Journal of Psychopharmacology
http://jop.sagepub.com

Evidence-based guidelines for management of attention-deficit/hyperactivity disorder in adolescents in transition to adult services and in adults: recommendations from the British Association for Psychopharmacology

D. J. Nutt, K. Fone, P. Asherson, D. Bramble, P. Hill, K. Matthews, K. A. Morris, P. Santosh, E. Sonuga-Barke, E. Taylor, M. Weiss and S. Young

J Psychopharmacol 2007; 21; 10 originally published online Nov 8, 2006;
DOI: 10.1177/0269881106073219

The online version of this article can be found at:
http://jop.sagepub.com/cgi/content/abstract/21/1/10

Published by:
SAGE Publications
http://www.sagepublications.com

On behalf of:
British Association for Psychopharmacology

Psychopharm

Journal of Psychopharmacology
21(1) (2007) 10–41

ISSN 0269-8811
SAGE Publications Ltd, London, Thousand Oaks, CA and New Delhi
10.1177/0269881106073219

Evidence-based guidelines for management of attention-deficit/hyperactivity disorder in adolescents in transition to adult services and in adults: recommendations from the British Association for Psychopharmacology

D. J. Nutt *Psychopharmacology Unit, University of Bristol, Bristol, UK.*
K. Fone *University of Nottingham, Nottingham UK.*
P. Asherson *MRC Social Genetic Developmental Psychiatry, Institute of Psychiatry, King's College London, UK.*
D. Bramble *Telford & Wrekin PCT, Shrewsbury, UK.*
P. Hill *London, UK.*
K. Matthews *University of Dundee, Dundee UK.*
K. A. Morris *c/o Psychopharmacology Unit, University of Bristol, Bristol, UK.*
P. Santosh *Institute of Psychiatry, London, UK.*
E. Sonuga-Barke *University of Southampton, Southampton, UK.*
E. Taylor *Institute of Psychiatry, London, UK.*
M. Weiss *University of British Columbia, Vancouver, Canada.*
S. Young *Bethlem Royal Hospital, Kent, UK.*

For the Consensus Group (other invited participants at the consensus meeting 'ADHD in transition from child to adult' are listed in the Acknowledgements).

Abstract

Attention-deficit/hyperactivity disorder (ADHD) is an established diagnosis in children, associated with a large body of evidence on the benefits of treatment. Adolescents with ADHD are now leaving children's services often with no readily identifiable adult service to support them, which presents problems as local pharmacy regulations often preclude the prescription of stimulant drugs by general practitioners (GPs). In addition, adults with ADHD symptoms are now starting to present to primary care and psychiatry services requesting assessment and treatment. For these reasons, the British Association for Psychopharmacology (BAP) thought it timely to hold a consensus conference to review the body of evidence on childhood ADHD and the growing literature on ADHD in older age groups. Much of this initial guidance on managing ADHD in adolescents in transition and in adults is based on expert opinion derived from childhood evidence. We hope that, by the time these guidelines are updated, much evidence will be available to address the many directions for future research that are detailed here.

Keywords

ADHD, hyperkinetic disorders, hyperactivity, impulsivity, psychostimulants, psychotherapy, co-morbidities

Corresponding author: Prof. David J. Nutt, Psychopharmacology Unit, Dorothy Hodgkin Building, Whitson St, Bristol BS1 3NY, UK.
Email: david.j.nutt@bristol.ac.uk

Introduction

In recent years, UK health services have proven inadequate in meeting the needs not only of children with ADHD in transition from children's services, but also of the growing number of adults newly presenting with ADHD symptoms, often after their child has been given the diagnosis. Specialist services are now being established to manage adolescents in transition and adults with ADHD. The BAP thought it helpful to act as the vehicle to prepare a consensus document on best practice in an area that is both controversial and rapidly changing.

The BAP is an association of psychiatrists, psychopharmacologists and pre-clinical scientists who are interested in the broad field of drugs and the brain. BAP is the largest national organization of its kind worldwide, and publishes the *Journal of Psychopharmacology*. The association started publishing consensus statements more than a decade ago, and the first BAP guidelines on depression were considered a landmark publication when published in 1993 (Montgomery *et al*., 1993). That document, which was updated in 2000 (Anderson *et al*., 2000), has become the standard of care in many countries because it is considered an accessible consensus to guide practising psychiatrists. The BAP now has a target of publishing one consensus statement per year in the *Journal of Psychopharmacology*. Recent guidelines have covered management of bipolar disorder (Goodwin, 2003) and drug treatments for addiction (Lingford-Hughes *et al*., 2004), with guidelines on anxiety published late last year (Baldwin *et al*., 2005). Forthcoming consensus conferences are planned on child psychopharmacology, old age psychopharmacology and schizophrenia, all of which will utilize a similar style and process. All guidelines are available via the BAP website (http://www.bap.org.uk) and the intention is to update each guideline every 5 years.

Method

A consensus conference was held at the Novartis Foundation building, London on 24 February 2005. The meeting was sponsored by unrestricted educational grants from Cephalon, Janssen, Lilly, Shire UK and Shire US pharmaceutical companies, which had no input into and no responsibility for the meeting and its content. Those invited to attend the meeting included BAP members, representative clinicians from services with a strong interest in ADHD, and other recognized experts and advocates in the field, including a representative from Canada who had recently participated in that country's consensus statement on adult ADHD (www.caddra.ca). Observers from the sponsoring companies were invited to attend but not to participate in the proceedings or in drafting the guidelines. All attendees completed conflict of interest statements that are held at the BAP office as per usual BAP policy.

Speakers were asked to present a review of the literature and identification of the standard of evidence in their area, with an emphasis on meta-analyses, systematic reviews and randomized controlled trials (RCTs) where available. Each presentation was followed by a lengthy discussion that aimed to reach consensus where the evidence and/or clinical experience was considered adequate, or otherwise to flag the area as a direction for future research. A draft of the taped proceedings was drawn up by an attending clinician writer and circulated to all speakers and other participants for comment. Key subsequent publications were added by the writer and speakers at draft stage. All comments were incorporated as far as possible in the final document, which represents the views of all participants, although the authors take final responsibility for the document.

Categories of evidence for causal relationships, observational relationships and strength of recommendations are given in Table 1 and are taken from Shekelle *et al*. (1999). The strength of recommendation reflects not only the quality of the evidence, but also the importance of the area under study. For example, it is possible to have methodologically sound (category I) evidence about an area of practice that is clinically irrelevant, or has such a small effect that it is of little practical importance and therefore attracts a lower strength of recommendation. However, more commonly, it has been necessary to extrapolate from the available evidence (e.g. in childhood) leading to weaker levels of recommendation (B, C or D) based upon category I evidence statements.

Scope of the guidelines

Our intention is to present a comprehensive statement to guide clinicians, who are managing adolescents with ADHD in transition from children's services, and adults newly presenting with ADHD symptoms. Although rigorous evidence exists in a few areas, overall there is a dearth of evidence that pertains to adolescents and especially adults. Many of the statements in this document are therefore based on the experience of experts who are currently treating this adolescent or adult group, with extrapolation from the greater body of rigorous data in children. We anticipate that the situation with regard to research on adult ADHD is likely to change markedly in the future. Until that time, these guidelines must be considered a first attempt to reach consensus in an area that continues to attract controversy, and in which we cannot be certain that childhood findings will be confirmed in older age groups. We hope that the body of evidence may be considered far more definitive when these guidelines are due for updating.

Our consensus on adolescents in transition and adults with ADHD is based on the premise that a clinical entity, ADHD, exists in childhood and, moreover, that the condition may persist in some form in older age groups. The meeting recognized the fact that even ADHD in childhood is a controversial diagnosis to make in some quarters of society; thus, a diagnosis in older age groups might be more controversial in these quarters. The crux of the controversy seems to be whether the symptoms of ADHD need to be understood as a medical condition or whether the behaviours identified as ADHD are an extreme of the normal spectrum of human behaviours (e.g. 'very naughty little boys'). A further dimension is whether such behaviours necessitate pharmacological treatment or whether non-pharmacological modifications are sufficient to manage them.

The consensus of the meeting is that the extreme behaviours characterized under current diagnostic systems represent a clinical condition in so much as the behaviours cause problems for the

Table 1 Categories of evidence and strength of recommendations

Categories of evidence for causal relationships and treatment	
Ia:	Evidence from meta-analysis of randomized controlled trials
Ib:	Evidence from at least one randomized controlled trial
IIa:	Evidence from at least one controlled study without randomization
IIb:	Evidence from at least one other type of quasi-experimental study
III:	Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies
IV:	Evidence from expert committee reports or opinions and/or clinical experience of respected authorities
Categories of evidence for observational relationships	
I:	Evidence from large, representative population samples
II:	Evidence from small, well-designed, but not necessarily representative samples
III:	Evidence from non-representative surveys, case reports
IV:	Evidence from expert committee reports or opinions and/or clinical experience of respected authorities
Strength of recommendation	
A	Directly based on category I evidence
B	Directly based on category II evidence or extrapolated from category I evidence
C	Directly based on category III evidence or extrapolated from category II evidence
D	Directly based on category IV evidence or extrapolated from category III evidence
S	Standard of clinical care

affected individual, are identified as problematic by others and may respond to various forms of clinical treatment or other forms of management, such as environmental restructuring. A diagnosis of ADHD is thus warranted to allow affected individuals to access appropriate forms of support from health care and other systems. We hope the controversy will be lessened over ADHD in older age groups, because in many cases, the affected individual will be the one to initiate clinical contact. Indeed, it is partly in response to the growing number of such requests that this consensus meeting was arranged.

With current science, it is not possible to determine whether ADHD is an extreme variant of normal behaviour or in a distinct category. However, current science does support the improvement of ADHD symptoms with treatments, particularly but not exclusively pharmacological. It is in this spirit that this consensus document is presented. The question of who should provide and pay for service provision is a matter of health policy and thus beyond the scope of our consensus, although we hope that this consensus will prompt this debate.

Neurodevelopmental background

The exact cause(s) of ADHD are unknown but the growing literature on genetics, neuroimaging and neuropsychology suggests features consistent with a neurodevelopmental condition in which multiple environmental and biological factors, of individually small effect, interact to produce an abnormal brain condition that manifests as cognitive and behavioural deficits (Sonuga-Barke *et al*., 2005). Subsequent bidirectional interactions then occur between these deficits and environmental and biological factors to modify the phenotype further, resulting in various diagnostic subgroups under the umbrella term ADHD. Overall, the literature on genetic, neurobiological and neuropsychological deficits shows marked disparities between subgroups. This may indicate that causation is likely to show marked heterogeneity, and/or that traditional theories on cause and effect in ADHD, that regard ADHD as a homogeneous condition characterized by a single causal pathway, are inadequate (Sonuga-Barke, 2003, 2005; Coghill *et al*., 2005; Castellanos *et al*., 2006).

Genetics and neuroscience

ADHD is highly heritable, with heritability estimates from twin studies in the range of 65–90% (Thapar *et al*., 2001) and average across 20 studies of 76% (Faraone *et al*., 2005b). Family studies report that both parents and siblings of a child with ADHD are around four to five times more likely to have ADHD than the general population (Faraone *et al*., 2000). Although ADHD is diagnosed using operational diagnostic criteria, measures of ADHD symptoms are continuously distributed in the general population. Mathematical modelling using De Fries and Fulker (DF) analysis supports the hypothesis that ADHD is the extreme of behaviours that vary genetically throughout the entire population (Gjone *et al*., 1996; Levy *et al*., 1997; Willcutt *et al*., 2000; Price *et al*., 2001). These data suggest that genetic influences on ADHD are distributed throughout the population and correlate with quantitative trait measures of ADHD symptoms. This is important since this implies that ADHD is best perceived as a quantitative trait, or series of quantitative traits, rather than a categorical disorder. The implication for clinical practice is that, similar to other common psychiatric disorders such as anxiety and depression, appropriate clinical cut-offs need to be established that link ADHD symptoms to significant clinical impairments; given that ADHD is a developmental disorder, this will require establishment of age- and gender-specific norms. A particular issue for the diagnosis of ADHD in adults is that the age-appropriate expression of clinical symptoms has yet to be firmly established.

Genetic influences on ADHD are likely to be the result of multiple genes of small effect size and are expected to interact with environmental risk factors (Asherson *et al*., 2005). Four linkage scans have been completed and highlight a number of potential chromosomal regions containing genes that increase risk for ADHD, although there is as yet no clear consensus across the various data sets, and no genes have been identified that account for linkage signals (Fisher *et al*., 2002; Smalley *et al*., 2002; Bakker *et al*., 2003; Ogdie *et al*., 2003; Arcos-Burgos *et al*., 2004; Ogdie *et al*., 2004; Hebebrand *et al*., 2005). Genetic association studies have focused on the analysis of *monoamine system genes*, due to the marked and rapid response of ADHD symptoms to stimulants that block the reuptake of dopamine and norepinephrine (see later). Several genes have been reported to be associated with ADHD in multiple studies, with small but significant effects confirmed by meta-analysis (Asherson *et al*., 2005; Faraone *et al*., 2005b, Thapar *et al*., 2005a). The best evidence for association is with DNA variants of the *dopamine D4 (DRD4)* and *D5 (DRD5)* receptors and the dopamine transporter (DAT1), with strong additional evidence for associations with the *serotonin IB receptor (5-HT$_{1B}$)*, *serotonin transporter (SERT)* and *synaptosomal associated protein-25 (SNAP-25)*. Gene–environment interactions have been reported between *DAT1* and maternal use of tobacco (Kahn *et al*., 2003) and alcohol (Brookes *et al*., 2006) during pregnancy on the risk of ADHD, and between *catechol O-methyltransferase* and low birth weight on risk for antisocial outcomes among ADHD cases (Thapar *et al*., 2005b). Although most studies have focused on children with ADHD, it is interesting to note that the only two studies to investigate the *DRD4* association in adults with ADHD were both positive (Muglia *et al*., 2000; Lynn *et al*., 2005).

Neuroimaging studies (Bush *et al*., 2005) have documented significant overall and regional reductions in white matter volumes between unmedicated ADHD patients, including those never exposed to relevant medication, and healthy controls (Castellanos *et al*., 2002). Medicated patients differ from unmedicated patients, but not from healthy controls, in overall and regional (frontal, parietal and temporal) white matter volumes. These studies have clearly demonstrated differences in the anatomy and processing of patients with ADHD compared with controls, although these differences do not have the sensitivity or specificity in individuals to contribute to differential diagnosis (Seidman *et al*., 2005).

Several neuroimaging studies, though not all (van Dyck *et al*., 2002), have indicated that striatal DAT binding is increased compared with controls in ADHD patients (Krause *et al*., 2000; Madras *et al*., 2002; Spencer *et al*., 2005a; Volkow *et al*., 2005) including studies in adults (Dougherty *et al*., 1999; Dresel *et al*., 2000; Krause *et al*., 2000), suggesting increased density of the transporter protein in the striatum. In addition, there is evidence from two out of four studies that the *DAT1* risk genotype for ADHD is associated with increased striatal DAT binding (Heinz *et al*., 2000; Jacobsen *et al*., 2000; Martinez *et al*., 2001; Cheon *et al*., 2003). Moreover, other groups have reported that methylphenidate treatment, which increases extracellular dopamine in the human striatum (Volkow *et al*., 2001), is accompanied by reductions in DAT binding to control values (Dresel *et al*., 2000; Spencer *et al*., 2005a; Volkow *et al*., 2005).

Environment

Detailed coverage of the diverse literature on the influence of environmental factors was beyond the scope of the meeting and thus is briefly reviewed in this document. It is noted that environmental factors of significance include pregnancy and birth factors, prematurity, diet, institutional care and other aspects of the psychosocial environment (see Biederman, 2005 for a recent review). Several studies also suggest that childhood environmental factors shape the phenotypic expression of ADHD, and co-morbidity with other behavioural disorders, by acting on genetic influences (e.g. Hudziak *et al*., 2005; Burt *et al*., 2005; Dick *et al*., 2005; Jester *et al*., 2005 I–II). Furthermore, predictors of persistence into adulthood include family history of ADHD, psychiatric co-morbidity and psychosocial adversity (Biederman, 2005). In terms of treatment, various dietary manipulations can improve ADHD symptoms in at least some children (Egger *et al*., 1985; Carter *et al*., 1993; Boris and Mandel, 1994; Rowe and Rowe, 1994; Schmidt *et al*., 1997; Dykman and Dykman, 1998; Richardson and Puri, 2002 Ib), although the mechanism of these improvements is unknown. Activities in natural 'green' settings have been linked with symptom improvement in a national sample (Kuo and Taylor, 2004 I). These and other findings (e.g. that brain abnormalities may not determine phenotype (Castellanos *et al*., 2002 IIa)) could suggest a greater importance of environmental factors in some individuals, both in childhood and in older age groups. Environmental restructuring might be particularly important as part of the management of adults with ADHD, in our experience (see 'Psychotherapeutic approaches' below).

Cognition

Neuropsychological research, mainly in children, has documented various deficits in executive function (especially inhibition), motivation and reinforcement, attention, timing, memory and energetics (covered in detail in 'Neuropsychological assessment' below (Doyle *et al*., 2005)). This research has clarified that although about a third of patients have difficulties with one or another neuropsychological test of executive functioning, this is neither universal nor diagnostic. Functional neuroimaging studies have often suggested that brain activation is abnormal during affected tasks compared with controls, and specifically is more diffuse than in controls with failure of inhibitory functions. For example, Tamm *et al*. (2004) have linked a key deficit – abnormal response inhibition on a Go/No Go task – with abnormal activation patterns in specific temporal regions compared with controls. This has led to the hypothesis that individuals with ADHD may have to use other brain regions, when faced with attention demanding tasks, that are perhaps less efficient (Bush *et al*., 2005). Recent evidence also suggests that this is reversible with medication.

