pucci ML, Solanto MV. Managing ADHD across the lifespan in the primary care setting. *Postgrad. Med.* 123(5), 14–26 (2011).
- 19 Asherson P, Akehurst R, Kooij JJ *et al*. Under diagnosis of adult ADHD: cultural influences and societal burden. *J. Atten. Disord.* 16(5 Suppl.), 20S–38S (2011).
- 20 Asherson P. Clinical assessment and treatment of attention deficit hyperactivity disorder. *Exp. Rev. Neurotherapeutics* 5(4), 525–539 (2005).
- 21 Skirrow C, Asherson P. Emotional lability, comorbidity and impairment in adults with attention-deficit hyperactivity disorder. *J. Affect. Disord.* 147(1–3), 80–86 (2013).
- Case-control study showing significant connections between adult ADHD and rapid changes from normal mood to elation, depression, anger and frustration.
- 22 Larsson H, Lichtenstein P, Larsson JO. Genetic contributions to the development of ADHD subtypes from childhood to

- adolescence. *J. Am. Acad. Child Adolesc. Psychiatry* 45(8), 973–981 (2006).
- 23 Huntley Z, Young S. Alcohol and substance use history among ADHD adults: the relationship with persistent and remitting symptoms, personality, employment, and history of service use. *J. Atten. Disord.* 18(1), 82–90 (2014).
- 24 Faraone SV, Biederman J, Mick E. The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. *Psychol. Med.* 36(2), 159–165 (2006).
- 25 Brod M, Schmitt E, Goodwin M, Hodgkins P, Niebler G. ADHD burden of illness in older adults: a life course perspective. *Qual. Life Res.* 21(5), 795–799 (2012).
- 26 Haavik J, Halmoy A, Lundervold AJ, Fasmer OB. Clinical assessment and diagnosis of adults with attention-deficit/hyperactivity disorder. *Expert Rev. Neurother.* 10(10), 1569–1580 (2010).
- 27 Wilens TE, Morrison NR, Prince J. An update on the pharmacotherapy of attention-deficit/hyperactivity disorder in adults. *Exp. Rev. Neurother.* 11(10), 1443–1465 (2011).
- **Comprehensive review of the safety and efficacy of currently available drugs for adult ADHD.**
- 28 Biederman J, Mick E, Faraone SV. Age-dependent decline of symptoms of attention deficit hyperactivity disorder: impact of remission definition and symptom type. *Am. J. Psychiatry* 157(5), 816–818 (2000).
- 29 Kooij JJ, Huss M, Asherson P *et al.* Distinguishing comorbidity and successful management of adult ADHD. *J. Atten. Disord.* 16(5 Suppl.), 3S–19S (2012).
- 30 Wilens TE, Biederman J, Faraone SV, Martelon M, Westerberg D, Spencer TJ. Presenting ADHD symptoms, subtypes, and comorbid disorders in clinically referred adults with ADHD. *J. Clin. Psychiatry* 70(11), 1557–1562 (2009).
- 31 Cumyn L, French L, Hechtman L. Comorbidity in adults with attention deficit hyperactivity disorder. *Can. J. Psych.* 54(10), 673–683 (2009).
- 32 Sprafkin J, Gadow KD, Weiss MD, Schneider J, Nolan EE. Psychiatric comorbidity in ADHD symptom subtypes in clinic and community adults. *J. Attention Disord.* 11(2), 114–124 (2007).
- 33 Skirrow C, McLoughlin G, Kuntsi J, Asherson P. Behavioral, neurocognitive and treatment overlap between attention-deficit/hyperactivity disorder and mood instability. *Expert Rev. Neurother.* 9(4), 489–503 (2009).
- 34 Barkley RA, Fischer M. The unique contribution of emotional impulsiveness to impairment in major life activities in hyperactive children as adults. *J. Am. Acad. Child Adolesc. Psychiatry* 49(5), 503–513 (2010).