Various studies are aimed at linking the specific neuropsychological traits (known as endophenotypes – e.g. delay aversion, executive motor inhibition, deficit in arousal/activation regulation) that may underpin symptoms and behaviours, with neurobiological changes (e.g. dysfunction in frontostriatal circuitry, reward systems and catecholamine function (Waldman, 2005; Willcutt *et*

al., 2005)). The effects of the identified genetic variants on brain functioning and resultant phenotypic traits remain unclear, so the possibility remains that such variants could contribute to several phenotypes of which one is currently classified as ADHD.

Finally, neuropsychological deficits neither consistently predict behaviours nor outcome of treatment (e.g. Rhodes *et al*., 2004, 2005). This could reflect a lack of specificity of the deficit tested to the diagnostic group under study or the fact that treatment efficacy is not mediated via those structures and functions involved in the causative pathway(s) of ADHD.

Natural history

Several major prospective follow-up studies have documented the natural history of ADHD, especially as patients transit through adolescence into adulthood (Hechtman and Weiss, 1983; Barkley *et al*., 1990; Weiss and Hechtman, 1993; Biederman *et al*., 1996a; Biederman *et al*., 1996b; Faraone *et al*., 1996; Biederman *et al*., 1998; Mannuzza *et al*., 1998; Mick *et al*., 2004; Faraone *et al*., 2006). These studies suggest that a large proportion of child patients show ADHD symptoms that persist to adolescence (estimated variously at 50–60%) or adulthood (10–66%; Hill and Schoener, 1996; Spencer *et al*., 1996; Faraone *et al*., 1996; Biederman *et al*., 2000; Barkley, 2002; Faraone *et al*., 2006). A recent meta-analysis of studies that followed children identified with ADHD and matched controls into adulthood has been completed (Faraone *et al*., 2006). When the definition of ADHD included only those that met full diagnostic criteria for ADHD, the rate of persistence was approximately 15% at age 25 years. However the rate was far higher, approximately 65%, when individuals fulfilling the DSM-IV definition of ADHD in partial remission were included, referring to the persistence of some symptoms associated with significant clinical impairments. Prevalence rates of adult ADHD estimated at around 4% have been found in several different studies, using DSM-IV criteria, but will vary depending on clinical measures used and the precise way in which the diagnostic criteria are applied (Hill and Schoener, 1996; Gallagher and Blader, 2001; Bloom and Dey, 2004; Faraone and Biederman, 2005; Kooij *et al*., 2005; Kessler *et al*., 2006; Faraone *et al*., 2006).

While some symptoms (e.g. hyperactivity) tend to diminish or present differently with age, perhaps due to self-medication, adaptation and neurodevelopment, other symptoms, especially inattention, (Millstein *et al*., 1998) are more likely to persist and may have a greater impact on adults. Community follow-up of young people with untreated 'hyperactivity' suggests that impulsiveness declines in absolute terms, but remains deviant relative to that of age-matched peers (Taylor *et al*., 1996). These studies have investigated the frequency of these symptoms in adults but no study to date has evaluated the relative impairment caused by continuation of the various symptoms that do remain in the adult population. Attentional difficulties are likely to persist at least in their impact on functioning. Symptoms diminish in frequency and severity as a consequence of natural developmental processes seen in all children and may further diminish, at least in part, due to learned skills, coping strategies and environmental restructuring. However, the overall impact may worsen due to the increased demands of an adult environment. While the full complement of diagnostic deficits can often disappear in adulthood, at an age-related rate dependent on criteria, impairment persists and may

Consensus: ADHD as a neurodevelopmental condition

- ADHD is a neurodevelopmental psychiatric condition that most likely results from the interaction of multiple genetic and environmental factors, each of small effect, with different patterns creating multiple pathways to symptoms each marked and mediated by different deficit profiles (B).
- ADHD is currently understood to be a life-long condition and currently a diagnosis of adult ADHD needs to include childhood impairment (either prospectively or retrospectively) (C). The status of disorder of later onset needs to be established.
- In the absence of specific markers common to the entire group of ADHD patients, assessment and treatment are guided by phenotype (symptoms/behaviours/impairments).
- Co-morbidity is common in both childhood and adulthood, and may determine outcomes (D). Clinical assessment of ADHD needs to include careful evaluation for other disorders.
- Expression of ADHD and co-morbidities is highly heterogeneous, thus management needs to be individualized (C).

Key uncertainties

- A better aetiological theory is needed that accounts for the causal heterogeneity in the condition (Coghill *et al*., 2005; Sonuga-Barke, 2005)
- Is ADHD a categorical difference or the end of spectrum of a population trait?
- How does phenotype match to genetic, neuropsychological and neuroimaging markers?
- What are the best ways to subdivide ADHD into subtypes?
- What underpins the relation between ADHD and environmental factors, such as diet and sleep?
- How many adults with adult ADHD currently receive alternative diagnoses and treatments within adult psychiatric and primary care services?
- Should screening of parents and children of referred patients be considered, and what would be the resource implications of this?

worsen in a subset. In such patients, impairment is usually pervasive or affects more than one domain of activities and may manifest as: educational, organizational or occupational failures; substance use disorders and other dependent, risky, antisocial or forensic behaviours; emotional and relationship difficulties and increased medical morbidity (Millstein *et al*., 1998; Swensen *et al*., 2000).

Co-morbidity is widely considered to be a common finding in adolescent and adult ADHD patients, and will affect outcomes (see 'Comorbid disorders and special situations'). Epidemiological and clinical studies have shown that more than 80% of adults with ADHD will have another disorder, and the finding that co-morbidity in adults is similar to that in children, but increases with time, raises the question of whether some of this co-morbidity may be driven by untreated ADHD. Common co-morbid disorders in adulthood include anxiety, depression and antisocial behaviour disorders, and persisting neurodevelopmental disorders such as dyslexia (Heiligenstein and Keeling, 1995; Biederman *et al*., 1996b; Marks *et al*., 2001; Biederman, 2004; McGough *et al*., 2005; Kessler *et al*., 2006). The frequency of self-medication and substance use disorders is thought to increase with age but no studies have confirmed this supposition.

Diagnosis and assessment

Several issues arise when considering the diagnostic process for adult ADHD. Two major sets of criteria are used worldwide to diagnose conditions characterized by inattention and/or hyperactivity – the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition text revision (DSM-IV-TR, APA, 2000), which recognizes ADHD, and the *International Classification of Diseases*, tenth edition (ICD-10, WHO, 1992), which encompasses hyperkinetic disorders. Due to differences in criteria, each system identifies different clinical entities with different names – ADHD (APA, 2000) or hyperkinetic disorders (WHO, 1992); the latter generally describes a more restricted and severe subset of DSM-IV combined-type ADHD. We have chosen to use the term ADHD as shorthand for ADHD and hyperkinetic disorders, except where the two are contrasted.

In the absence of any definitive and objective test (e.g. genetic or neuropsychological), the purpose of the diagnostic process needs consideration. Currently, diagnosis is a process of identifying extreme behaviour that requires and is amenable to professional help. However, this process can be used to validate observers' views of extreme behaviour rather than to identify markers of an underlying pathological process, with manifestations that map to the label of ADHD. As in most areas of medicine, ADHD is diagnosed clinically. The only valid 'test' for ADHD is the use of rating scales that have been normed on large populations, and can identify whether the child is affected by this disorder, other disorders and functional impairment compared with age- and gender-matched peers. The use of rating scales combined with a developmental history, observation, family and other risk factors, and impairments consistent with the disorder allows a high level of diagnostic certainty between clinicians and predicting response to treatment (Barkley, 2006). Treatment response is not considered sufficient to make a diagnosis of ADHD; although the criteria for hyperkinetic disorders better predicts treatment response than the criteria for ADHD, treatment response varies between individuals, while other disorders can respond to current therapeutic options.

The two diagnostic systems have various limitations, not least the internal tautology that the definition of ADHD or hyperkinetic disorders rests solely on the criteria that have been established. For example, the possibility exists that boys are diagnosed with ADHD more often than girls because the diagnostic criteria relate to disruptive behaviours as markers that are more prevalent in male children. Importantly, these systems do not include associated symptoms, reported by patients which could arguably be the main target of treatments.

Diagnostic systems

Although DSM-IV-TR and ICD-10 have criteria to diagnose childhood ADHD, these have not been adapted to be appropriate to adults – e.g. there is no age adjustment to the criteria appropriate to adults. The associated symptoms are similar in the two classifications and full criteria are given in the Appendix.

DSM-IV-TR The DSM-IV-TR (APA, 2000) requires all the following criteria for a diagnosis of ADHD:

- Either at least six of nine symptoms of inattention or at least six of nine symptoms of hyperactivity/impulsivity persisting for at least 6 months to a maladaptive degree, inconsistent with developmental level. DSM-IV-TR allows for ADHD 'in partial remission' that can usefully be applied to adults who had ADHD and have persistence of some of the symptoms associated with continued clinical impairments, but who no longer fulfil the full criteria.
- Some symptoms that caused impairment were present before age 7 years.
- Some impairment from symptoms is present in at least two settings (e.g. at home and at school/work).
- Clear evidence of clinically significant impairment in social, academic or occupational functioning.
- Symptoms do not occur exclusively during a pervasive developmental disorder or psychotic disorder and are not better accounted for by another mental health disorder.

DSM-IV-TR distinguishes three subtypes of ADHD on the basis of clinical symptoms: (a) predominantly inattentive type, (b) predominantly hyperactive/impulsive type or (c) combined type (presence of inattention and hyperactivity/impulsivity). These subtypes are defined by the absence of a six of nine symptom cut-off in any one of the domains, although the patient may still have significant symptoms (five of nine), impairment, or be markedly discrepant for age and gender norms in the area in which they fail to meet this cut-off criterion.

ICD-10 Two types of WHO criteria exist (WHO, 1992) – the general criteria and the diagnostic criteria for research (DCR),

which are more specific than the general criteria and closer to the DSM-IV-TR criteria. The diagnostic basis of ICD-10 hyperkinetic disorders is the existence of both impaired attention and overactivity evident in more than one situation (e.g. home, educational settings, clinic). The presence or absence of conduct disorder constitutes the basis for the main subdivision of hyperkinetic disorders – disturbance of activity and attention versus hyperkinetic conduct disorder.

For the general ICD-10 diagnosis, behavioural problems should be longstanding and have started before age 6 years. The caveat is made that due to wide normal variation in activity, only extreme degrees of hyperactivity should lead to a diagnosis in preschool children. Associated features are not necessary or sufficient for the diagnosis but help sustain the disorder, including; disinhibition in social relationships, recklessness in situations involving some danger, and impulsive flouting of social rules (as shown by intruding on or interrupting others' activities, prematurely answering questions before they have been completed or difficulty in waiting turns).

The ICD-10 DCR recognizes seven criteria:

- Demonstrable abnormalities at home: at least three of five problems of inattention, at least three of five problems of hyperactivity, at least one of three problems of hyperactivity.
- Demonstrable abnormalities at school or nursery: at least two of four attentional problems and at least three of five activity problems.
- Directly observed abnormality of attention or inactivity.
- Does not meet criteria for pervasive developmental disorders, mania, depressive or anxiety disorder.
- Onset before the age of 7 years.
- Duraction of at least six months.
- IQ above 50.

Thus the DSM-IV-TR criteria identify a broader group of patients than the ICD-10 (Tripp *et al*., 1999). No definitive system exists to diagnose adult ADHD, while use of these childhood diagnostic systems in adults raises various difficulties, not least the alteration of symptoms in adulthood. Thus, the consensus group thought it would be helpful to present an extended checklist of adult symptoms in this document, based on childhood diagnostic symptoms plus additional adult symptoms (APA, 2000; WHO, 1992; Wender, 1995).

Rating scales Various rating scales have been developed to help diagnose adult ADHD, including three self-report scales. The 61-item Wender Utah Rating Scale focuses on retrospective symptoms in childhood plus current hyperactivity, inattention and other symptoms. It relies on retrospective recall by the individual but has been validated against parent report and found to be reliable (Ward *et al*., 1993). Others include the Adult Self Report Scale (Adler *et al*., 2004; Kessler *et al*., 2005), Conners Adult ADHD Rating Scale (Conners *et al*., 1998), the 40-item Brown Adult Attention Deficit Disorder Scale (Brown, 1996) and the Barkley Self, Other and Past ADHD symptom checklists (Barkley and Murphy, 2006). None of these scales is sufficient for diagnostic purposes but may be useful in conjunction with a formal clinical evaluation, or serially to evaluate symptom changes. Several different types of scales may be helpful: screens for adult ADHD symptoms, screen for co-morbidity (Gadow *et al*., 1999), and examination of impact of ADHD on functional impairment (Weiss and Weiss, 2004). Generic functioning scales have shown poor correlation with ADHD symptoms, making it clear that ADHD specific functional scales are needed (Gordon *et al*., 2006).

Proposed BAP extended adult symptom checklist

1 Lack of attention to detail or carelessness
2 Inattention in tasks or activities the patient finds tedious
3 Difficulty listening
4 Failure to follow instructions
5 Starting many tasks while having difficulty finishing them
6 Poor organizational skills
7 Avoidance of, dislike of, or inability to expend sustained mental effort
8 Losing or misplacing things
9 Ready distractibility
10 Forgetfulness
11 Fidgeting
12 Restlessness or an inability to sit still in low-stimulation situations
13 Inappropriate or excessive activity or an internal feeling of restlessness or edginess
14 Difficulty keeping quiet; talking out of turn
15 Unfocused mental activity; difficulty turning thoughts off
16 Blurting out responses; poor social timing in dialogue
17 Trouble waiting if there is nothing to do
18 Interrupting or intruding on others
19 Irritability, impatience or frustration
20 Affective lability or hot temper
21 Stress intolerance
22 Impulsivity or risk-taking in activities

Two shorter scales have been developed to allow a rapid initial screen in various clinical settings, and are based on the 18 symptoms listed in both the DSM-IV-TR and the ICD-10 DCR criteria. The six-item Adult ADHD Self-Report Scale screener (ASRS-v1.1, Adler *et al*., 2004; Kessler *et al*., 2005) is patient-rated while the ADHD Rating Scale (ADHDRS-IV-Inv, Adler *et al*., 2005b) is clinician administered with good reliability and moderate agreement between raters. The ASRS (available at www.med.nyu.edu/psych/assets/adhdscreen18.pdf) and the Canadian Consensus screening checklist (www.caddra.ca) are given in the Appendix. Other scales can be downloaded from www.caddra.ca and www.adhd.net.

Neuropsychological assessment

Many studies in children but few in adolescents have documented various deficits of neuropsychological testing. The limited liter-

Table 2 Summary of evidence on neuropsychological assessment

	Child (approx 6 to 12)			Adolescence (approx 12 to 18)			Adulthood		
Test	Quality	Quantity	Strength	Quality	Quantity	Strength	Quality	Quantity	Strength
Inhibition-based executive functions									
CPTcomm	A	A	III	D	D	II	A	B	III
CPT-omm	A	A	III	D	D	I	A	B	III
SST-RT	A	A	III	D	C	III	A	C	III
WM-spati	A	A	III	D	B	III	A	C	II
WM-verb	A	A	III	D	B	III	A	B	II
ToL/H	A	A	III	D	D	II	A	D	III
Trials-B	A	A	III	D	E	–	A	B	III
StroopIntf	A	A	II	D	C	II	A	C	I
WCST-Per	A	A	III	D	D	I	A	C	I
Timing									
Time-Dis	B	C	III	E	E	–	E	E	–
Time-Rep	B	B	III	B	D	III	B	D	III
Energetics									
ISI effects	C	B	III	E	E	–	E	–	–
Reward and punishment processing									
Reward	B	B	II	E	E	–	E	–	–
Punishment	B	B	II	E	E	–	E	–	–
Delay aversion									
Delay	B	B	III	D	D	II	E	–	–

Quality: quantitative review (A); qualitative review (B); no review (C); no studies (D)
Quantity: more than ten studies (A); five to ten studies (B); two to four studies (C); one study (D); no studies (E)
Strength: I=no effect d<0.2; II=small effect d 0.2–0.4; III=moderate d 0.4–0.7; IV=large d 0.7–1.0; V=very large d>1.0
Tests are: Continuous Performance Test commission errors; Continuous Performance Test ommission errors; Stop Signal Reaction Times; Spatial working memory; Verbal working memory; Tower of London/Hanoi; Trials-B; Stroop interference; Wisconsin card sorting task; Time discrimination; Time reproduction; Interstimulus interval effects; responses to reward, punishment; Choice for delayed rewards

ature in adults reports similar patterns, although marked heterogeneity exists (Schoeclin and Engel, 2005; Frazier *et al*., 2004; Harvey *et al*., 2004; Seidman *et al*., 2004; Nigg, 2005). Commonly reported impairments are found in tasks involving executive functions, selective and sustained attention, response inhibition, working memory and reward-related motivation. Findings on specific tests in various domains are shown in Table 2.

However as suggested above, the traditional neuropsychological model of ADHD, which holds that symptoms are the product of a common core deficit expressed by all affected individuals, is now contentious (Sonuga-Barke, 2002, 2003, 2005; Castellanos *et al*., 2006). The emerging consensus is that ADHD is a neuropsychologically heterogeneous disorder, with different patterns of impairments seen in different individuals (Sonuga-Barke, 2002, 2003, 2005; Coghill *et al*., 2005). Alternate theories include a failure of specific response-inhibition mechanisms (Willcutt *et al*., 2005), altered reward or motivational pathways (Luman *et al*., 2005), abnormal processing of time-related cues (Toplak and Tannock, in submission), non-working memory (Rhodes *et al*., 2004, 2005) and diffuse abnormalities in energetics (Seargant, 2005). Current thinking is that these impairments may reflect dysregulation in distinct underlying neural circuitries, that is: frontal, (dorsolateral prefrontal cortex), dorsal and medial striatal function reflecting executive function deficits; cerebellum and its outputs affecting timing (with modulation by norepinephrine); ventro-striatal-prefrontal (orbito-frontal) circuitry affecting reward and punishment processing, motivation and delay aversion (with modulation by dopamine); temporal and amygdalo-hippocampal

circuitry affecting non-working memory; and distributed circuitry implicated in abnormal cognitive energetics.

While little is known about the value of neuropsychological assessment in differential diagnosis in adults and adolescents (Lovejoy *et al*., 1999) most studies in children reveal that tests of executive function and attention show good positive predictive power but poor negative predictive power (Barkley *et al*., 1992; Sharma *et al*., 1991; Grodzinsky and Barkley, 1999; Rielly *et al*., 1999; Doyle *et al*., 2000; Dickerson Mayes *et al*., 2001; Berlin *et al*., 2004). Thus, use of such tests alone will lead to false-negative diagnoses (children without neuropsychological executive impairment will still have the condition), which is unsurprising given the heterogeneity of neuropsychological findings.

The effect of co-morbidities on such tests is not well researched. General intelligence testing can be useful to relate IQ to the level of academic and occupational achievement and to investigate or exclude learning disabilities. However, it raises the issue of labelling based on IQ testing alone. This is particularly important for individuals with ADHD since it is possible that IQ testing results will show increased variation in this group and are likely to be affected by the attention and motivation of individuals and/or by underachievement in education. For example, a recent study of the WISC-IV in 118 children showed the working memory tests to be the lowest score in all 118 children, thus lowering the overall IQ score secondary to a deficit considered specific to ADHD (Mayes and Calhoun, 2006).

Until the heterogeneity of ADHD is better characterized and an optimal battery of tests in multiple domains is compiled, the practical value of experimental neuropsychological assessment may lie in profiling areas of particular deficits in individual cases, which may then help to indicate specific solutions to task-related impairments, and then to monitor outcomes. Further, neuropsychological subtyping of patterns of deficits might shed more light on the underlying pathological processes and potentially help tailor treatments to phenotype.

Assessment and differential diagnosis

The importance of a full clinical assessment needs to be emphasized, including neurodevelopmental history (Weiss and Murray, 2003, 2004; Biederman, 2005; Asherson, 2005). It may be worth setting aside any preconceptions of an individual's diagnosis from previous contacts with health services and starting from first principles, using standard assessment techniques available in psychiatric services. The presence of ADHD symptoms needs to be elicited plus symptoms of differential and co-morbid disorders (see also 'Co-morbid disorders and special situations'), and their impact on various domains of functioning needs to be assessed. The differential diagnosis of ADHD includes neurodevelopmental disorders (learning disability, autistic spectrum disorders, communication difficulties, etc.), anxiety, depression, bipolar disorder, substance use disorders and personality disorders. Some clinicians also advocate a full examination including neurology, since subtle deficits like gaze instability and word-finding defects have been reported (Weiss and Murray, 2004 IV). The clinical assessment may generate hypotheses about specific disorders or deficits in an individual, which can then be explored further with rating scales, and where indicated neuropsychology. Treatment response is not thought to be sufficiently specific to form part of the diagnostic assessment (IV).

Diagnostic difficulties in adults A diagnosis of adult ADHD may be made under several circumstances. The most straightforward scenario is the persistence of symptoms or problem behaviours in individuals in transition from child and adolescent mental health services. Individuals that present in adulthood may self-report symptoms of ADHD or observations of others. ADHD might also be identified through presentation with a co-morbid diagnosis such as substance use disorders or a difficulty in a domain of functioning (e.g. referral from occupational health services). The availability of management strategies suggests the possibility of screening – either in the parents or siblings of those identified with ADHD or in children and adults with problem behaviours. This latter strategy might present a potential source of gender bias since a focus on conduct disorder and related behaviours might be one explanation of the high male: female ratio among children diagnosed with ADHD (Pineda *et al*., 1999; Jackson and King, 2004). Some evidence suggests that equal numbers of women and men are affected with ADHD as adults (Murphy and Barkley, 1996; Rowland *et al*., 2002), which raises the possibility that girls with ADHD are underdiagnosed.

Diagnosis of ADHD in adults raises other issues in addition to those already identified. The importance of making a diagnosis in adults is the identification of impairments that are amenable to treatment. Moreover, being given a diagnosis of adult ADHD may help individuals understand why their attainment has failed to correlate with that expected of them, but can also reduce self-esteem, which may itself have an adverse impact on functioning. The diagnostic and assessment process is further complicated by differences in co-morbidities, which may be a more important focus for management than core ADHD symptoms.

To make a diagnosis of ADHD in adults, current diagnostic systems require the presence of ADHD symptoms from childhood. Whilst this is unlikely to be a problem for individuals in transition from children's services, presentation for the first time in adulthood raises the question of whether ADHD is always a continuum from childhood deficits or whether adult-onset ADHD can occur. A view shared by many clinicians is that whilst symptoms are likely to have been present throughout development, there are groups for whom these symptoms only become impairing at particular stages of development, often around significant transitions, e.g. from primary to secondary school or from school to college or to work. Whilst the current diagnostic frameworks would not formally recognize these cases as late-onset ADHD, they will meet all criteria for diagnosis excepting that for onset of impairment.

Another requirement for diagnosis is the number of symptoms reported but, given the natural history of the disorder and other sources of heterogeneity, many adults may not reach full diagnostic criteria. Furthermore, adults have a greater ability to adapt to their environment and the demands that this places on them, which may alter the ways in which symptoms are expressed. However,

Recommendations – diagnosis and assessment

Diagnosis in adulthood requires specialist skills – i.e. those used by psychiatrists – but should involve primary care practitioners, who should be trained to be aware of the diagnosis (D). Assessment includes symptoms (past and present), impairments in different contexts, influence of changing demands through life, exclusion of differentials, and application of clinical examination, rating scales and other tools as indicated.

- Diagnosis has a major impacts, so the purpose of diagnosis is to identify those who are likely to benefit from treatment options where these are available (D).
- Preferable diagnostic and assessment criteria are an extended checklist based on DSM-IV-TR and ICD-10 and adult symptoms (D) (see panel and Appendix).
- Assessment needs to confirm impairment in different scenarios: (a) a history of childhood ADHD or suggestive symptoms (impairments/failure of attainment/demands and co-morbidity), (b) current evidence of symptoms leading to pervasive impairment in more than one domain (given context demands and skills) (D).
- Multiple informants need to be used where possible (at least one contemporary and one developmental) with consent, especially for younger patients (D).
- Current neuropsychological tests based solely on executive function are likely to be of limited diagnostic value, though test batteries that assess multiple domains of neuropsychological performance may be useful to determine individual deficits and to suggest tailored management strategies (D).
- Sensitive use of general intelligence tests can be useful to ascertain potential attainment, and to diagnose co-morbid learning disabilities (D). Interest, reward and educational achievement are important complicating factors (D).
- Clinicians need to be aware of the impact of diagnosis and testing on the individual, particularly on self-esteem (D).
- Treatment response cannot be used to make a diagnosis of ADHD (D).

Key uncertainties

- What criteria and checklists are required to incorporate better subjective adult symptomatology, to highlight possible neuropsychological deficits and to map treatment responses?
- What will be the impact of extending the symptom checklists on sensitivity and specificity of diagnosis?
- How can the diagnostic process avoid gender and other biases and match to an underlying pathological process reflected in symptoms rather than to external complaints?
- What is the practical place of neuropsychology (who to test, with what, and when with what value)?
- What can neuropsychological subtyping tell us about different neuropsychological traits (endophenotypes) within ADHD and their relationship with causation, behaviours, co-morbidity and treatment responses?
- What are the natural history or neurodevelopmental milestones in different domains of neuropsychological functioning especially in relation to transitions between childhood/adolescence and adulthood?
- Can a diagnostically useful battery of tests that measures across domains of functioning, be compiled to improve diagnosis?
- What are the useful thresholds regarding diagnosis to determine whether symptoms will or will not be amenable to treatment?
- Since the current subtypes are based on male child norms that are problematic, what further research is needed on subtypes? Of note, the inattentive subtype includes patients who have never had problems with hyperactivity, but also those who have subthreshold hyperactivity and impulsive symptoms that are representative of the combined type. There are very few patients who are just hyperactive and no research to indicate that these people are impaired or simply not reporting problems with attention.

some will still have substantial impairments amenable to treatment, which will not be highlighted by use of diagnostic systems but rather through a detailed assessment of associated impairments (Weiss and Murray, 2004). Epidemiological data support the validity of applying a lower threshold in adults (e.g. four or five out of nine criteria), as this lower threshold correlates significantly with impairment (Kooij *et al*., 2005). The emphasis on functional impairment has several effects. First, it permits recognition of the need for treatment in those patients who are impaired but subsyndromal. Second, it raises questions about the value of treatments in patients with symptoms and no evidence of current impairment, thus narrowing diagnostic criteria to those who are actually having problems.

Use of the current childhood diagnostic systems (APA, 2000; WHO, 1992) in adults requires validation of ADHD symptomatology from observers since self-reported symptoms are not included. However, individuals who present in adulthood with ADHD report their symptoms but may also lack insight into their current symptoms (Magnusson *et al*., 2006). In addition, the need to collect data on possible impairments as a child raises the possibility of recall bias in the individual, especially for symptoms such as impulsivity and their impact. Use of informants, if available, to

report on current and childhood behaviour requires consent and could be unreliable depending on the nature of the informant and their relationship to the individual (e.g. partner, parent, employer, etc.) but is nevertheless useful.

Treatment

Physicians identify and treat patients based on symptoms. However, patients come to clinical practice with the hope of functional change, which is the key goal of management. Change in psychological functioning and functioning in other domains is essential since 'pills don't build skills' and treatment of inattention and other core symptoms is not beneficial if patients have nothing to do. A package of care needs to be developed from available options on an individual basis after a thorough assessment (Weiss and Murray, 2004; Asherson, 2005, IV).

Drug treatment in childhood

Drug treatment for children with ADHD has substantially increased in the past decade, in part due to increased recognition of the disorder and perhaps also due to changing views on the impairment thresholds for drug treatment. In the UK, GP prescribing of methylphenidate has increased sixfold (PPA data www.publications.doh.gov.uk/prescriptionstatistics/index.htm), although rates remain about 20 times lower than in the USA for both prescribing and treatment. Therapeutic agents licensed in the UK and comparative costs are listed in Table 3, and are all used in primary care. These agents plus mixed amfetamine salts (Adderall) are generally available elsewhere. Safety alerts have been issued over atomoxetine use in childhood, concerning rare hepatotoxicity (one possible case, one probable case in 3.8 million) and, recently, increased suicidal thoughts (five cases out of 1357 cases) or behaviour (one case). All of these rare events are below the prevalence of similar events in the general population.

An appraisal for the National Institute for Clinical Excellence (NICE, 2006 Ia) has identified 65 acceptable trial reports on the first-line agents, although most are of low quality, and the heterogeneity of measures, methods and participants has precluded a meta-analysis. Qualitative assessment suggests that all agents are more effective than placebo and have similar efficacy, although there have been few head-to-head comparisons. Cost-effectiveness modelling indicates that use of all three agents sequentially is beneficial, and although the order of sequential prescribing is not clear on a clinical basis, dexamfetamine would be first line on the basis of cost alone. However, these agents are not equivalent in terms of side effects (for example, dexamfetamine is considered by many to have greater abuse potential than methylphenidate), and the response to different agents varies both between individuals and at different doses.

Table 3 Agents licensed in children (data from the British National Formulary 2005)

Generic	Proprietary	Annual cost
Methylphenidate hydrochloride	Equasym	30 mg/day = £182
	Ritalin	30 mg/day = £203
	Concerta XL	36 mg/day = £444
	Equasym XL	30 mg/day = £578 (E)
Dexamfetamine sulfate	Dexedrine	15 mg/day = £75
Atomoxetine	Strattera	40 mg once daily = £712
		40 mg twice daily = £1424

Note – prices may change and the dosages given are not necessarily equipotent.

The effects of drug treatment require careful monitoring and dose adjustment. Scales such as the Clinical Global Adjustment Scale (Shaffer *et al*., 1983), the ADHD checklists (Adler *et al.*, 2005; Barkley, 2006) and Conners' scales (Conners *et al*., 1998) are useful tools for disease monitoring and service audit. Patients and parents should be questioned for concordance over reported effects, as well as compliance. Any history of tolerance or diurnal changes in symptom control should be specifically elicited. Adolescents need to be advised of the potential interaction with recreational drugs, including possibly cannabis, although strong warnings against substance use might need to be balanced against the need to engage the patient with treatment. Substance use or dependence might need to be addressed prior to being able to intervene effectively in ADHD.

Various questions remain open over prescribing in childhood, and would benefit from future research. Comparable data on cost effectiveness of different drugs are lacking, as are data on long-term effects, including adverse events and effects on different symptom domains, including broader areas of functioning such as social adjustment. Data are also lacking regarding the effects of longer acting preparations on phenomena such as tolerance and sensitization. The mechanisms of diurnal and long-term changes in symptoms per se are not well understood nor is the basis of variation in effective medication dosages, though increasing dose with increasing body size is well recognized. Better outcome measures are required to assess broader effects, including quality of life measures because the QALY is inadequate in this scenario.

Drug treatment of adults

Drug treatment of adults with ADHD is relatively new, having been prompted by the entry into adult services of people previously treated in children's services. However, clinical experience in specialist adult ADHD clinics suggests that the majority of adult patients are diagnosed as adults, while most adolescent patients stop or are taken off medication. While it is not known whether all findings in children can be extrapolated to adults, psychostimulants have comparable effects in adults as in children and adolescents (Faraone *et al*., 2004; Kooij *et al*., 2004; Spencer *et al*., 2005b 1a). Global functioning and adult symptoms such as unstable mood and ceaseless mental activity are thought to respond as well to psychostimulants as do other core symptoms (Asherson, 2005).

Prescribing and monitoring strategies are no more complex than those used in the management of children, and can be based

on usual approaches utilized in adult services. However, a rigorous approach to diagnosis is warranted since adult patients are perceived to present commonly with and be treated for anxiety and depression either as the primary disorder or as part of a personality disorder. It is important that such patients are correctly diagnosed and treated within adult psychiatric services, since symptoms can respond to treatment. Moreover, specialist services are able to monitor treated patients in a similar manner to those with other conditions, for compliance, response and potential adverse effects, including physical side effects like hypertension and weight loss, and effects on co-morbid symptoms. The best outcomes for monitoring response within trials and for individuals are not known but may include ratings of core and co-morbid symptoms and effects on various domains of functioning. In general, compliance may be better in adults than in children, although the reverse may also be true. Patients may discontinue treatment due to disorganization, difficulty with persistence, negative and uninformed media (leading for example to employer prejudice), fears over dependency, mistaking the treatment as the cause of the stigma of the disorder, and lack of knowledge on other long-term effects.

Atomoxetine is licensed in the USA for the treatment of adult ADHD and in the UK for the treatment of adults who have previously been treated for ADHD as children. No agent is currently licensed in the UK for adults newly diagnosed with ADHD so prescribing is off-label. The drugs of first choice for the treatment of adult ADHD are classified as either psychostimulants (e.g. methylphenidate, amfetamines (Maidment, 2003a)) or non-stimulant (e.g. atomoxetine (Thomason and Michelson, 2004)) (see Table 3). Other non-stimulant agents reported to have some efficacy include alpha2 adrenoceptor agonists (clonidine and guanfacine), tricyclic antidepressants, bupropion, modafinil and venlafaxine (Maidment, 2003b). No efficacy has been found for selective serotonin-reuptake inhibitors, which may be because effective agents generally act via dopamine and/or norepinephrine as discussed next. In general, core symptoms are thought to respond better to psychostimulants and atomoxetine than to antidepressants, although no head-to-head studies have been done (Biederman and Spencer, 2001; Maidment, 2003a; Maidment, 2003b).

Mechanisms of drug action All effective agents thus far identified act on dopamine and/or norepinephrine neurotransmission, either as agonists or as reuptake inhibitors with the exception of modafinil, whose mechanism of action remains unclear (Fone and Nutt, 2005). Methylphenidate is a potent inhibitor of dopamine reuptake (Andersen, 1989; Thomason and Michelson, 2004), by binding to the cocaine-binding site on the DAT, but *in vitro* data on reuptake inhibition suggest that it also has a very high affinity for the norepinephrine transporter (NET). The primary action of dexamfetamine is inhibition of dopamine reuptake but in addition, amfetamines can cross the cell membrane by a mechanism independent of the transporter, and interact with the vesicular monoamine transporter 2 (VMAT2), thereby displacing vesicular dopamine and causing the release of newly synthesized intraneuronal monoamine (Ferris and Tang, 1979; Fleckenstein and Hanson, 2003). Atomoxetine is a relatively selective NET inhibitor, having approximately a 300-fold higher affinity for NET than DAT, (Thomason and Michelson, 2004; Gehlert *et al*., 1995). Neuroimaging studies in humans have failed to clarify the relative therapeutic benefit resulting from targeting DAT or NET independently. In particular, no high-affinity ligands exist to visualize the norepinephrine transporter in the human brain making it difficult to establish the therapeutic importance of NET inhibition. Nonetheless, imaging studies indicate that methylphenidate binds strongly to DAT and indirect evidence suggests that this elevates dopamine levels within an hour when given in therapeutic doses by oral administration (Volkow *et al*., 1998; Krause *et al*., 2000). These changes are accompanied by an increase in synaptic dopamine that is dependent on cell-firing rates. Thus, following methylphenidate administration, a salient stimulus is found to elicit greater synaptic dopamine levels than a neutral stimulus (Volkow *et al*., 2005).