- 35 Shaw P, Stringaris A, Nigg J, Leibenluft E. Emotion dysregulation in Attention Deficit Hyperactivity Disorder. *Am. J. Psychiatry* doi:10.1176/appi.ajp.2013.13070966 (2014) (Epub ahead of print).
- 36 Klein RG, Mannuzza S, Olazagasti MA *et al.* Clinical and functional outcome of childhood attention-deficit/hyperactivity disorder 33 years later. *Arch. Gen. Psychiatry* 15, 1–9 (2012).
- 37 Lichtenstein P, Halldner L, Zetterqvist J *et al.* Medication for attention deficit–hyperactivity disorder and criminality. *N. Engl. J. Med.* 367(21), 2006–2014 (2012).
- **Groundbreaking research demonstrating significant decreases in criminal convictions among adults with ADHD receiving drug treatment.**
- 38 Young SJ, Adamou M, Bolea B *et al.* The identification and management of ADHD offenders within the criminal justice system: a consensus statement from the UK Adult ADHD Network and criminal justice agencies. *BMC Psychiatry* 11, 32 (2011).
- 39 Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult outcome of hyperactive children: adaptive functioning in major life activities. *J. Am. Acad. Child Adolesc. Psychiatry* 45(2), 192–202 (2006).
- 40 Biederman J, Petty CR, Woodworth KY, Lomedico A, Hyder LL, Faraone SV. Adult outcome of attention-deficit/hyperactivity disorder: a controlled 16-year follow-up study. *J. Clin. Psychiatry* 73(7), 941–950 (2012).
- 41 van de Glind G, van den Brink W, Koeter MW *et al.* Validity of the Adult ADHD Self-Report Scale (ASRS) as a screener for adult ADHD in treatment seeking substance use disorder patients. *Drug Alcohol Depend.* 132(3), 587–596 (2013).
- 42 Fried R, Petty CR, Surman CB *et al.* Characterizing impaired driving in adults with attention-deficit/hyperactivity disorder: A controlled study. *J. Clin. Psychiatry* 67(4), 567–574 (2006).
- 43 Weafer J, Camarillo D, Fillmore MT, Milich R, Marczynski CA. Simulated driving performance of adults with ADHD: comparisons with alcohol intoxication. *Exp. Clin. Psychopharmacol.* 16(3), 251–263 (2008).
- 44 Merkel RL Jr, Nichols JQ, Fellers JC *et al.* Comparison of on-road driving between young adults with and without ADHD. *J. Atten. Disord.* doi:10.1177/1087054712473832 (2013) (Epub ahead of print).
- 45 Chang Z, Lichtenstein P, D’Onofrio BM, Sjolander A, Larsson H. Serious transport accidents in adults with attention-deficit/hyperactivity disorder and the effect of medication: a population-based study. *JAMA Psychiatry* doi:10.1001/jamapsychiatry.2013.4174 (2014) (Epub ahead of print).
- 46 Barbaresi WJ, Colligan RC, Weaver AL, Voigt RG, Killian JM, Katusic SK. Mortality, ADHD, and psychosocial adversity in adults with childhood ADHD: a prospective study. *Pediatrics* 131(4), 637–644 (2013).
- 47 Moffitt TE, Arseneault L, Belsky D *et al.* A gradient of childhood self-control predicts health, wealth, and public safety. *Proc. Natl Acad. Sci. USA* 108(7), 2693–2698 (2011).
- 48 Agarwal R, Goldenberg M, Perry R, IsHak WW. The quality of life of adults with attention deficit hyperactivity disorder: a systematic review. *Innov. Clin. Neurosci.* 9(5–6), 10–21 (2012).
- 49 Lehti V, Niemelä S, Heinze M *et al.* Childhood predictors of becoming a teenage mother among Finnish girls. *Acta Obstet. Gynecol. Scand.* 91(11), 1319–1325 (2012).
- 50 Hosain GM, Berenson AB, Tennen H, Bauer LO, Wu ZH. Attention deficit hyperactivity symptoms and risky sexual behavior in young adult women. *J. Womens Health (Larchmt)*. 21(4), 463–468 (2012).