Animal studies show that psychostimulants induce an increase in cFos-like immunoreactivity consistent with it causing neuronal activation in the striatum, including the caudate, and in the mediofrontal cortex (Lin *et al*., 1996). However, microdialysis in rats shows that intraperitoneal methylphenidate increases the synaptic overflow of hippocampal norepinephrine and striatal dopamine efflux to a similar magnitude (Kuczenski and Segal, 2001). Furthermore, with oral methylphenidate, hippocampal norepinephrine efflux is evoked by lower doses than are required to elicit nucleus accumbens dopamine efflux (Kuczenski and Segal, 2002). In contrast, atomoxetine causes a selective increase in cFos within the prefrontal cortex without increasing expression within the nucleus accumbens or striatum, consistent with it being a selective inhibitor of NET as indicated from *in vitro* data (Bymaster *et al*., 2002). Yet, systemic atomoxetine administration produced an equivalent threefold increase in prefrontal norepinephrine and dopamine efflux measured by microdialysis (Bymaster *et al*., 2002), whereas extracellular norepinephrine but not dopamine is increased in other brain regions, including the hippocampus (Swanson *et al*., 2006). The prefrontal cortex contains very low levels of DAT but dopamine and norepinephrine have very similar affinity for NET, so it is possible that dopamine reuptake may occur via NET in this brain area. Furthermore, adrenoceptor agonists (guanfacine and clonidine), which are thought to activate prefrontal cortex postsynaptic alpha2 adrenoceptors, have been shown to improve performance of non-human primates in a spatial working memory task (Avery *et al*., 2000).

Clinical efficacy Discussions on clinical efficacy are limited by the lack of head-to-head studies with adequate and unbiased methodology. In general, all agents with evidence of efficacy in adults can reduce core symptoms, although effects on different symptoms and global functioning may vary between agents and individuals. In the absence of any obvious prescribing hierarchy, choice of agent may depend on pharmacological factors other than efficacy (particularly abuse potential, side-effect profile and toxicity in overdose), as well as individual factors (such as patient choice and co-morbidity). The effect of genotype on treatment response is unclear, although a poor response to methylphenidate has been reported in children homozygous for the less common nine-repeat DAT1 genotype (Stein *et al*., 2005).

In children and adolescents, over 200 trial reports indicate around a 70% short-term response rate with methylphenidate treatment (Smith *et al*., 2000 Ib; Schachter *et al*., 2001). A recent meta-analysis of several adult trials of methylphenidate indicates that response rates and effect size of treatment in adults is comparable with, although somewhat lower than, those in children (Faraone *et al*., 2004 Ia). Notably, greater response rates were identified by physician ratings compared with self-report, and in global functioning rather than core symptomatology. Long-acting preparations are reported to have similar response rates and effect sizes to standard methylphenidate (Santosh and Taylor, 2000 Ib). It should be noted, however, that the long-acting preparations may improve compliance, minimise abuse, diminish rebound symptoms and address impairment later in the day, which has been shown to lead to preferential effectiveness in children (Steele *et al*., 2006).

The meta-analysis found response rates varied between trials (25–78%); this report and a subsequent trial (76%) indicate that greater responses are found with higher dosing regimes (1 mg/kg) that are comparable with those effective in children (Faraone *et al*., 2004; Spencer *et al*., 2005b Ia). Other factors found to correlate with response include reduced level of functioning (psychiatric outpatients versus high functioning academic underachievers) and psychiatric co-morbidity, although the latter was not confirmed in the latest trial (Spencer *et al*., 2005b).

Similar but more limited findings are reported for dexamfetamine (dextro- or D-amfetamine) (Arnold *et al*., 1989; Paterson *et al*., 1999; Taylor and Russo, 2000, 2001 Ib), Adderall mixed amfetamine salts (Spencer *et al*., 2001; Biederman *et al*., 2005 Ib), the psychostimulant pemoline (Wilens *et al*., 1999b Ib), and the dopaminergic agent bupropion (Wender and Reimherr, 1990; Wilens *et al*., 2001 Ib). However, pemoline is associated with hepatotoxicity (Marotta and Roberts, 1998 III) and has been withdrawn from use.

Several randomized, double-blind placebo-controlled trials have confirmed the efficacy of atomoxetine in children and adolescents (Thomason and Michelson, 2004 Ib), and similar findings with an effect size of 0.35–0.4 have been reported from two trials in adults (Michelson *et al*., 2003; Faraone *et al*., 2005a Ib). However, effects on overall functioning are debated, while no long-term efficacy trials have yet been reported, although an interim analysis in adults has been reported (Adler *et al*., 2005a). Thus, its place in clinical practice is not yet fully defined. Other norepinephrine uptake blocking agents such as desipramine (Wilens *et al*., 1996 Ib) have similar effects in trials while open studies on venlafaxine report comparable responses (Adler *et al*., 1995; Hedges *et al*., 1995; Findling *et al*., 1996 IIb). It is not known whether other noradrenergic agents like reboxetine, duloxetine and lofepramine have any efficacy in ADHD. Guanfacine is reported in one small trial to have similar efficacy to dexamfetamine (Taylor and Russo, 2001 Ib), as is the non-stimulant wakefulness-promoting agent modafinil (Taylor and Russo, 2001 Ib)

Monitoring and adverse effects During review of drug treatments, patients should be specifically questioned about efficacy on core symptoms and in various domains of functioning, as well as effects on co-morbid symptoms and side effects noted. The findings of the MTA study strongly suggest that active and fairly intensive monitoring of drug treatments improves effectiveness (MTA Cooperative Group, 1999). Patients do not always report psychiatric effects, which they may not realize can be induced by medication. Therefore, direct questioning about changes in affect, anger or personality should be part of the follow-up interview. The physician also needs to ask directly about difficulty with compliance, since this is often problematic in ADHD and may not be reported spontaneously. Diurnal changes in effects should also be sought, since these may be ameliorated by adjustment of dose timing or with longer-acting preparations. In addition, long-term monitoring of blood pressure, pulse and weight is indicated. All the treatments for ADHD are associated with mild statistical increases in blood pressure and pulse which may not be problematic in children, but could be problematic in those with antecedent cardiac disease, hypertension or those who engage in extreme sports. Treatment adjustment should be guided by report of symptoms and functioning in various domains as well as rating scores. Optimal outcome is the dose which leads to best functional

Guidance on prescribing

Off-label. Prescribing for adult ADHD is necessarily off-label since no agent is licensed for this indication – although atomoxetine is licensed for use in adults but only when ADHD treatment was initiated in childhood. The BNF (Joint Formulary Committee, 2005) states: 'Unlicensed use of medicines becomes necessary if the clinical need cannot be met by licensed medicines; such use should be supported by appropriate evidence and experience.' However, the BNF also states that prescribing medicines outside the recommendations of marketing authorization alters (and probably increases) the doctor's professional responsibility. This latter statement might explain a reluctance to prescribe beyond marketing authorization by clinicians, particularly in primary care. Although controlled evidence for prescribing in adults is not extensive, this consensus statement can be considered to meet the criteria for adequate evidence and experience in prescribing standard medications to adults with ADHD, when done in the context or with support of specialist psychiatric services. However, it is noted that supplementary prescribers are not contracted for unlicensed prescribing.

Controlled drugs. Prescriptions for psychostimulants (CD) are subject to prescription requirements, which might be altered in the future, notably for computer prescribing. Currently in the UK, prescriptions must be indelible, signed and dated by the prescriber with their address, and must always state *in the prescriber's own handwriting*: name and address of patient; the form and strength of a preparation (e.g. 10 mg tablets); total quantity or number of dose units in words and figures (e.g. 900 mg = nine hundred milligrams OR −90 = ninety doses); the dose (e.g. 10 mg tds).

outcome, balancing adverse effects against benefits for that individual.

Various concerns have been raised over long-term treatment effects, including the potential for tolerance over time, and adverse effects of psychostimulants such as psychosis, sensitization, dependency and withdrawal reactions (Ashton *et al*., 2006). Few data exist to guide clinicians since no long-term treatment trials have been conducted in adults with ADHD. The long-term effects were reviewed in an analysis of existing short- and long-term follow-up studies of stimulants in children with ADHD (Hechtman and Greenfield, 2003). The conclusions were that children with ADHD treated with stimulants for as long as 2 years continue to benefit from the treatment, with improvements observed in ADHD symptoms, co-morbid oppositional defiant disorder and academic and social functioning, with no significant problems of tolerance or adverse effects. Long-term, prospective follow-up studies into adulthood show that stimulant treatment in childhood has slight benefits regarding social skills and self-esteem. Long-term adverse effects from stimulant treatment in childhood regarding adult height or future substance abuse have not been supported by existing studies.

Substance use is a particular concern, both surrounding the abuse potential of psychostimulants and the effect of treatment on co-morbid substance use disorders. Abuse potential is related to the route of administration and the rate of absorption/bioavailability of the drug, and may relate to the resultant rate of dopamine release, which is higher for dopamine releasers than pure reuptake inhibitors (Kollins, 2003). Slow-release preparations have less abuse potential and are less amenable to use through abused routes such as snorting. They are to be preferred for patients with a history of, or risk factors for, drug misuse.

Diversion of psychostimulants is reported, in particular for short-acting preparations. Very few clinical studies have evaluated the risk/benefit ratio of long-term stimulant medication at therapeutic doses on human brain and behaviour (Volkow and Insel, 2003) – imaging studies indicate that cocaine induces a similar blockade of striatal DAT to that seen with methylphenidate (Volkow *et al*., 1999). Circumstantial evidence exists for sensitization and tolerance, which can be precursors to dependency; in particular, from baseline data of COMACs (Swanson *et al*., 2004; Sonuga-Barke *et al*., 2005) and from the titration phase of the MTA (Galanter *et al*., 2003), in which possible rebound was seen that might be due to tolerance (Sonuga-Barke *et al*., 2004).

Co-morbid substance use is common in untreated ADHD (see also 'Substance use disorders' below). Treatment in children has been repeatedly shown to be linked to a reduction in acquiring substance misuse, but the effect of treatment at other ages is not known. A meta-analysis of six trials in children found a 1.9-fold reduction in incidence of substance use in medicated compared with unmedicated patients (Wilens *et al*., 2003 Ia). Notably, studies of methylphenidate-treated rats have found that treatment during the equivalent age to human childhood reduces the reward-related effects of cocaine (Carlezon *et al*., 2003), while treatment during the equivalent age to adulthood enhances cocaine reward (Brandon *et al*., 2001). However, clinical experience suggests probable lower use of recreational drugs in medicated adults, although adolescence might carry a differing vulnerability. Thus, rigorous studies are needed to determine the long-term effects of pharmacotherapy in different age groups, particularly on co-morbid recreational substance use. Research is also needed to determine whether treatment of ADHD in patients currently using cannabis and/or alcohol on a daily basis is effective.

Recommendations – drug treatments

- Proven drug treatments in children include psychostimulants (A) and atomoxetine (A) as first-line treatments, with imipramine, which is metabolized to desipramine, (B) and bupropion (B) as second-line treatments and clonidine and guanfacine as possible adjunctive treatment (D).
- Adult patients with ADHD are most likely to present to primary care, but drug treatment is best initiated and optimized by secondary/specialist services (D).
- Drug treatment needs to be chosen and adapted to best fit the individual, including the patient's preferences and concerns (D).
- Meta-analysis of methlyphenidate in adults demonstrates similar drug response effect sizes to that seen in children (A).
- The limited evidence in adults suggests that agents that enhance synaptic dopamine have far better efficacy than other treatments for core symptoms – amfetamines, methylphenidate and atomoxetine are all effective but not equivalent, since they have different actions and hazards (A).
- Drug prescribing in adults is usually off-label but clinicians are supported in prescribing by these BAP guidelines (D).
- Drug treatment requires regular, preferably structured, monitoring and review (e.g. for dose adjustment). For uncomplicated cases this should be every 6–12 months.
- Clinicians need regularly to assess patients on medication for ADHD and other symptoms, global and specific functioning, adverse effects, concordance of effects (e.g. between patient, doctor, informants), psychiatric side effects, cardiovascular effects, compliance and tolerance (daily and long term) (D, S).
- Drug treatment should NOT be initiated if the diagnosis is uncertain or benefit is unlikely (D).
- Abuse potential is related to drug action and formulation – abuse by patients seems low, but diversion can occur with stimulants for performance enhancement or weight loss (D). Slow-release preparations of these agents or atomoxetine are to be preferred for patients with a history or who are at risk of drug misuse (D). Controlled studies are required to confirm these observations.

Key uncertainties

- Can we extrapolate from treatment studies in children?
- Can drug treatment be continued and monitored in primary care with training and support? With such an arrangement, what would the workload and resources implications be for both primary and secondary care?
- How is individual outcome of drug treatment best assessed?
- How do classes of drugs compare with each other in head-to-head comparisons and with psychotherapeutic approaches in adults?
- What factors underlie individual differences in drug response, tolerance and other side effects and how is treatment best matched to individuals and types of impairments?
- What is the effectiveness of various drug treatments beyond clinical ADHD trials?
- Do different drug treatments have differential effects on different underlying deficits (endophenotypes)?
- What are the effects of different drug treatments on symptoms beyond ADHD core (e.g. functioning/impairment), risk–benefit analysis and tolerance?
- What are effects of long-term drug treatment and how feasible are long-term follow-up studies given likely high dropout rates?
- What are better measures of effectiveness and cost effectiveness for drug trials?
- What are the important interactions with other prescribed psychoactive medications (e.g. SSRIs) and with recreational drugs?
- When are drug treatments best avoided (e.g. women of child-bearing age, certain age groups, patients with nothing to do)?
- What to offer drug non-responders?

Psychotherapeutic approaches

The Multimodal Treatment Study in ADHD (MTA Cooperative Group, 1999) has provided definitive evidence on the role of psychotherapy in childhood, with the conclusion that psychotherapy provides a small additional benefit when added to drug treatment. Compared with children, adults are mostly self-referred and thus are self-selected and generally more motivated. However, adults have usually left the education system where skills are taught and may also be affected by lifetime failures and effects of co-morbidity. Good evidence of the effects of psychotherapy in adulthood is sparse. Moreover, the usefulness of published studies is limited due to small numbers, lack of evidence on long-term unmedicated patients, failure to consistently rate effects beyond core and co-morbid symptoms, exclusion of patients with extreme symptoms or co-morbidity, and analysis of completers only.

Clinical experience indicates that general psychotherapeutic support and psycho-education around the time of adult diagnosis, treatment initiation and review seems helpful. Aims of psycho-education are to inform on the condition, natural history and prognosis, to prevent further negative effects on self-esteem or unrealistic expectations of treatment and to give perspective to individual neurodevelopmental history. Advice to and screening of family members may also be initiated at this time. A review of the psychosocial environment is essential to assess specific limitations in various domains, the level of executive demands and coping skills already acquired. Assistance with improving coping skills and efforts at environmental restructuring may have a powerful impact on the functioning of adults with ADHD. Group therapy, where available, may help with social isolation, especially around the critical period where treatment initiation can enhance experience of failure and lead to loss of self-esteem, depression and substance use (Safren *et al*., 2005a).

In terms of psychotherapy, an initial retrospective notes review conducted by Ratey *et al*. (1992 III) found that a dynamic psychotherapeutic approach led to decreased self-esteem and increased frustration. In a review of 36 patients improved but not remitted on medication, 85% of those who also had co-morbidity found benefits of adapted cognitive–behavioural therapy on anxiety, depression and functioning (Wilens *et al*., 1999a III). Two controlled, non-randomized studies are reported. Seventeen patients given psycho-education and organizational skills teaching versus no treatment found improvements in organization, attention and emotional stability but a reduction in self-esteem (Wiggins *et al*., 1999 IIa). In 15 patients, dialectical behaviour therapy showed improvements in ADHD symptoms, depression and functioning compared to control treatment (Hesslinger *et al*., 2002 IIa).

Three RCTs are published, with some good effect sizes reported in terms of core symptoms, and providing some insights into the interaction of psychotherapy with medication. A cognitive remediation programme using a brain injury model in 44 patients versus waiting list controls showed moderate effects on core symptoms and organization with minimal improvement of self-esteem and anger (Stevenson *et al*., 2002 Ib). Notably, effects on core symptoms and organizational skills were maintained at 1 year while effects on anger were not. A retrospective examination of the effects of cognitive remediation found no difference between medicated and unmedicated patients but numbers were small (Stevenson *et al*., 2002 Ib).

Weiss and the ADHD Research Group have examined the effects of individualized problem-focused therapy in 33 patients on dexamfetamine versus those on placebo (unpublished data Ib). Problem-focused therapy was found to be more effective in reducing core symptoms and improving functioning in medicated patients than controls. Modified cognitive–behavioural therapy plus medication demonstrated greater benefits than psychotherapy or medication alone particularly on ADHD symptoms, with lesser effects on anxiety and depression in 32 patients (Safren *et al*., 2005b Ib).

Recommendations – psychotherapeutic approaches

- General psychotherapeutic support to the individual, family and others around time of diagnosis and treatment initiation is helpful to inform on the condition and prognosis, to prevent negative effects on self-esteem or unrealistic expectations of treatment, to adapt positive and negative coping strategies and to give perspective to individual neurodevelopmental history (D).
- Structured, adapted psychotherapies may be useful to build confidence, develop executive skills, address anxiety and depression and improve functioning (B), while group therapy may help for social isolation (C/D).
- Evidence in childhood suggests that psychotherapies are beneficial for co-morbid anxiety and for functional outcomes beyond the core symptoms, when added to drug treatment (B). Since adults are self-referred, may no longer have access to school or skills development and are motivated once symptoms improve, there is reason to suggest that non-pharmacological treatments may be useful in augmenting the functional outcomes of medication alone (D).
- Involvement of educational/occupational psychologists and other relevant personnel for environmental restructuring can maximize functioning at college/work (D).

Key uncertainties

- Whether and what types of therapy might best work for the different aspects of ADHD (different core symptoms, global functioning) and for different co-morbidities?
- How best to combine drug treatments, psycho-education, psychotherapeutic approaches, and environmental restructuring?
- Can psychotherapy be used with good effect in adults unable to take, or who do not respond to, medication?
- What is the natural history of the outcomes of psychotherapeutic approaches and what follow-up approaches are needed to reinforce effects over time?