- 51 Ramos Olazagasti MA, Klein RG, Mannuzza S *et al.* Does childhood attention-deficit/hyperactivity disorder predict risk-taking and medical illnesses in adulthood? *J. Am. Acad. Child Adolesc. Psychiatry* 52(2), 153–162.e4 (2013).
- 52 Ding YC, Chi HC, Grady DL *et al.* Evidence of positive selection acting at the human dopamine receptor D4 gene locus. *Proc. Natl Acad. Sci. USA* 99(1), 309–314 (2002).
- 53 Faraone SV, Biederman J, Monuteaux MC. Toward guidelines for pedigree selection in genetic studies of attention deficit hyperactivity disorder. *Genet. Epidemiol.* 18(1), 1–16 (2000).
- 54 Chen W, Zhou K, Sham P *et al.* DSM-IV combined type ADHD shows familial association with sibling trait scores: a sampling strategy for QTL linkage. *Am. J. Med. Genet. B Neuropsychiatr. Genet.* 147B(8), 1450–1460 (2008).

- 55 Chronis-Tuscano A, Stein MA. Pharmacotherapy for parents with attention-deficit hyperactivity disorder (ADHD): impact on maternal ADHD and parenting. *CNS Drugs*. 26(9), 725–732 (2012).
- 56 Margari F, Craig F, Petruzzelli MG, Lamanna A, Matera E, Margari L. Parents psychopathology of children with attention deficit hyperactivity disorder. *Res. Dev. Disabil.* 34(3), 1036–1043 (2013).
- 57 Agha SS, Zammit S, Thapar A, Langley K. Are parental ADHD problems associated with a more severe clinical presentation and greater family adversity in children with ADHD? *Eur. Child Adolesc. Psychiatry* 22(6), 369–377 (2013).
- 58 Nikolas M, Klump KL, Burt SA. Youth appraisals of inter-parental conflict and genetic and environmental contributions to attention-deficit hyperactivity disorder: examination of G×E effects in a twin sample. *J. Abnorm. Child Psychol.* 40(7), 543–554 (2012).
- 59 Sprich S, Biederman J, Crawford MH, Mundy E, Faraone SV. Adoptive and biological families of children and adolescents with ADHD. *J. Am. Acad. Child Adolesc. Psychiatry* 39(11), 1432–1437 (2000).
- 60 Larsson H, Chang Z, D’Onofrio BM, Lichtenstein P. The heritability of clinically diagnosed attention deficit hyperactivity disorder across the lifespan. *Psychol. Med.* doi:10.1017/S0033291713002493 (2013) (Epub ahead of print).
- 61 Larsson H, Asherson P, Chang Z *et al.* Genetic and environmental influences on adult attention deficit hyperactivity disorder symptoms: a large Swedish population-based study of twins. *Psychol. Med.* 43(1), 197–207 (2013).
- 62 Burt SA. Are there shared environmental influences on attention-deficit/hyperactivity disorder? Reply to Wood, Buitelaar, Rijdsdijk, Asherson, and Kuntsi [corrected] (2010). *Psychol. Bull.* 136(3), 341–343 (2010).
- 63 Stevens SE, Sonuga-Barke EJ, Kreppner JM *et al.* Inattention/overactivity following early severe institutional deprivation: presentation and associations in early adolescence. *J. Abnorm. Child Psychol.* 36, 385–398 (2008).
- 64 Banerjee TD, Middleton F, Faraone SV. Environmental risk factors for attention-deficit hyperactivity disorder. *Acta Paediatr.* 96(9), 1269–1274 (2007).
- 65 Primich C, Iennaco J. Diagnosing adult attention-deficit hyperactivity disorder: the importance of establishing daily life contexts for symptoms and impairments. *J. Psychiatric Mental Health Nursing* 19(4), 362–373 (2012).
- 66 Craig WS. Adult attention deficit hyperactivity disorder. *J. Mens Health* 8, 299–305 (2011).