Thus, various forms of structured, intensive, skills-based treatment may improve likelihood of remission, especially when combined with medication. Effects of psychotherapy on core symptoms including disorganization seem substantial, with potential effects on functioning and modest effects on co-morbid symptoms. The effect on self-esteem seems often poor or even negative, since skills-based treatment may reveal low functioning. Psychotherapy data have particular implications for patients who have a poor response to or who are unable to take medication (e.g. women who wish to become pregnant), while such interventions might be particularly helpful for patients who are parents and others with a high-level need for learned skills, including those with few activities in their lives. A future direction for research is on therapies that emphasize interventions to address disinhibition and impulsivity, interpersonal skills and stress management.

Co-morbidity and special situations

Co-morbidity could be considered the rule rather than the exception when ADHD persists into adulthood (IV), yet much of the available evidence is from childhood populations. A key difficulty in the diagnostic process is determining the relationship between symptoms attributable to ADHD and other symptoms. Thus, symptoms may represent core ADHD symptomatology, complications or consequences of ADHD, including self-medication, a separate co-morbidity, a differential diagnosis or even the effects of prescribed medication. An accurate diagnostic attribution is important to determine the likelihood of a given treatment modality improving specific symptoms as well as to determine an individual diagnostic hierarchy for targeting treatments. Given the neurodevelopmental background and natural history of ADHD, and many common co-morbidities, an accurate diagnostic attribution could also inform on the likely course and complications of the disorder. Much experience with co-morbidity comes from specialist paediatric clinic populations, which are likely to have increased co-morbidity compared with the general population. Specialist clinics need to have skills to differentiate or exclude key co-morbidities, as these will impact on management, which in turn will impact on co-morbidities. This is an argument for establishment of neurodevelopmental clinics that can provide appropriate specialist training in assessment and management to patients of all ages (IV).

Key co-morbidities

Evidence on co-morbidities is fairly strong – at all ages, the disruptive and antisocial behaviours predominate; in childhood and adolescence, other neurodevelopmental disorders are the main additional co-morbidities, while in adults substance use and mood disorders predominate. Several co-morbid studies of adults with ADHD have been completed (Kooij *et al*., 2001; Biederman, 2004; Secnik *et al*., 2005; Kessler *et al*., 2005, 2006; Torgersen *et al*., 2006). Co-morbid disorders in adults can be classified into (1) ongoing developmental disorders such as learning disabilities, oppositional defiant disorder, conduct disorder, autism spectrum conditions, Tourette and tic disorders, and developmental delay, and (2) disorders that may first present in childhood but are familiar to adult psychiatry such as anxiety and mood disorders, post-traumatic stress disorder, substance use/dependence, sleep disorders and personality disorders. Up to 90% of adults will have one or another of these co-morbidities. Epidemiological data suggest that at least a third of patients will have had a lifetime

history of mood or anxiety disorders or other disruptive behaviour disorders. The prevalence of current co-morbid disorders is lower than a history of co-morbid disorders. Some co-morbid presentations such as problems with sleep and learning disabilities in adults have not yet been researched although they may be quite common. Clinically, this is of major importance since ADHD in adults rarely exists in isolation and outcome may be determined by co-morbid disorders that either preclude treatment, require treatment in their own right or are more severe than ADHD itself. A good assessment for ADHD in adults therefore requires a full mental status and psychiatric exam for other disorders as well as familiarity with both the co-morbid conditions of childhood and the co-morbid conditions of adulthood.

Childhood proportion of co-morbidities are given as follows: oppositional defiant disorder (40%); language disorders (30–35%); conduct disorder (20%); specific learning disability (15–25%); anxiety disorder (20–25%); mood disorder (15–20%); smoking (19%); substance use disorder (15%); autistic spectrum disorders (10%); tics (15–20%), often associated with Tourette's syndrome and obsessive–compulsive disorder; epilepsy; sleep disorders; sensory problems.

Conversely, ADHD as a co-morbidity correlates strongly with some disorders and needs to be specifically sought in these populations. For example, with Tourette's or chronic tic disorder, roughly one in two to three children will have ADHD while one in three will have obsessive–compulsive disorder, which will further impact on management. Many more may have poor social skills. Autistic spectrum disorders is another area in which ADHD symptoms occur commonly in the symptom profile, including: stereotyped mannerism (70%), stereotyped utterances (65%), inattention (60%), morbid/unusual preoccupation (65%), compulsions or rituals (50%), anxiety or fears (50%), hyperactivity (40%), depression/irritability/agitation (25%), self-injury (30%), tics (8%).

In Europe, bipolar disorder is a controversial diagnosis alongside a diagnosis of ADHD in childhood, and yet experts in other areas recognize that children with unstable mood and ADHD symptoms do exist (Geller *et al*., 2000a, 2000b; Craney and Geller, 2003; Post *et al*., 2004). Moreover, the combination of hypersexuality, grandiosity and a family history of bipolar illness is common in paediatric bipolar presentations, particularly in the context of neurodevelopmental disorders. A subgroup of these children may therefore be at risk of later adult bipolar disorder, which is conceptualized differently from childhood mood-related symptoms, such as dysphoric conduct disorder, in which ADHD symptoms, conduct disorder and depression co-exist. Thus the possibility exists that bipolar disorder is also a neurodevelopmental disorder that produces dysregulation of affect. This also implies that an early mood complication or a strong family history is more likely to predict a mood co-morbidity in the future.

In initiating medication for co-morbidities, it is important to consider on an individual basis the effectiveness, risk–benefit ratio and the likelihood of tolerance and other effects of a given treatment. Co-morbidity may increase the need for a combined treatment strategy with one or more medications plus a specific psychotherapeutic management – e.g. behavioural programmes for conduct disorder or cognitive–behavioural therapy for co-morbid mood disorders.

A common finding in childhood is that stimulant medication does work in some individuals with neurodevelopmental co-morbidity but that non-response or adverse effects may be more common. If stimulants prove unsuitable in the individual case, medication aimed at the co-morbid disorder or combined medication might overall provide a better response than medication aimed at ADHD, as argued with autistic spectrum disorders and bipolar symptoms. This begs the question of whether a diagnostic hierarchy exists for co-morbid disorders and the effect this has on treatment – for example, bipolar symptoms, autistic spectrum disorders and epilepsy treated before ADHD, which may be targeted before or alongside substance use disorders, conduct disorder and oppositional defiant disorder. Sleep problems, anxiety and depression may arise as a consequence of ADHD but may still require separate treatment, including antidepressants. Complex cases need to be considered on an individual basis and may need further specialist referral (e.g. for sleep assessment), especially in adulthood, where existing evidence and experience is even less than in childhood.

Evidence on management of bipolar symptoms comes mainly from expert experience outside Europe. One concern in this group is the potential for psychostimulants to enhance the likelihood of psychosis (DelBello *et al*., 2001), whether in children with prominent mood instability or in those with a strong family history of bipolar disorder. Risperidone and other atypical antipsychotics help with psychotic symptoms, mania and aggression but ADHD symptoms respond poorly. Sodium valproate may be useful in rapid cycling and mixed states. Since psychostimulants carry a potential risk of worsening or triggering bipolar symptoms, expert paediatric groups in Boston and Cincinnati treat mania prior to addressing the ADHD separately; however, their views remain controversial.

Depression can be treated with antidepressants, such as the SSRIs, which can be used safely with psychostimulants. Noradrenergic agents (atomoxetine, reboxetine) might be sensible for use in people with co-morbid anxiety and depression, though no research studies have been done to confirm this supposition, while methylphenidate was used as an antidepressant in the 1950s.

With autistic spectrum disorders, one in two children respond to medication compared with two in three of children with ADHD alone. Psychostimulant side effects are more common in autistic spectrum disorders, typically dysphoria and perseveration or cognitive rigidity, which needs to be monitored. A final dose of 20 to 30 mg/day of methylphenidate is usually sufficient. The key principles with dosing are to start low, go slow and monitor more frequently. Conversely, the effect of atypical antipsychotics on ADHD symptoms particularly hyperactivity in ASD is good, with an effect size of 1.4 (McCracken *et al*., 2002 Ia).

Evidence on the link between ADHD and children with epilepsy is somewhat stronger, occurring commonly in the context of learning disabilities. Adequate anticonvulsant cover is essential, and treatment of ADHD with stimulants may be indicated once anticonvulsant hyperactivity is ruled out. Little research exists in this area, and the research that does exist has studied methylphenidate only (Gross-Tsur *et al*., 1997; Gucuyener *et al*., 2003; Tan and Appleton, 2005; van der Feltz-Cornelis and Aldenkamp, 2006). However, psychostimulants, atomoxetine and antidepressants can lower seizure threshold.

Sleep disorders are a common complaint with some 40% of children with ADHD having sleep symptoms, which may be due to stimulant medication or due to inability to settle down at night due to ADHD. The latter will respond to a later dose of stimulant medication, although care should be given when administering late doses of psychostimulants as failure to clear medication completely by the time of the next morning dose might lead to the development of a steady state, which may increase risks of tolerance and sensitization. Another key co-morbidity that presents with sleep symptoms is an undiagnosed anxiety disorder (e.g. phobia of darkness). Treatment options include non-pharmacological measures to regulate sleep ('sleep hygiene'), melatonin, clonidine, trazodone and zolpidem. Recent clinical trials have demonstrated that patients with co-morbid ADHD and anxiety or tics may show improvement in both disorders with atomoxetine (Kratochvil *et al*., 2005).

At follow-up, clinicians need to assess the effects of ADHD treatment on all key symptoms, including those of other diagnoses, since ADHD medication may have either a positive or negative impact on co-morbid diagnoses. Psychostimulants often worsen sleep, mood, appetite, emotional lability, cognitive rigidity and other symptoms in practice so assessment of such effects is needed in future clinical trials and in populations that are excluded from clinical trials. The relationship between tics and ADHD grows stronger with time. Although research indicates that there is no statistically significant worsening of tics with stimulants or atomoxetine in children, individuals may nonetheless experience either improvement or deterioration in tics which needs to be treated accordingly (Gadow *et al*., 1995; Allen *et al*., 2005). Conversely, medication for co-morbid disorders might impact on ADHD. For example, our experience suggests that anticonvulsants might increase hyperactivity and restlessness as might drugs for sleep disorders, while atypical antipsychotics can worsen many core ADHD symptoms.

Co-morbid substance use disorders

Substance use disorders are common in ADHD and may persist into or arise in adulthood. Substance use may reflect a core deficit in ADHD, i.e. reduced reward mechanisms and impulsivity, it can arise via conduct disorder and antisocial behaviours, or develop through self-medication with stimulants, alcohol, cannabis or other sedatives. Substance use disorders thus represent a diagnostic difficulty in people with possible ADHD; in the presence of core symptoms of ADHD, substance use disorders could be considered a complication of ADHD. In childhood, stimulant medication does not cause but in fact reduces the incidence of substance use disorders (Wilens *et al*., 2003 Ia). However, effects in adulthood may vary among individuals – adult substance use may reduce with ADHD medication but others could be predisposed to the development of tolerance, sensitization and increased substance use, particularly with higher doses of psychostimulants (see 'Monitoring and adverse effects' above).

In general, substance use needs to be stable prior to initiating medication treatment of ADHD, especially in primary care. Few trials have examined the effects of treatment in adults with substance use disorder but methylphenidate has been used effectively in cocaine users (Levin *et al*., 1998 Ib), while history of drug

Recommendations – co-morbid conditions

- Clinicians need to screen for autistic spectrum, developmental disorders, communication difficulties, learning disabilities, tics and Tourette's syndrome, anxiety and affective disorders, substance use disorders and others (e.g. epilepsy, sleep disorders, sensory problems), but symptoms cannot be counted twice for ADHD and co-morbid disorders (C/D).
- Further specialist input or advice may be needed regarding co-morbidity (e.g. learning disability teams), since co-morbidity can have a greater impact on functioning than ADHD (D).
- Likely co-morbidities vary according to age of presentation and will alter treatment responses and outcomes, including adverse effects, but co-morbidity is not necessarily a barrier to treatment of ADHD (C/D).
- Treatment and monitoring need to be adapted according to co-morbidity (D). With neurodevelopmental co-morbidity, the key principles with dosing are to start low, go slow and monitor more frequently (D).
- Medication remains first line for ADHD with most co-morbid conditions (A).
- Combined treatment (including non-pharmacological treatment) is likely to be necessary in co-morbid conduct disorder, oppositional defiant disorder, autistic spectrum disorders, learning disability, anxiety and depressive disorders and personality disorders (B/D).
- ADHD and co-morbid bipolar disorder occur together and require atypical antipsychotic treatment initiated first (D).
- ADHD and co-morbid autistic spectrum disorders respond less well to treatment with more side effects than in ADHD alone (B).
- Psychostimulants can be used cautiously with co-morbid epilepsy since they could potentially lower seizure threshold (C).

Key uncertainties

- Does a diagnostic hierarchy for ADHD and co-morbidities exist?
- Which co-morbidities are part of the neurodevelopmental process that includes ADHD (cf. Learning disability, autistic spectrum disorders)?
- What is the impact of different treatments on different co-morbidities?

Recommendations – co-morbid substance use disorders

- Treatment of ADHD in childhood is likely to reduce later substance use disorders in most individuals (A), although later psychostimulant use and high doses might lead to tolerance or sensitization (B).
- Treatment of ADHD in adulthood might reduce concurrent substance use but extensive evidence is lacking (D).
- Patients who use recreational drugs need to be advised of possible interactions with their medication, particularly concurrent stimulant-type drugs. Psychostimulants, especially short-acting preparations, are best avoided in this population (D).

Key uncertainties

- Does timing of treatment relate to outcome in terms of substance use disorders?
- What is the ideal management of people with concurrent substance use disorders (e.g. detoxification/behavioural modification before, after or combined with ADHD treatment)?
- Is medication treatment for ADHD effective in patients with chronic, daily cannabis and/or alcohol use?

abuse has been reported as the best indicator of a response to methylphenidate (Mattes *et al*., 1984). The formulation of modified release methylphenidate, which cannot be used other than via the oral route, may be an alternative. Atomoxetine might be preferable in dependent patients due to an apparent lack of sensitization, tolerance and abuse potential plus its stability of action, evening effectiveness and lack of diversion compared with short-acting methylphenidate.

A key question with substance-using patients is the timing of medication in relation to detoxification or other programmes to reduce substance use. Detoxification before ADHD medication may lead to increased dropouts from drug services, but ADHD medication initiated before detoxification may carry issues for drug services which emphasize a drug-free approach, and might lead to tolerance or sensitization. It may be the case that simultaneous behavioural modification, including detoxification, is worthwhile alongside initiation of ADHD medication in this group, but for now the role of medication in the learning effect required to change substance-using behaviours is an important direction for future research.

People with learning disabilities

It is important to consider an ADHD diagnosis in a person with an intellectual or learning disability (LD) who presents with behavioural problems. There is good evidence to suggest that ADHD occurs in the context of LD and can be diagnosed with confidence in this context (Seager and O'Brien, 2003). The prevalence rate of ADHD in LD is up to ten times higher than that in the general population, with a predominance of hyperactive/hyperkinetic symptoms (Seager and O'Brien, 2003). The symptoms of ADHD are particularly more prevalent in association with various behavioural phenotypes (e.g. Williams, Velo-cardio-facial, Smith-Magenis, Fragile X and Foetal Alcohol syndromes), with the highest association in Foetal Alcohol Syndrome. Maternal alcohol intake in pregnancy is thus an important consideration in assessment of ADHD in a person with LD.

A diagnosis of ADHD should be sought in LD because ADHD adds considerably to overall impairment, particularly if undiagnosed. Standard rating scales may be used for assessment, although ratings are secondary to clinical assessment, including a full neurodevelopmental history and examination. A diagnosis of ADHD may be missed if symptoms are wrongly attributed to the person being developmentally immature or to side effects of medication.

There is good evidence to suggest that age, IQ, neurodisability and other co-morbidity are no barriers to standard treatment (Mayes *et al*., 1994 Ib). Few RCTs of methylphenidate treatment have been carried out specifically in LD children, and none in LD adults to date. Those studies of LD children have been small scale, of short duration and have limited follow-up (Mayes *et al*., 1994; Handen *et al*., 1999; Aman *et al*., 2003 Ib). No meta-analysis has yet been performed, but methylphenidate seems somewhat less effective, but rather more likely to produce side effects compared with its use in the general childhood population. Lower doses of methylphenidate (0.3 mg/kg/dose) appear to be better tolerated in LD children (Handen *et al*., 1999 Ib). Other treatments for ADHD have been poorly evaluated in LD children, although risperidone has been found useful for treating disruptive behaviours, such as hyperactivity, aggression and impulsivity (Aman *et al*., 2002 IIa). Little research exists on service provision or other specific treatment for LD adults with ADHD. The American Association on Mental Retardation Expert Consensus treatment guidelines (2000 IV) cover ADHD treatment but the expert advice is very age specific.

Various factors confound and complicate analysis of the extant research on ADHD in the context of LD, and the most important is the confusing nomenclature now employed to define the LD population – this includes the terms 'learning difficulty', 'intellectual disability', 'mental retardation' and 'mental handicap'. The lower end of the IQ range and developmental immaturity can complicate assessment, particularly of hyperactive/hyperkinetic symptoms, and ADHD may be misdiagnosed particularly if these developmental delays are missed because severe LD individuals are constitutionally inattentive, often impulsive and, particularly as children, physically overactive. Furthermore, changes in IQ and developmental maturity tend to have different trajectories in association with specific handicapping disorders such as Fragile X and Down's syndromes.

Other factors that complicate the assessment of ADHD symptoms in the LD population are its higher rates of physical and psychiatric co-morbidity (see above), treatment side effects, adverse

socio-environmental factors, including family distress through the burden of care and poor social support. Educational and occupational shortfalls can further obscure the picture. It is particularly important to note that LD patients are often on very complex drug regimens, which may consist of various psychotropic agents and anticonvulsants, with a high potential for drug interactions and side effects.

Previous professional therapeutic nihilism towards the mental health needs of LD children has merited their specific inclusion in the recently launched 'National Service Framework for Children, Young People and Maternity Services' (Department of Health, 2004). The expectation is that all children, irrespective of their intellectual ability, should have access to high quality services.

Recent patterns of UK ADHD prescribing practice have been documented by the 'Child and Adolescent Learning Disability Psychiatry Network Psychotropic Medication Prescribing Survey', which revealed that, across all prescribing practice, psychostimulants were the most commonly prescribed class, with methylphenidate the most commonly prescribed specific agent, ahead of the antipsychotics (unpublished data IV). ADHD in the context of LD is usually diagnosed in children by either psychiatrists in child and adolescent mental health services or by paediatricians in community child health. In LD adults, psychiatrists in adult learning disability services diagnose and manage the condition. Psychostimulants are the usual first-line drug treatment in children. Second-line treatment is commonly risperidone or carbamazepine, while methylphenidate may be co-administered (particularly with risperidone). Monitoring should be more frequent but for patients with specific co-morbidities and, particularly in the context of autism, this may pose important logistical obstacles – for example, touch defensiveness may prevent the measurement of accurate blood pressure or of pulses. General recognition exists of slightly lower efficacy and higher rates of side effects, especially in children with autistic spectrum disorders. In general, the prescribing principles of 'start low, go slow and monitor more frequently' are accepted (IV).

Transition to adult services occurs at age 18 in England (Department of Health, 2004) but while adult LD psychiatrists generally accept the diagnosis of LD with ADHD and diagnose and manage cases, general adult psychiatrists may not. Thus, many LD adults with ADHD may not have access to a specialist clinical service, although patients in this situation who also have a more severe degree of LD are more likely to receive ongoing care from an adult LD psychiatrist.

Further research and service developments are required to meet the needs of the growing numbers of LD children and adults being diagnosed with ADHD. In terms of clinical assessment, there is a pressing need to develop developmentally sensitive rating scales for ADHD symptomatology, both across the ability range of the entire LD population but also within genetically distinct handicapping conditions such as Down's syndrome. Also, studies of new formulations of agents for ADHD (such as liquids, sprinkles, patches and sublingual gels, which may be more easily ingested) seem warranted in LD populations in order to improve treatment concordance.

Finally, it must be emphasized that adolescents and adults with LD and ADHD are only part of a much wider population of patients with a spectrum of neurodevelopmental difficulties such as autism, to which similar principles and issues apply (see also 'Service models').

Offenders and the prison system

ADHD is a common factor associated with delinquency, adult criminal behaviour in men and women and recidivism (Bambinski *et al*., 1999; Pratt *et al*., 2002; Brassett-Grundy and Butler, 2004a,

Recommendations – people with learning disabilities (LD)

- ADHD is more commonly found in people with LD, and treatment is effective albeit with reduced efficacy and increased side effects (B). Thus, LD, IQ and neurodisability should be no barrier to treatment (B).
- More children with LD are entering adulthood, and a proportion would benefit from continuation of treatment, but appropriate services are needed for those who do not come under the care of adult LD teams (e.g. in community neurodevelopmental teams) (D).
- Drug treatment needs to be started at lowest doses in people with LD and be increased slowly (D).
- Increased monitoring is likely to be required, particularly in the context of complex drug regimens, though monitoring may present logistical difficulties (D).

Key uncertainties

- What is the effect of different developmental ages on expression of ADHD?
- What is the natural history of ADHD in different populations with LD?
- How many people with LD on ADHD treatment are affected by transition issues?
- Can new formulations of existing standard psychopharmacological agents, which are easier to ingest, improve treatment concordance in this group?
- How can professional disinterest be improved to improve the detection and treatment of ADHD in this vulnerable group?
- In adults with ADHD and specific reading, writing and arithmetic disabilities, what is the effect of educational remediation once attention problems have been treated?
- In adults with attention and processing problems, is medication a possible way of alleviating a learning problem?
- Does treatment of ADHD in adults raise the potential for long-term educational achievement?

2004b I). Court records data indicate that people with ADHD are four to five times more likely to be arrested, and often have a history of multiple arrests and convictions (Satterfield *et al*., 1982; Hechtman and Weiss, 1986; Lambert, 1988; Mannuzza *et al*., 1989; Satterfield *et al*., 1994 II). Using screening questionnaires, studies from various countries report 22–71% of prisoners as possibly having had a childhood diagnosis of ADHD, depending on the assessment tool and cut-offs applied. In adulthood, some 30–50% are screened as possibly being fully symptomatic, with a high proportion of inmates (15–50%) screened as being in partial remission of their symptoms (Eyestone and Howell, 1994; Vitelli, 1995; Dalteg and Levander, 1998 II; Dalteg *et al*., 1999; Rasmussen *et al*., 2001; Retz *et al*., 2004; Rosler *et al*., 2004).

Young and Gudjonsson (submitted II) have found antisocial behaviour and police contact are strongly associated with the extent and severity of ADHD symptoms. As the symptoms remit there is less antisocial behaviour, less contact with the police and fewer presentations to adult psychiatric services. However, forensic services have been slow to recognize and respond to the needs and complexities of defendants (and witnesses) with ADHD in the criminal justice system, and changes have been mainly in response to court judgements, while research is lacking. Thus, all aspects of the relationship between ADHD and offending in adolescents and adults represent a key direction for future research.

ADHD is important in relation to offending in several ways. People with ADHD may be vulnerable in all stages of the justice system. Behaviour in a police interview may be compromised by various factors, including inattention and impulsive responding, a motivation to get out of a police station or terminate an interview. Juveniles may be suggestible, and parental representation of such young people may be compromised by the parent having undiagnosed ADHD, and therefore not able to provide adequate support.

People with ADHD can also be vulnerable in court due to inattention and other symptoms, which could have implications for conviction and sentencing. Neuropsychological testing in this context might offer a measure of vulnerability and initiate special provisions for the defendant (Gujondsson and Young, in press III). In the case *R*. v. *Billy Joe Friend* (1997, Cr.App.R. 231), a convinction of murder was quashed since it was recognized that due to the previously unrecognized deficit of ADHD in adolescence, the defendant was unlikely to have effectively participated in trial proceedings and the jury was open to have drawn adverse inference from failure to give evidence. Of note, a previously diagnosed learning disability was not confirmed on neuro- psychological assessment in adulthood, probably due to the effects of symptom remission and prison education (Gudjonsson and Young, in press III).

In *R*. v. *David Blackender* (July, 2002, Central Criminal Court), the Crown accepted a conviction of manslaughter rather than murder on the grounds of diminished responsibility due to childhood ADHD. Blackender was given a life sentence; however, a minimum sentence of 2 years and 4 months was recommended provided he cooperated with treatment (including medication) and could demonstrate that he was not a risk to the public. Blackender was put on a licence for life, which meant that he could be recalled by the parole board if he did not cooperate. This put the onus of responsibility on Blackender; he could get out of prison early if he did well but was on a licence for life which provided a check or control of his behaviour.

Once incarcerated, people with ADHD may be a management problem especially when they have co-morbid personality disorder. In one series, 6% of people with personality disorders were screened to have full ADHD symptoms while 29% were in partial remission; the latter was associated with an excess of critical incidents (Young *et al*., 2003 II). Medication in this context has

Recommendations – offenders with ADHD

- ADHD symptoms are common in offenders, and may be co-morbid with a diagnosis of personality disorder, so screening for ADHD (including partial remission), may be indicated in anyone in contact with the criminal justice system (A).
- Neuropsychological profiling is useful in this situation to assess individual vulnerability in comparison to population standards (C).
- Special provisions may reduce vulnerability of people with ADHD within the judicial system (C).
- Management of affected offenders may improve outcomes in prison, including substance use, antisocial behaviour, critical incidents (B).
- Management of offenders might be done better in the context of psycho-educational rehabilitation, rather than with drug treatment alone (C).

Key uncertainties

- How are offenders with ADHD with or without personality disorder best identified and managed within the judicial and prison systems?
- What is the relationship between ADHD, personality disorder, offending behaviours and the amenability of symptoms to treatment?
- Could screening in schools for emotional/behavioural disorders ascertain ADHD diagnosis before potential for youth offending?
- What appropriate management could prevent the developmental sequence that leads towards offending, or reduce recidivism in those who have already offended?
- What are the legal implications of a diagnosis of ADHD?

been shown to markedly improve symptoms and functioning, and thus improve ability to access other services in a severely affected individual (Young and Harty, 2001 III). However, most studies to date have applied screening questionnaires to define groups that may be over inclusive. A large prison study is underway in Scotland that screens for ADHD as well as conducting neuropsychological assessment of inattention and impulsivity. This study will also evaluate psychopathology, personality, substance use, critical incidents, offending motivation and offending history.

Symptoms of ADHD or personality disorders may be constructed as part of the disorder or as criminal behaviour, but although impulsivity is recognized in this context, inattention is not. When such symptoms are constructed as part of a disorder, treatment may be possible, which experience suggests should involve medication, skills-based psycho-education and cognitive behavioural therapy (IV). The 'Reasoning & Rehabilitation' prosocial competence training programme is currently being developed by Young and Ross for delivery by professionals (not necessarily clinicians) to children, adolescents and adults with antisocial behaviour and symptoms of ADHD who have offended (Young and Ross, 2006, in preparation IV).

ADHD seems likely to represent a frequent part of the developmental sequence to criminal behaviour (Farrington, 1995 IV), since it contributes to problems at school, which can lead to exclusion and a subsequent change in culture and association with individuals with similar behaviours. The Dorset ADHD group has been involved in training for custody officers and national offenders management services (including prison staff and probation officers) to raise awareness of ADHD in youth offending. Such services may be guided in the UK by local authority protection of vulnerable adults policy or related local or regional policy, including the Disability Discrimination Act and the Human Rights Act. However, referral for treatment at this point may miss an opportunity to alter the developmental sequence, so the role of screening for ADHD in emotional/behavioural disorder schools needs to be evaluated. If ADHD is detected by youth offending teams, which now have screening tools in place, or the forensic psychiatric system, then programmes could be initiated as a condition of sentence, which would render the treatment of ADHD in the justice system closer to that of schizophrenia.

Service models

ADHD has been described as one of the most common neurobehavioural disorders of childhood (Remschmidt and Global ADHD Working Group, 2005). Currently, UK management of ADHD in children and adolescents mostly involves primary care with specialist input on assessment and management from Childhood and Adolescent Mental Health Services (CAMHS), community paediatricians, sub-speciality learning disability teams where the latter exist, and other youth services (e.g. youth offending teams). Children's clinical services in England and Wales now have a National Service Framework (Department of Health, 2004). Recent guidelines are available on management of children with ADHD from the European Society for Child and Adolescent Psychiatry (Taylor *et al*., 2004; Banaschewski *et al*., 2006) and the Global ADHD Working Group (Remschmidt and Global ADHD Working Group, 2005), and a suggested protocol for the organization of services within the NHS for children and adolescents with ADHD has recently been published (Coghill, 2006). No guidelines or protocol currently exist in the UK to guide practitioners on management of adolescents in transition or newly presenting adults.

The usual skills available to general adult psychiatric services should be sufficient to support the assessment of adolescents required to transit from children's services together with newly presenting adults, while adolescents and adults with learning disabilities may be assessed in learning disability teams. However, currently, expertise and capacity does not exist in many specialist services to manage such patients, and is not included in the training curriculum for adult psychiatrists. The situation is similar in primary care, so this is rapidly becoming an issue of support and service provision that needs to be addressed at local and higher levels. One initiative to guide development of services for ADHD is being led by the Dorset ADHD Support Group, which has outlined ADHD 'Across The Lifespan', which suggests staged, lifelong ADHD service provision,

Recommendations – service models

- Appropriate service provision and expertise are needed to manage adolescents in transition from children's services and newly presenting adults, with primary care and specialist involvement, although some of these patients will have received other diagnoses (D,S).
- Appropriate service provision and expertise are needed to diagnose and treat newly presenting cases in adulthood, some of whom are already being treated within the system for other, sometimes incorrect, diagnoses such as anxiety, depression and personality disorder (D).
- ADHD is part of a broader population of neurodevelopmental disorders, and similar services are required for the larger group of people with neurodevelopmental conditions (D).
- A working group could consider the community neurodevelopmental team as a model for lifelong care, based on existing psychiatric and sub-speciality (e.g. learning disability) services (D).

Key uncertainties

- Should screening of parents and children of referred patients be considered?
- What are the available expertise and funding implications of managing these patients?

and 'Equality in Justice', regarding criminal justice system provisions for people with ADHD (Alsop, 2005).

Adolescents and adults with ADHD are only part of the population of individuals affected by neurodevelopmental disorders that lead to loss of functioning and impairments. Moreover, services based on individual disease groupings are not efficient in terms of capacity, skills and training. Thus, recognition across adult services of the similar issues affecting such patients is important if appropriate assessment and evidence-based management strategies are to be offered to this growing population. Our strong consensus of an ideal service model is the multidisciplinary community neurodevelopmental team, perhaps based at regional level, which can offer lifelong support where necessary on both assessment and management of individuals without the need to transit services. Such teams could be developed from existing psychiatric and other services and would form the basis for training and education on neurodevelopmental disorders.

Conclusion

Although there are many areas of research that remain, work to date has established clearly that ADHD in childhood may continue into adulthood and cause significant impairment throughout the life cycle. The prevalence of ADHD in childhood and adulthood is considered to be about 4% so this is a common disorder. It is becoming increasingly evident that this common and impairing disorder is costly and treatable, providing a significant opportunity to relieve the burden of suffering for the patient and family, but also to alleviate social costs in unemployment, crime, incarceration, smoking, substance use and driving accidents. This information needs to be addressed by the National Health Service so that resources can be redirected to provide appropriate and evidence-based care for adults with ADHD.

Acknowledgements

We thank Cephalon, Janssen, Lilly, Shire UK and Shire US for unrestricted educational grants. Many thanks go to Susan Chandler, the BAP executive officer, for organizing the logistics of the meeting. Participants at the consensus meeting other than the authors were: Marios Adamou, Margaret Alsop, Gillian Baird, Andrea Bilbow, Jessica Bramham, David Coghill, Val Curran, Tony Hale, Chris Hollis, Andy Jackson, Geoff Kewley, Amanda Kirby, Ian Maidment, Alison Munden, Nikos Myttas, Clare Stanford, Morris Zwi. These participants included representatives from the patient support organizations ADDISS (www.addiss.co.uk) and Dorset ADHD Support Group (www.dorsetadhd.org.uk). Observers were also present from Cephalon, Janssen, Lilly, Shire UK and US pharmaceutical companies.

References

Adler L A, Kessler R C, Spencer T (2004) Adult ADHD Self-Report Scale-v 1.1 (ASRS-v1.1) Symptom Checklist. New York, NY. Available at: www.med.nyu.edu/psych/assets/adhdscreen18.pdf

Adler L A, Resnick S, Kunz M, Devinsky O (1995) Open-label trial of venlafaxine in adults with attention deficit disorder. Psychopharmacol Bull *31*: 785–788

Adler L A, Spencer T J, Milton D R, Moore R J, Michelson D (2005a) Long-term, open-label study of the safety and efficacy of atomoxetine in adults with attention-deficit/hyperactivity disorder: an interim analysis. J Clin Psychiatry *66*: 294–299

Adler L A, Spencer T, Faraone S V, Reimherr F W, Kelsey D, Michelson D, Biederman J (2005b) Training raters to assess adult ADHD: reliability of ratings. J Atten Disord *8*: 121–126

Allen A J, Kurlan R M, Gilbert D L, Coffey B J, Linder S L, Lewis D W, Winner P K, Dunn D W, Dure L S, Sallee F R, Milton D R, Mintz M I, Ricardi R K, Erenberg G, Layton L L, Feldman P D, Kelsey D K, Spencer T J (2005) Atomoxetine treatment in children and adolescents with ADHD and comorbid tic disorders. Neurology *65*: 1941–1949

Alsop M (2005) Equality in Justice, ADHD Across the Lifespan. Dorset ADHD Support Group, Weymouth (www.dorsetadhd.org.uk)

Aman M G, Buican B, Arnold L E (2003) Methylphenidate treatment in children with borderline IQ and mental retardation: analysis of three aggregated studies. J Child Adolesc Psychopharmacology *13*: 29–40

Aman M G, Smedt G D, Derivan A, Lyons B, Findling R L (2002) Double-blind, placebo-controlled study of risperidone for the treatment of disruptive behaviours in children with subaverage intelligence. Am J Psychiatry *159*: 1337–1346

American Association on Mental Retardation, Rush A J, Frances A (2000) Expert Consensus Guidelines Series: Treatment of psychiatric and behavioral problems in mental retardation. Am J Mental Retardation *105*: 178–188

American Psychiatric Association (2000) Diagnostic and Statistical Manual of Mental Disorders version IV text revision. American Psychiatric Association, Washington DC

Andersen P H (1989) The dopamine inhibitor GBR 12909: selectivity and molecular mechanism of action. Eur J Pharmacol *166*: 493–504

Anderson I M, Nutt D J, Deakin J F (2000) Evidence-based guidelines for treating depressive disorders with antidepressants: a revision of the 1993 British Association for Psychopharmacology guidelines. British Association for Psychopharmacology. J Psychopharmacol *14*: 3–20

Arcos-Burgos M, Castellanos F X, Pineda D, Lopera F, Palacio J D, Palacio L G, Rapoport J L, Berg K, Bailey-Wilson J E, Muenke M (2004) Attention-deficit/hyperactivity disorder in a population isolate: linkage to loci at 4q13.2, 5q33.3, 11q22, and 17p11. Am J Hum Genet *75*: 998–1014