- 67 Langley K, Heron J, Smith GD, Thapar A. Maternal and paternal smoking during pregnancy and risk of ADHD symptoms in offspring: testing for intrauterine effects. *Am. J. Epidemiol.* 176, 261–268 (2012).
- 68 Coghill DR, Seth S, Pedroso S, Usala T, Currie J, Gagliano A. Effects of methylphenidate on cognitive functions in children and adolescents with attention-deficit/hyperactivity disorder: evidence from a systematic review and a meta-analysis. *Biol. Psychiatry*. doi:10.1016/j.biopsych.2013.10.005 (2013) (Epub ahead of print).
- 69 Paloyelis Y, Rijdsdijk F, Wood AC, Asherson P, Kuntsi J. The genetic association between ADHD symptoms and reading difficulties: the role of inattentiveness and IQ. *J. Abnorm. Child Psychol.* 38(8), 1083–1095 (2010).
- 70 Nakao T, Radua J, Rubia K, Mataix-Cols D. Gray matter volume abnormalities in ADHD: voxel-based meta-analysis exploring the effects of age and stimulant medication. *Am. J. Psychiatry* 168(11), 1154–1163 (2011).
- 71 Frodl T, Skokauskas N. Meta-analysis of structural MRI studies in children and adults with attention deficit hyperactivity disorder indicates treatment effects. *Acta Psychiatr. Scand.* 125(2), 114–126 (2012).
- 72 Cortese S, Kelly C, Chabernaud C *et al.* Toward systems neuroscience of ADHD: a meta-analysis of 55 fMRI studies. *Am. J. Psychiatry* 169(10), 1038–1055 (2012).
- 73 Fassbender C, Zhang H, Buzy WM *et al.* A lack of default network suppression is linked to increased distractibility in ADHD. *Brain Res.* 1273, 114–128 (2009).
- 74 Fair DA, Posner J, Nagel BJ *et al.* Atypical default network connectivity in youth with attention-deficit/hyperactivity disorder. *Biol. Psychiatry* 68(12), 1084–1091 (2010).
- 75 Kuntsi J, Wood AC, Rijdsdijk F *et al.* Separation of cognitive impairments in attention-deficit/hyperactivity disorder into 2 familial factors. *Arch. Gen. Psychiatry* 67(11), 1159–1167 (2010).
- 76 Bond DJ, Hadjipavlou G, Lam RW *et al.* The Canadian Network for Mood and Anxiety Treatments (CANMAT) task force recommendations for the management of patients with mood disorders and comorbid attention-deficit/hyperactivity disorder. *Ann. Clin. Psychiatry* 24(1), 23–37 (2012).
- 77 Conner’s Adult ADHD Diagnostic Interview for DSM-IV. [www.mhs.com/product.aspx?gr=cli&prod=c\\_aadid&id=overview](http://www.mhs.com/product.aspx?gr=cli&prod=c_aadid&id=overview)
- 78 Kooij JJ, Francken, MH. DIVA 2.0 (2010). [www.psyq.nl/files/1263005/DIVA\\_2\\_EN.pdf](http://www.psyq.nl/files/1263005/DIVA_2_EN.pdf)
- Recommended diagnostic interview for ADHD in adults can be downloaded from [www.divacenter.eu](http://www.divacenter.eu)
- 79 Kessler RC, Adler L, Ames M *et al.* The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. *Psychol. Med.* 35(2), 245–256 (2005).
- 80 National Comorbidity Survey. Adult ADHD Self-Report Scales, version 1.1. Harvard Medical School. [www.hcp.med.harvard.edu/ncs/asrs.php](http://www.hcp.med.harvard.edu/ncs/asrs.php)
- 81 Ward MF, Wender PH, Reimherr FW. The Wender Utah Rating Scale: an aid in the retrospective diagnosis of childhood attention deficit hyperactivity disorder. *Am. J. Psychiatry* 150(6), 885–890 (1993).
- 82 Barkley R, Murphy K. *A Clinical Workbook: Attention-Deficit Hyperactivity Disorder*. Guilford Press, New York, NY, USA (1998).
- 83 Weiss MD, Weiss JR. A guide to the treatment of adults with ADHD. *J. Clin. Psychiatry*. 65(Suppl. 3), 27–37 (2004).
- 84 Brod M, Johnston J, Able S, Swindle R. Validation of the adult attention-deficit/hyperactivity disorder quality-of-life Scale (AAQoL): a disease-specific quality-of-life measure. *Qual. Life Res.* 15(1), 117–129 (2006).
- 85 Weiss MD. [www.caddra.ca/cms4/pdfs/caddraGuidelines2011WFIRS\\_P.pdf](http://www.caddra.ca/cms4/pdfs/caddraGuidelines2011WFIRS_P.pdf)
- 86 Leon AC, Olfson M, Portera L, Farber L, Sheehan DV. Assessing psychiatric impairment in primary care with the Sheehan Disability Scale. *Int. J. Psychiatry Med.* 27(2), 93–105 (1997).
- 87 Ronald A, Simonoff E, Kuntsi J, Asherson P, Plomin R. Evidence for overlapping genetic influences on autistic and ADHD behaviours in a community twin sample. *J. Child Psychol. Psychiatry* 49(5), 535–542 (2008).
- 88 Faraone SV, Kunwar A, Adamson J, Biederman J. Personality traits among ADHD adults: implications of late-onset and subthreshold diagnoses. *Psychol. Med.* 39(4), 685–693 (2009).
- 89 European Medicines Agency. Committee for Medical Product for Human Use. EMEA/CHMP/EWP/431734/2008 (2008).

- 90 Huss M, Ginsberg Y, Tvedten T *et al.* Methylphenidate hydrochloride modified-release in adults with attention deficit hyperactivity disorder: a randomized double-blind placebo-controlled trial. *Adv. Ther.* 31(1), 44–65 (2014).
- **A unique study with dual primary endpoints for symptoms and functioning, demonstrating that the efficacy and safety of drug therapy can be sustained for at least 40 weeks in adults.**
- 91 Rösler M, Fischer R, Ammer R, Ose C, Retz W. A randomised, placebo-controlled, 24-week, study of low-dose extended-release methylphenidate in adults with attention-deficit/hyperactivity disorder. *Eur. Arch. Psychiatry Clin. Neurosci.* 259(2), 120–129 (2009).
- 92 Faraone SV, Biederman J, Spencer T *et al.* Efficacy of atomoxetine in adult attention-deficit/hyperactivity disorder: a drug–placebo response curve analysis. *Behav. Brain Funct.* 1, 16 (2005).
- 93 Adler L, Spencer T, Brown TE *et al.* Once-daily atomoxetine for adult attention-deficit/hyperactivity disorder: a 6-month, double-blind trial. *J. Clin. Psychopharmacol.* 29(1), 44–50 (2009).
- 94 Wigal T, Brams M, Gasior M, Gao J, Squires L, Giblin J, on behalf of the 316 Study Group. Randomized, double-blind, placebo-controlled, crossover study of the efficacy and safety of lisdexamfetamine dimesylate in adults with attention-deficit/hyperactivity disorder: novel findings using a simulated adult workplace environment design. *Behav. Brain Funct.* 6, 34 (2010).
- 95 Retz W, Rösler M, Ose C *et al.* Multiscale assessment of treatment efficacy in adults with ADHD: a randomized placebo-controlled, multi-centre study with extended-release methylphenidate. *World J. Biol. Psychiatry* 13(1), 48–59 (2012).
- 96 Biederman J, Mick E, Surman C *et al.* A randomized, 3-phase, 34-week, double-blind, long-term efficacy study of osmotic-release oral system-methylphenidate in adults with attention-deficit/hyperactivity disorder. *J. Clin. Psychopharmacol.* 30(5), 549–553 (2010).