Arnold L E, Kleykamp D, Votolato N A, Taylor W A, Kontras S B, Tobin K (1989) Gamma-linolenic acid for attention-deficit hyperactivity disorder: placebo-controlled comparison to D-amphetamine. Biol Psychiatry *25*: 222–228

Asherson P (2005) Clinical assessment and treatment of attention deficit hyperactivity disorder in adults. Expert Rev Neurotherapeutics *5*: 525–539

Asherson P, Kuntsi J, Taylor E (2005) Unravelling the complexity of attention-deficit hyperactivity disorder: a behavioural genomic approach. Brit J Psychiatry *187*: 103–105

Ashton C H, Gallagher P, Moore B (2006) The adult psychiatrist's dilemma: psychostimulant use in attention deficit/hyperactivity disorder. J Psychopharmacol *20*: 602–610

Avery R A, Franowicz J S, Studholme C, van Dyck C H, Amsten A F (2000) The alpha-2A-adrenoceptor agonist, guanfacine, increases regional cerebral blood flow in dorsolateral prefrontal cortex of monkeys performing a spatial working memory task. Neuropsychopharmacology *23*: 240–249

Bakker S C, van der Meulen E M, Buitelaar J K, Sandkuijl L A, Pauls D L, Monsuur A J, van't Slot R, Minderaa R B, Gunning W B, Pearson P L, Sinke R J (2003) A whole-genome scan in 164 Dutch sib pairs with attention-deficit/hyperactivity disorder: suggestive evidence for linkage on chromosomes 7p and 15q. Am J Hum Genet *72*: 1251–1260

Baldwin D S, Anderson I M, Nutt D J, Bandelow B, Bond A, Davidson J R T, den Boer J A, Fineberg N A, Knapp M, Scott J, Wittchen H-U (2005) Evidence-based guidelines for the pharmacological treatment of

anxiety disorders: recommendations from the British Association of Psychopharmacology. J Psychopharm *19*: 567–596

Bambinski L M, Hartsough C S, Lambert N M (1999) Childhood conduct problems, hyperactivity-impulsivity, and inattention as predictors of adult criminal activity. J Child Psychol Psychiatry *40*: 347–355

Banaschewski T, Coghill D, Santosh P, Zuddas A, Asherson P, Buitelaar J, Danckaerts M, Dopfner M, Faraone S V, Rothenberger A, Sergeant J, Steinhausen H-C, Sonuga-Barke E J S, Taylor E (2006) Long-acting medications for the hyperkinetic disorders – a systematic review and European treatment guideline Eur Child Adolesc Psychiatry [Epub ahead of print, May]

Barkley R A (2002) Major life activity and health outcomes associated with attention-deficit/hyperactivity disorder. J Clin Psychiatry *63* (suppl. 12): 10–15

Barkley R A (2006) Attention Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment, 3rd edn. Guilford Press, New York

Barkley R A, Murphy K (2006) Attention Deficit Hyperactivity Disorder: A Clinical Workbook, 3rd edn. Guilford Press, New York

Barkley R A, Grodzinsky G, DuPaul G J (1992) Frontal lobe functions in attention deficit disorder with and without hyperactivity: a review and research report. J Abnorm Child Psychol *20*: 163–188

Barkley R A, Fischer M, Edelbrock C S, Smallish L (1990) The adolescent outcome of hyperactive children diagnosed by research criteria: I. An 8-year prospective follow-up study. J Am Acad Child Adolesc Psychiatry *29*: 546–557

Berlin L, Bohlin G, Nyberg L, Janols L O (2004) How well do measures of inhibition and other executive functions discriminate between children with ADHD and controls? Neuropsychol Dev Cogn C Child Neuropsychol *10*: 1–13

Biederman J, Mick E, Faraone S V (1998) Normalized functioning in youths with persistent attention-deficity/hyperactivity disorder. J Pediatr Oct *133*(4): 544–551

Biederman J (2004) Impact of comorbidity in adults with attention-deficit/hyperactivity disorder. J Clin Psychiatry *65* (suppl. 3): 3–7

Biederman J (2005) Attention-deficit/hyperactivity disorder: a selective overview. Biol Psychiatry *57*: 1215–1220

Biederman J, Spencer T J (2001) Psychopharmacology of adults with attention-deficit/hyperactivity disorder. Primary Psychiatry *11*: 57–62

Biederman J, Mick E, Faraone S V (2000) Age-dependent decline of symptoms of attention deficit hyperactivity disorder: impact of remission definition and symptom type. Am J Psychiatry *157*: 816–818

Biederman J, Spencer T J, Wilens T E, Weisler R H, Read S C, Rulloch S J, SLI381.304 study group (2005) Long-term safety and effectiveness of mixed amphetamine salts extended release in adults with ADHD. CNS Spectr *10* (suppl. 20): 16–25

Biederman J, Faraone S V, Milberger S, Jetton J G, Chen L, Mick E, Greene R W, Russell R L (1996a) Is childhood oppositional defiant disorder a precursor to adolescent conduct disorder? Findings from a four-year follow-up study of children with ADHD. J Am Acad Child Adolesc Psychiatry *35*: 1193–1204

Biederman J, Faraone S, Milberger S, Guite J, Mick E, Chen L, Mennin D, Marrs A, Ouellette C, Moore P, Spencer T, Norman D, Wilens T, Kraus I, Perrin J (1996b) A prospective 4-year follow-up study of attention-deficit hyperactivity and related disorders. Arch Gen Psychiatry *53*: 437–446

Bloom B, Dey A N (2004) Summary health statistics for U.S. children: National Health Interview Survey. Vital Health Stat *10*: 1–85

Boris M, Mandel F S (1994) Foods and additives are common causes of the attention deficit hyperactive disorder in children. Ann Allergy *72*: 462–468

Brandon C L, Marinelli M, Baker L K, White F J (2001) Enhanced reactivity and vulnerability to cocaine following methylphenidate treatment in adolescent rats. Neuropsychopharmacology *25*: 651–661

Brassett-Grundy A, Butler N (2004a) Attention-Deficit/Hyperactivity Disorder: An overview and review of the literature relating to the correlates and lifecourse outcomes for males and females. Bedford Group for Lifecourse and Statistical Studies Occasional Paper: No. 1. Institute of Education, University of London

Brassett-Grundy A, Butler N (2004b) Prevalence and Adult Outcomes of Attention-Deficit/Hyperactivity Disorder: Evidence from a 30-year prospective longitudinal study. Bedford Group for Lifecourse and Statistical Studies Occasional Paper: No. 2. Institute of Education, University of London

Brookes K, Mill J, Guindalini C, Curran S, Xu X, Knight J, Chen C K, Huang Y S, Sethna V, Taylor E, Chen W, Breen G, Asherson P (2006) A common haplotype of the dopamine transporter gene associated with attention deficit/hyperactivity disorder and interacting with maternal use of alcohol during pregnancy. Arch Gen Psychiatry *63*: 74–81

Brown T E (1996) Brown Attention-Deficit Disorder Scales. The Psychological Corporation, San Antonio, TX

Burt S A, McGue M, Krueger R F, Iacono W G (2005) Sources of covariation among the child-externalizing disorders: informant effects and the shared environment. Psychol Med *35*: 1133–1144

Bush G, Valera E M, Seidman L J (2005) Functional neuroimaging of attention-deficit/hyperactivity disorder: a review and suggested future directions. Biol Psychiatry *57*: 1273–1284

Bymaster F P, Katner J S, Nelson D L, Hemrick-Luecke S K, Threlkeld P G, Heiligenstein J H, Morin S M, Gehlert D R, Perry K W (2002) Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder. Neuropsychopharmacology *27*: 699–711

Carlezon WA Jr, Mague S D, Andersen S L (2003) Enduring behavioral effects of early exposure to methylphenidate in rats. Biol Psychiatry *54*: 1330–1337

Carter C M, Urbanowicz M, Hemsley R, Mantilla L, Strobel S, Graham P J, Taylor E (1993) Effects of a few food diet in attention deficit disorder. Arch Dis Child *69*: 564–568

Castellanos F X, Lee P P, Sharp W, Jeffries N O, Greenstein D K, Clasen L S, Blumenthal J D, James R S, Ebens C L, Walter J M, Zijdenbos A, Evans A C, Giedd J N, Rapoport J L (2002) Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. JAMA *288*: 1740–1748

Castellanos X, Sonuga-Barke E J S, Tannock R, Milham M (2006) Characterising cognition in ADHD: beyond executive dysfunction. Trends Cogn Sci *10*: 117–123

Cheon K A, Ryu Y H, Kim Y K, Namkoong K, Kim C H, Lee J D (2003) Dopamine transporter density in the basal ganglia assessed with [123I]IPT SPET in children with attention deficit hyperactivity disorder. Eur J Nucl Med Mol Imaging *30*: 306–311

Coghill D (2006) Making the most of scant resources. In Yule W (ed.), The ADHD Spectrum. ACAMH Occasional papers 24, ACAMH, London

Coghill D, Nigg J, Rothenberger A, Sonuga-Barke E, Tannock R (2005) Whither causal models in the neuroscience of ADHD? Dev Sci *8*: 105–114

Conners C K, Erhardt D, Sparrow E, Conners M A (1998) CAARS Adult ADHD Rating Scales. Multi Health Systems Inc., New York

Craney J L, Geller B (2003) A prepubertal and early adolescent bipolar disorder-I phenotype: review of phenomenology and longitudinal course. Bipolar Disord *5*: 243–256

Dalteg A, Levander S (1998) Twelve thousand crimes by 75 boys: a 20-year follow-up study of childhood hyperactivity. J Forensic Psychiatry *9*: 39–57

Dalteg A, Lindgren M, Levander S (1999) Retrospectively rated ADHD is linked to specific personality characteristics and deviant alcohol reaction. J Forensic Psychiatry *10*: 623–634

DelBello M P, Soutullo C A, Niemeier R T, Wigh W L, McElroy S L, Strakowski S M (2001) Prior stimulant treatment in adolescents with bipolar disorder: association with age at onset. Bipolar Disord *3*: 53–57

Department of Health (2004) National Service Framework for Children, Young People and Maternity Services. Department of Health Publications. Available at: http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/ChildrenServices/fs/en

Dick D M, Viken R J, Kaprio J, Pulkkinen L, Rose R J (2005) Understanding the covariation among childhood externalizing symptoms: genetic and environmental influences on conduct disorder, attention deficit hyperactivity disorder, and oppositional defiant disorder symptoms. J Abnorm Child Psychol *33*: 219–229

Dickerson Mayes S, Calhoun S L, Crowell E W (2001) Clinical validity and interpretation of the Gordon Diagnostic System in ADHD assessments. Neuropsychol Dev Cogn C Child Neuropsychol *7*: 32–41

Dougherty D D, Bonab A A, Spencer T J, Rauch S L, Madras B K, Fischman A J (1999) Dopamine transporter density in patients with attention deficit hyperactivity disorder. Lancet *354*: 2132–2133

Doyle A E, Biederman J, Siedman L J, Weber W, Faraone S V (2000) Diagnostic efficiency of neuropsychological test scores for discriminating boys with and without attention deficit-hyperactivity disorder. J Consult Clin Psychol *68*: 477–488

Doyle A E, Willcutt E G, Siedman L J, Biederman J, Chouinard V A, Silva J, Faraone S V (2005) Attention-deficit/hyperactivity disorder endophenotypes. Biol Psychiatry *57*: 1324–1335

Dresel S, Krause J, Krause K H, LaFougere C, Brinkbaumer K, Kung H F, Hahn K, Tatsch K (2000) Attention deficit hyperactivity disorder: binding of [99mTc]TRODAT-1 to the dopamine transporter before and after methylphenidate treatment. Eur J Nucl Med *27*: 1518–1524

Dykman K D, Dykman R A (1998) Effect of nutritional supplements on attentional-deficit hyperactivity disorder. Integr Physiol Behav Sci *33*: 49–60

Egger J, Carter C M, Graham P J, Gumley D, Soothill J F (1985) Controlled trial of oligoantigenic treatment in the hyperkinetic syndrome. Lancet *9*(1): 540–545

Eyestone L L, Howell R J (1994) An epidemiological study of attention-deficit hyperactivity disorder and major depression in a male prison population. Bull Am Acad Psychiatry Law *22*: 181–193

Faraone S V, Biederman J (2005) What is the prevalence of adult ADHD? Results of a population screen of 966 adults. J Atten Disord *9*: 384–391

Faraone S V, Biederman J, Mick E (2006) The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. Psychol Med *36*: 159–165

Faraone S V, Biederman J, Monuteaux M C (2000) Toward guidelines for pedigree selection in genetic studies of attention deficit hyperactivity disorder. Genet Epidemiol *18*: 1–16

Faraone S V, Biederman J, Mennin D, Gershon J, Tsuang M T (1996) A prospective four-year follow-up study of children at risk for ADHD: psychiatric, neuropsychological, and psychosocial outcome. J Am Acad Child Adolesc Psychiatry *35*: 1449–1459

Faraone S V, Spencer T, Aleardi M, Pagano C, Biederman J (2004) Meta-analysis of the efficacy of methylphenidate for treating adult attention-deficit/hyperactivity disorder. J Clin Psychopharmacol *24*: 24–29

Faraone S V, Biederman J, Spencer T, Michelson D, Adler L, Reimherr F, Glatt S J (2005a) Efficacy of atomoxetine in adult attention-deficit/hyperactivity disorder: a drug-placebo response curve analysis. Behav Brain Funct *1*: 16

Faraone S V, Perlis R H, Doyle A E, Smoller J W, Goralnick J J, Holmgren M A, Sklar P (2005b) Molecular genetics of attention-deficit/hyperactivity disorder. Biol Psychiatry *57*: 1313–1323

Farrington D P (1995) The Twelfth Jack Tizard Memorial Lecture. The development of offending and antisocial behaviour from childhood: key findings from the Cambridge Study in Delinquent Development. J Child Psychol Psychiatry *36*: 929–964

Ferris R M, Tang F L (1979) Comparison of the effects of the isomers of amphetamine, methylphenidate and deoxypipradrol on the uptake of l-[3H]norepinephrine and [3H]dopamine by synaptic vesicles from rat whole brain, striatum and hypothalamus. J Pharmacol Exp Ther *210*: 422–428

Findling R, Schwartz M A, Flannery D J, Manos M J (1996) Venlafaxine in adults with attention-deficit/hyperactivity disorder: an open clinical trial. J Clin Psychiatry *57*: 184–189

Fisher S E, Francks C, McCracken J T, McGough J J, Marlow A J, MacPhie I L, Newbury D F, Crawford L R, Palmer C G, Woodward J A, Del'Homme M, Cantwell D P, Nelson S F, Monaco A P, Smalley S L (2002) A genomewide scan for loci involved in attention-deficit/hyperactivity disorder. Am J Hum Genet *70*: 1183–1196

Fleckenstein A E, Hanson G R (2003) Impact of psychostimulants on vesicular monoamine transporter function. Eur J Pharmacol *479*: 283–289

Fone K C, Nutt D J (2005) Stimulants: use and abuse in the treatment of attention deficit hyperactivity disorder. Curr Opin Pharmacol *5*: 87–93

Frazier T M, Demaree H A, Youngstrom E A (2004) Meta-analysis of intellectual and neuropsychological test performance in ADHD. Neuropsychology *18*: 543–555

Gadow K, Sprafkin J, Weiss M (1999) Adult Inventories-4. Available at: www.checkmateplus.com

Gadow K D, Nolan E E, Sprafkin J, Sverd J (1995) School observations of children with attention deficit hyperactivity disorder and comorbid tic disorder: effects of methylphenidate treatment. J Dev Behav Pediatr *16*: 167–177

Galanter C A, Carlson G A, Jensen P S, Greenhill L L, Davies M, Li W, Chuang S Z, Elliott G R, Arnold L E, March J S, Hechtman L, Pelham W E, Swanson J M (2003) Response to methylphenidate in children with attention deficit hyperactivity disorder and manic symptoms in the multimodal treatment study of children with attention deficit hyperactivity disorder titration trial. J Child Adolesc Psychopharmacol *13*: 123–136

Gallagher R, Blader J (2001) The diagnosis and neuropsychological assessment of adult attention deficit/hyperactivity disorder. Scientific study and practical guidelines. Ann N Y Acad Sci *931*: 148–171

Gehlert D R, Schober D A, Hemrick-Luecke S K, Krushinski J, Howbert J J, Roberston D W, Fuller R W, Wong D T (1995) Novel halogenated analogs of tomoxetine that are potent and selective inhibitors of norepinephrine uptake in brain. Neurochem Int *26*: 47–52

Geller B, Zimerman B, Williams M, Bolhofner K, Craney J L, DelBello M P, Soutullo C A (2000a) Six month stability and outcome of a prepubertal and early adolescent bipolar disorder phenotype. J Child Adolesc Psychopharm *10*: 165–174

Geller B, Zimerman B, Williams M, Bolhofner K, Craney J L, DelBello M P, Soutullo C A (2000b) Diagnostic characteristics of 93 cases of a prepubertal and early adolescent bipolar disorder phenotype by gender, puberty, and comorbid ADHD. J Child Adolesc Psychopharmacol *10*: 157–164

Gjone H, Stevenson J, Sundet J M (1996) Genetic influence on parent-reported attention-related problems in a Norwegian general population twin sample. J Am Acad Child Adolesc Psychiatry *35*: 588–596

Gordon M, Antshel K, Faraone S, Barkley R, Lewandowski L, Hudziak

J J, Biederman J, Cunningham C (2006) Symptoms versus impairment: the case for respecting DSM-IV's Criterion D. J Atten Disord *9*: 465–475

Goodwin G M for the Consensus Group of the British Association of Psychopharmacology (2003) Evidence-based guidelines for treating bipolar disorder: recommendations from the British Association for Psychopharmacology. J Psychopharmacol *17*: 149–173