- 97 Young JL, Sarkis E, Qiao M, Wietecha L. Once-daily treatment with atomoxetine in adults with attention-deficit/hyperactivity disorder: a 24-week, randomized, double-blind, placebo-controlled trial. *Clin. Neuropharmacol.* 34(2), 51–60 (2011).
- 98 Ginsberg Y, Lindefors N. Methylphenidate treatment of adult male prison inmates with attention-deficit hyperactivity disorder: randomised double-blind placebo-controlled trial with open-label extension. *Br. J. Psychiatry* 200(1), 68–73 (2012).
- 99 Adler LA, Spencer T, McGough JJ, Jiang H, Muniz R. Long-term effectiveness and safety of dexamethylphenidate extended-release capsules in adult ADHD. *J. Atten. Disord.* 12(5), 449–459 (2009).
- 100 Biederman J, Spencer TJ, Wilens TE, Weisler RH, Read SC, Tullloch SJ, on behalf of the SLI381.304 Study Group. Long-term safety and effectiveness of mixed amphetamine salts extended release in adults with ADHD. *CNS Spectr.* 10(12 Suppl. 20), 16–25 (2005).
- 101 Knouse LE, Cooper-Vince C, Sprich S, Safren SA. Recent developments in the psychosocial treatment of adult ADHD. *Expert Rev. Neurother.* 8(10), 1537–1548 (2008).
- 102 Cox DJ, Humphrey JW, Merkel RL, Penberthy JK, Kovatchev B. Controlled-release methylphenidate improves attention during on-road driving by adolescents with attention-deficit/hyperactivity disorder. *J. Am. Board Fam. Pract.* 17(4), 235–239 (2004).
- 103 Verster JC, Bekker EM, de Roos M *et al.* Methylphenidate significantly improves driving performance of adults with attention-deficit hyperactivity disorder: a randomized crossover trial. *J. Psychopharmacol.* 22(3), 230–237 (2008).
- 104 Lichtenstein P, Larsson H. Medication for attention deficit-hyperactivity disorder and criminality. *N. Engl. J. Med.* 368, 775–776 (2013).
- 105 Koesters M, Becker T, Kilian R, Fegert JM, Weinmann S. Limits of meta-analysis: methylphenidate in the treatment of adult attention-deficit hyperactivity disorder. *J. Psychopharmacol.* 23(7), 733–744 (2009).
- 106 Marchant BK, Reimherr FW, Halls C, Williams ED, Strong RE. OROS methylphenidate in the treatment of adults with ADHD: a 6-month, open-label, follow-up study. *Ann. Clin. Psychiatry* 22(3), 196–204 (2010).
- 107 Rösler M, Retz W, Fischer R *et al.* Twenty-four-week treatment with extended release methylphenidate improves emotional symptoms in adult ADHD. *World J. Biol. Psychiatry* 11(5), 709–718 (2010).
- 108 Faraone SV, Glatt SJ. A comparison of the efficacy of medications for adult attention-deficit/hyperactivity disorder using meta-analysis of effect sizes. *J. Clin. Psychiatry* 71(6), 754–763 (2010).
- 109 Cooper WO, Habel LA, Sox CM *et al.* ADHD drugs and serious cardiovascular events in children and young adults. *N. Engl. J. Med.* 365(20), 1896–1904 (2011).
- 110 Westover AN, Halm EA. Do prescription stimulants increase the risk of adverse cardiovascular events? A systematic review. *BMC Cardiovasc. Disord.* 12, 41 (2012).
- 111 Castells X, Ramos-Quiroga JA, Rigau D *et al.* Efficacy of methylphenidate for adults with attention-deficit hyperactivity disorder: a meta-regression analysis. *CNS Drugs* 25(2), 157–169 (2011).
- 112 Urban KR, Waterhouse BD, Gao WJ. Distinct age-dependent effects of methylphenidate on developing and adult prefrontal neurons. *Biol. Psychiatry* 72(10), 880–888 (2012).
- 113 Wang G-J, Volkow ND, Wigal T *et al.* Long-term stimulant treatment affects brain dopamine transporter level in patients with Attention Deficit Hyperactive Disorder. *PLoS ONE* 8(5), e63023 (2013).
- 114 Volkow ND, Ding YS, Fowler JS *et al.* Dopamine transporters decrease with age. *J. Nucl. Med.* 37(4), 554–559 (1996).
- 115 Manor I, Vurembrandt N, Rozen S, Gevah D, Weizman A, Zalsman G. Low self-awareness of ADHD in adults using a self-report screening questionnaire. *Eur. Psychiatry* 27(5), 314–320 (2012).
- 116 Söderström S, Pettersson R, Nilsson KW. Quantitative and subjective behavioural aspects in the assessment of attention-deficit hyperactivity disorder (ADHD) in adults. *Nord. J. Psychiatry* 68(1), 30–37 (2014).
- 117 Fredriksen M, Halmøy A, Faraone SV, Haavik J. Long-term efficacy and safety of treatment with stimulants and atomoxetine in adult ADHD: a review of controlled and naturalistic studies. *Eur. Neuropsychopharmacol.* 23(6), 508–527 (2013).
- 118 Brams M, Weisler R, Findling RL *et al.* Maintenance of efficacy of lisdexamfetamine dimesylate in adults with attention-deficit/hyperactivity disorder: randomized withdrawal design. *J. Clin. Psychiatry* 73, 977–983 (2012).
- 119 Marchant BK, Reimherr FW, Halls C *et al.* Long-term open-label response to atomoxetine in adult ADHD: influence of sex, emotional dysregulation, and double-blind response to atomoxetine. *Atten. Defic. Hyperact. Disord.* 3(3), 237–244 (2011).
- 120 Reimherr FW, Marchant BK, Strong RE *et al.* Emotional dysregulation in adult ADHD and response to atomoxetine. *Biol. Psychiatry* 58(2), 125–131 (2005).
- 121 Mao AR, Babcock T, Brams M. ADHD in adults: current treatment trends with consideration of abuse potential of

- medications. *J. Psychiatr. Pract.* 17(4), 241–250 (2011).
- 122 Perwien AR, Hall J, Swensen A, Swindle R. Stimulant treatment patterns and compliance in children and adults with newly treated attention-deficit/hyperactivity disorder. *J. Managed Care Pharm.* 10(2), 122–129 (2004).
- 123 McCarthy S, Wilton L, Murray ML, Hodgkins P, Asherson P, Wong IC. Persistence of pharmacological treatment into adulthood, in UK primary care, for ADHD patients who started treatment in childhood or adolescence. *BMC Psychiatry* 12, 219 (2012).
- 124 McCarthy S, Asherson P, Coghill D *et al.* Attention-deficit hyperactivity disorder: treatment discontinuation in adolescents and young adults. *Br. J. Psychiatry* 194(3), 273–277 (2009).
- 125 McCarthy S, Wilton L, Murray ML, Hodgkins P, Asherson P, Wong IC. The epidemiology of pharmacologically treated attention deficit hyperactivity disorder (ADHD) in children, adolescents and adults in UK primary care. *BMC Pediatr.* 12, 78 (2012).
- 126 Wong IC, Asherson P, Bilbow A *et al.* Cessation of attention deficit hyperactivity disorder drugs in the young (CADDY) – a pharmacoepidemiological and qualitative study. *Health Technol. Assess.* 13(50), iii–iv, ix–xi, 1–120 (2009).
- 127 Zetterqvist J, Asherson P, Halldner L, Langstrom N, Larsson H. Stimulant and non-stimulant attention deficit/hyperactivity disorder drug use: total population study of trends and discontinuation patterns 2006–2009. *Acta Psychiatr. Scand.* 128, 70–77 (2013).
- 128 van den Ban E, Souverein PC, Swaab H, van Engeland H, Egberts TC, Heerdink ER. Less discontinuation of ADHD drug use since the availability of long-acting ADHD medication in children, adolescents and adults under the age of 45 years in the Netherlands. *Atten. Defic. Hyperact. Disord.* 2(4), 213–220 (2010).
- 129 Adler LA, Lynch LR, Shaw DM *et al.* Medication adherence and symptom reduction in adults treated with mixed amphetamine salts in a randomized crossover study. *Postgrad. Med.* 123(5), 71–79 (2011).
- 130 Adler LD, Nierenberg AA. Review of medication adherence in children and adults with ADHD. *Postgrad. Med.* 122(1), 184–191 (2010).
- 131 Philipsen A, Richter H, Peters J *et al.* Structured group psychotherapy in adults with attention deficit hyperactivity disorder: results of an open multicentre study. *J. Nerv. Ment. Dis.* 195(12), 1013–1019 (2007).
- 132 Solanto MV, Marks DJ, Wasserstein J *et al.* Efficacy of meta-cognitive therapy (MCT) for adult ADHD. *Am. J. Psychiatry* 167(8), 958–968 (2010).
- 133 Weiss M, Murray C, Wasdell M, Greenfield B, Giles L, Hechtman L. A randomized controlled trial of CBT therapy for adults with ADHD with and without medication. *BMC Psychiatry* 12, 30 (2012).
- 134 Rostain AL, Ramsay JR. A combined treatment approach for adults with ADHD – results of an open study of 43 patients. *J. Atten. Disord.* 10(2), 150–159 (2006).
- 135 Emilsson B, Gudjonsson G, Sigurdsson JF *et al.* Cognitive behaviour therapy in medication-treated adults with ADHD and persistent symptoms: a randomized controlled trial. *BMC Psychiatry* 11, 116 (2011).
- 136 Knouse LE, Safren SA. Current status of cognitive behavioral therapy for adult attention-deficit hyperactivity disorder. *Psychiatr. Clin. North Am.* 33(3), 497–509 (2010).
- 137 Bramham J, Young S, Bickerdike A, Spain D, McCartan D, Xenitidis K. Evaluation of group cognitive behavioral therapy for adults with ADHD. *J. Atten. Disord.* 12(5), 434–441 (2009).
- 138 Safren SA, Sprich S, Mimiaga MJ *et al.* Cognitive behavioral therapy vs relaxation with educational support for medication-treated adults with ADHD and persistent symptoms: A randomized controlled trial. *JAMA* 304(8), 875–880 (2010).
- 139 Zylowska L, Ackerman DL, Yang MH *et al.* Mindfulness meditation training in adults and adolescents with ADHD: a feasibility study. *J. Atten. Disord.* 11(6), 737–746 (2008).
- 140 Mitchell JT, McIntyre EM, English JS, Dennis MF, Beckham JC, Kollins SH. A pilot trial of mindfulness meditation training for ADHD in adulthood: impact on core symptoms, executive functioning, and emotion dysregulation. *J. Atten. Disord.* doi:10.1177/1087054713513328 (2013) (Epub ahead of print).
- 141 Philipsen A. Differential diagnosis and comorbidity of attention-deficit/hyperactivity disorder (ADHD) and borderline personality disorder (BPD) in adults. *Eur. Arch. Psychiatry Clin. Neurosci.* 256(Suppl. 1), i42–46 (2006).
- 142 Skirrow C, Hosang GM, Farmer AE, Asherson P. An update on the debated association between ADHD and bipolar disorder across the lifespan. *J. Affect. Disord.* 141, 143–159 (2012).
- 143 Swift KD, Hall CL, Marimuttu V, Redstone L, Sayal K, Hollis C. Transition to adult mental health services for young people with attention deficit/hyperactivity disorder (ADHD): a qualitative analysis of their experiences. *BMC Psychiatry* 13, 74 (2013).
- **Patients describe graduating from pediatric to adult ADHD care in their own words, offering insights on how to support continued treatment adherence and enduring patient-caregiver relationships.**
- 144 Hall CL, Newell K, Taylor J, Sayal K, Swift KD, Hollis C. ‘Mind the gap’ – mapping services for young people with ADHD transitioning from child to adult mental health services. *BMC Psychiatry* 13, 186 (2013).