Grodzinsky G M, Barkley R A (1999) Predictive power of frontal lobe tests in the diagnosis of attention deficit hyperactivity disorder. Clin Neuropsychol *13*: 12–21

Gross-Tsur V, Manor O, van der Meere J, Joseph A, Shalev R S (1997) Epilepsy and attention deficit hyperactivity disorder: is methylphenidate safe and effective? J Pediatr *130*: 40–44

Gucuyener K, Erdemoglu A K, Senol S, Serdaroglu A, Soysal S, Kockar A I (2003) Use of methylphenidate for attention-deficit hyperactivity disorder in patients with epilepsy or electroencephalographic abnormalities. J Child Neurol *18*: 109–112

Gudjonsson G, Young S (2006) An overlooked vulnerability in a defendant: Attention Deficit Hyperactivity Disorder (ADHD) and a miscarriage of justice. Legal & Criminological Psychology *11*: 211–218

Handen B L, Feldman H M, Lurier A, Murray P J (1999) Efficacy of methylphenidate among preschool children with developmental disorders and ADHD. J Am Assoc Child Adolesc Psychiatry *38*: 805–812

Harvey A S, Epstein J N, Curry J F (2004) Neuropsychology of adults with AD/HD: A meta-analytic review. Neuropsychology *18*: 485–503

Hebebrand J, Dempfle A, Saar K, Thiele H, Herpertz-Dahlmann B, Linder M, Kiefl H, Remschmidt H, Hemminger U, Warnke A, Knolker U, Heiser P, Friedel S, Hinney A, Schafer H, Nurnberg P, Konrad K (2005) A genome-wide scan for attention-deficit/hyperactivity disorder in 155 German sib-pairs. Mol Psychiatr *11*: 196–205

Hechtman L, Greenfield B (2003) Long-term use of stimulants in children with attention deficit hyperactivity disorder: safety, efficacy, and long-term outcome. Paediatr Drugs *5*: 787–794

Hechtman L, Weiss G (1983) Long-term outcome of hyperactive children. Am J Orthopsychiatry *53*: 532–541

Hechtman L, Weiss G (1986) Controlled prospective fifteen-year follow-up of hyperactives as adults: non-medical drug and alcohol use and anti-social behaviour. Am J Orthopsychiatry *54*: 415–425

Hedges D, Reimherr F W, Rogers A, Strong R, Wender P H (1995) An open trial of venlafaxine in adult patients with attention deficit hyperactivity disorder. Psychopharmacol Bull *31*: 779–783

Heiligenstein E, Keeling R P (1995) Presentation of unrecognized attention deficit hyperactivity disorder in college students. J Am Coll Health *43*: 226–228

Heinz A, Goldman D, Jones D W, Palmour R, Hommer D, Gorey J G, Lee K S, Linnoila M, Weinberger D R (2000) Genotype influences in vivo dopamine transporter availability in human striatum. Neuropsychopharmacology *22*: 133–139

Hesslinger B, Tebartz van Elst L, Nyberg E, Dykierek P, Richter H, Berner M, Ebert D (2002) Psychotherapy of attention deficit hyperactivity disorder in adults: a pilot study using a structured skills training program. Eur Arch Psychiatry Clin Neurosci *252*: 177–184

Hill J C, Schoener E P (1996) Age-dependent decline of attention deficit hyperactivity disorder. Am J Psychiatry *153*: 1143–1146

Hudziak J J, Derks E M, Althoff R R, Rettew D C, Boomsma D I (2005) The genetic and environmental contributions to attention deficit hyperactivity disorder as measured by the Conner's Rating Scales-Revised. Am J Psychiatry *162*: 1614–1620

Jackson D A, King A R (2004) Gender differences in the effects of oppositional behavior on teacher ratings of ADHD symptoms. J Abnorm Child Psychol *32*: 215–224

Jacobsen L K, Staley J K, Zoghbi S S, Seibyl J P, Kosten T R, Innis R B, Gelernter J (2000) Prediction of dopamine transporter binding availability by genotype: a preliminary report. Am J Psychiatry *157*: 1700–1703

Jester J M, Nigg J T, Adams K, Fitzgerald H E, Puttler L I, Wong M M, Zucker R A (2005) Inattention/hyperactivity and aggression from early childhood to adolescence: heterogeneity of trajectories and differential influence of family environment characteristics. Dev Psychopathol *17*: 99–125

Joint Formulary Committee (2005) *British National Formulary, 50 ed.* British Medical Association and Royal Pharmaceutical Society of Great Britain, London

Kahn R S, Khoury J, Nichols W C, Lanphear B P (2003) Role of dopamine transporter genotype and maternal prenatal smoking in childhood hyperactive-impulsive, inattentive, and oppositional behaviors. J Pediatr *143*: 104–110

Kessler R C, Adler L, Ames M, Demler O, Faraone S, Hiripi E, Howes M J, Jin R, Secnik K, Spencer T, Ustun T B, Walters E E (2005) The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. Psychol Med *35*: 245–256

Kessler R C, Adler L, Barkley R, Biederman J, Conners C K, Demler O, Faraone S V, Greenhill L L, Howes M J, Secnik K, Spencer T, Ustun T B, Walters E E, Zaslavsky AM (2006) Prevalence of adult ADHD in the United States: results from the National Comorbidity Survey Replication (NCS-R). Am J Psychiatry *163*: 716–723

Kollins S H (2003) Comparing the abuse potential of methylphenidate versus other stimulants: a review of available evidence and relevance to the ADHD patient. J Clin Psych *64* (suppl. II): 14–18

Kooij J J, Aeckerlin L P, Buitelaar J K (2001) [Functioning, comorbidity and treatment of 141 adults with attention deficit hyperactivity disorder (ADHD) at a psychiatric outpatient department]. Ned Tijdschr Geneeskd *145*: 1498–501

Kooij J J, Burger H, Boonstra A M, Van der Linden P D, Kalma L E, Buitelaar J K (2004) Efficacy and safety of methylphenidate in 45 adults with attention-deficit/hyperactivity disorder. A randomized placebo-controlled double-blind cross-over trial. Psychol Med *34*: 973–982

Kooij J J, Buitelaar J K, van den Oord E J, Furer J W, Rijnders C A, Hodiamont P P (2005) Internal and external validity of attention-deficit hyperactivity disorder in a population-based sample of adults. Psychol Med *35*: 817–827

Kratochvil C J, Newcorn J H, Arnold L E, Duesenberg D, Emslie G J, Quintana H, Sarkis E H, Wagner K D, Gao H, Michelson D, Biederman J (2005) Atomoxetine alone or combined with fluoxetine for treating ADHD with comorbid depressive or anxiety symptoms. J Am Acad Child Adolesc Psychiatry *44*: 915–924

Krause K H, Dresel S H, Krause J, Kung H F, Tatsch K (2000) Increased striatal dopamine transporter in adult patients with attention deficit hyperactivity disorder: effects of methylphenidate as measured by single photon emission computed tomography. Neurosci Lett *285*: 107–110

Kuczenski R, Segal D S (2001) Locomotor effects of acute and repeated threshold doses of amphetamine and methylphenidate: relative roles of dopamine and norepinephrine. J Pharmacol Exp Ther *296*: 876–883

Kuczenski R, Segal D S (2002) Exposure of adolescent rats to oral methylphenidate: preferential effects on extracellular norepinephrine and absence of sensitization and cross-sensitization to methamphetamine. J Neurosci *22*: 7264–7271

Kuo F E, Taylor A F (2005) A potential natural treatment for attention-deficit/hyperactivity disorder: evidence from a national study. Am J Public Health *94*: 1580–1586

Lambert N M (1988) Adolescent outcomes for hyperactive children. Perspectives on general and specific patterns of childhood risk for adoles-

cent educational, social and mental health problems. Am Psychologist *43*: 786–799

Levin F R, Evans S M, McDowell D M, Kleber H D (1998) Methylphenidate treatment for cocaine abusers with adult attention-deficit/hyperactivity disorder: a pilot study. J Clin Psychiatry *59*: 300–305

Levy F, Hay D A, McStephen M, Wood C, Waldman I (1997) Attention-deficit hyperactivity disorder: a category or a continuum? Genetic analysis of a large-scale twin study. J Am Acad Child Adolesc Psychiatry *36*: 737–744

Lin J S, Hou Y, Jouvet M (1996) Potential brain neuronal targets for amphetamine-, methylphenidate-, and modafinil-induced wakefulness, evidenced by c-fos immunocytochemistry in the cat. Proc Natl Acad Sci U S A *93*: 14128–14133

Lingford-Hughes A R, Welch S, Nutt D J (2004) Evidence-based guidelines for the pharmacological management of substance misuse, addiction and comorbidity: recommendations from the British Association of Psychopharmacology. J Psychopharmacol *18*: 293–335

Lovejoy D W, Ball J D, Keats M, Stutts M L, Spain E H, Janda L, Janusz J (1999) Neuropsychological performance of adults with attention deficit hyperactivity disorder (ADHD): diagnostic classification estimates for measures of frontal lobe/executive functioning. J Int Neuropsychol Soc *5*: 222–233

Luman M, Oosterlaan J, Sergeant J (2005) The impact of reinforcement contingencies on ADHD: a review and theoretical appraisal. Clin Psychol Rev *25*: 183–213

Lynn D E, Lubke G, Yang M, McCracken J T, McGough J J, Ishii J, Loo S K, Nelson S F, Smalley S L (2005) Temperament and character profiles and the dopamine D4 receptor gene in ADHD. Am J Psychiatry *162*: 906–913

McCracken J T, McGough J, Shah B, Cronin P, Hong D, Aman M G, Arnold L E, Lindsay R, Nash P, Hollway J, McDougle C J, Posey D, Swiezy N, Kohn A, Scahill L, Martin A, Koenig K, Volkmar F, Carroll D, Lancor A, Tierney E, Ghuman J, Gonzalez N M, Grados M, Vitiello B, Ritz L, Davies M, Robinson J, McMahon D, Research Units on Pediatric Psychopharmacology Autism Network (2002) Risperidone in children with autism and serious behavioral problems. N Engl J Med *347*: 314–321

McGough J J, Smalley S L, McCracken J T, Del'Homme M, Lynn D E, Loo S (2005) Psychiatric comorbidity in adult attention deficit hyperactivity disorder: findings from multiplex families. Am J Psychiatry *162*: 1621–1627

Madras B K, Miller G M, Fischman A J (2002) The dopamine transporter: relevance to attention deficit hyperactivity disorder (ADHD). Behav Brain Res *130*: 57–63

Magnusson P, Smari J, Sigurdardottir D, Baldursson G, Sigmundsson J, Kristjansson K, Sigurdardottir S, Hreidarsson S, Sigurbjornsdottir S, Gudmundsson O O (2006) Validity of self-report and informant rating scales of adult ADHD symptoms in comparison with a semistructured diagnostic interview. J Atten Disord *9*: 494–503

Maidment I D (2003a) Efficacy of stimulants in adult ADHD. Ann Pharmacother *37*: 1884–1890

Maidment I D (2003b) The use of antidepressants to treat attention deficit hyperactivity disorder in adults. J Psychopharmacol *17*: 332–336

Mannuzza S, Klein R G, Konig P H, Giampino T L (1989) Hyperactive boys almost grown up: IV. Criminality and its relationship to psychiatric status. Arch Gen Psychiatry *46*: 1073–1079

Mannuzza S, Klein R G, Bessler A, Malloy P, LaPadula M (1998) Adult psychiatric status of hyperactive boys grown up. Am J Psychiatry *155*: 493–498

Marks D J, Newcorn J H, Halperin J M (2001) Comorbidity in adults with attention-deficit/hyperactivity disorder. Ann N Y Acad Sci *931*: 216–238

Marotta P J, Roberts E A (1998) Pemoline hepatotoxicity in children. J Pediatr *132*: 894–897

Martinez D, Gelernter J, Abi-Dargham A, van Dyck C H, Kegeles L, Innis R B, Laruelle M (2001) The variable number of tandem repeats polymorphism of the dopamine transporter gene is not associated with significant change in dopamine transporter phenotype in humans. Neuropsychopharmacology *24*: 553–560

Mattes J A, Boswell L, Oliver H (1984) Methylphenidate effects on symptoms of attention deficit disorder in adults. Arch Gen Psychiatry *41*: 1059–1063

Mayes S D, Calhoun S L (2006) WISC-IV and WISC-III profiles in children with ADHD. J Atten Disord *9*: 486–493

Mayes S D, Crites D L, Bixler E O, Humphrey F J 2nd, Mattison R E (1994) Methylphenidate and ADHD: influence of age, IQ and neurodevelopmental status. Dev Med Child Neurol *36*: 1099–1107

Michelson D, Adler L, Spencer T, Reimherr F W, West S A, Allen A J, Kelsey D, Wernicke J, Dietrich A, Milton D (2003) Atomoxetine in adults with ADHD: two randomized, placebo-controlled studies. Biol Psychiatry *53*: 112–120

Mick E, Faraone S V, Biederman J (2004) Age-dependent expression of attention-deficit/hyperactivity disorder symptoms. Psychiatr Clin North Am *27*: 215–224

Millstein R, Wilens T, Biederman J, Spencer T (1998) Presenting ADHD symptoms and subtypes in clinically referred adults with ADHD. Attention *2*: 159–166

Montgomery S A, Cowen P J, Deakin W, Freeling P, Hallstrom C, Katona C, King D, Leonard B, Levine S, Phanjoo A, Peet M, Thompson C (1993) Guidelines for the treating depressive illness with antidepressants. A statement from the British Association for Psychopharmacology. J Psychopharmacol *7*: 19–23

MTA Cooperative Group (1999) A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. Multimodal Treatment Study of Children with ADHD. Arch Gen Psychiatry *56*: 1073–1086

Muglia P, Jain U, Macciardi F, Kennedy J L (2000) Adult attention deficit hyperactivity disorder and the dopamine D4 receptor gene. Am J Med Genet *96*: 273–277

Murphy K R, Barkley R A (1996) Parents of children with attention-deficit/hyperactivity disorder: psychological and attentional impairment. American J Orthopsychiatry *66*: 93–102

NICE (2006) Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents – guidance. National Institute for Health and Clinical Excellence (TA098). Available at: www.nice.org.uk/

Nigg J T (2005) Neuropsychologic theory and findings in attention-deficit/hyperactivity disorder: the state of the field and salient challenges for the coming decade. Biol Psychiatry *57*: 1424–1435

Ogdie M N, Fisher S E, Yang M, Ishii J, Francks C, Loo S K, Cantor R M, McCracken J T, McGough J J, Smalley S L, Nelson S F (2004) Attention deficit hyperactivity disorder: fine mapping supports linkage to 5p13, 6q12, 16p13, and 17p11. Am J Hum Genet *75*: 661–668

Ogdie M N, Macphie I L, Minassian S L, Yang M, Fisher S E, Francks C, Cantor R M, McCracken J T, McGough J J, Nelson S F, Monaco A P, Smalley S L (2003) A genomewide scan for attention-deficit/hyperactivity disorder in an extended sample: suggestive linkage on 17p11. Am J Hum Genet *72*: 1268–1279

Paterson R, Douglas C, Hallmayer J, Hagan M, Krupenia Z (1999) A randomised, double-blind, placebo-controlled trial of dexamphetamine in adults with attention deficit hyperactivity disorder. Aust N Z J Psychiatry *33*: 494–502

Pineda D, Ardila A, Rosselli M, Arias B E, Henao G C, Gomez L F, Mejia

S E, Miranda M L (1999) Prevalence of attention-deficit/hyperactivity disorder symptoms in 4- to 17-year-old children in the general population. J Abnorm Child Psychol *27*: 455–462

Post R M, Chang K D, Findling R L, Geller B, Kowatch R A, Kutcher S P, Leverich G S (2004) Prepubertal bipolar I disorder and bipolar disorder NOS are separable from ADHD. J Clin Psychiatry *65*: 898–902

Pratt T C, Cullen F T, Blevins K R, Daigle L, Unnever J D (2002) The relationship of attention deficit hyperactivity disorder to crime and delinquency: a meta-analysis. Int J Police Sci Management *4*: 344–360

Price T S, Simonoff E, Waldman I, Asherson P, Plomin R (2001) Hyperactivity in preschool children is highly heritable. J Am Acad Child Adolesc Psychiatry *40*: 1362–1364

Rasmussen K, Almik R, Levander S (2001) Attention deficit hyperactivity disorder, reading disability and personality disorders in a prison population. J Am Acad Psychiatry Law *296*: 186–193

Ratey J J, Greenberg M S, Bemporad J R, Lindem K J (1992) Unrecognized attention-deficit hyperactivity disorder in adults presenting for outpatient psychotherapy. J Child Adolesc Psychopharmacology *2*: 267–275

Remschmidt H, Global ADHD Working Group (2005) Global consensus on ADHD/HKD. Eur Child Adolesc Psychiatry *14*: 127–137

Retz W, Retz-Junginger P, Hengesch G, Schneider M, Thome J, Pajonk F G, Salahi-Disfan A, Rees O, Wender P H, Rosler M (2004) Psychometric and psychopathological characterization of young male prison inmates with and without attention deficit/hyperactivity disorder. Eur Arch Psychiatry Clin Neurosci *254*: 201–208

Rielly N E, Cunningham C E, Richards J E, Elbard H J, Mahoney W J (1999) Detecting attention deficit hyperactivity disorder in a communications clinic: diagnostic utility of the Gordon Diagnostic System. J Clin Exp Neuropsychol *21*: 685–700

Rhodes S M, Coghill D R, Matthews K (2004) Methylphenidate restores visual memory, but not working memory function in attention deficit-hyperkinetic disorder. Psychopharmacology (Berl) *175*: 319–330

Rhodes S M, Coghill D R, Matthews K (2005) Neuropsychological functioning in stimulant-naive boys with hyperkinetic disorder. Psychol Med *35*: 1109–1120

Richardson A J, Puri B K (2002) A randomized double-blind, placebo-controlled study of the effects of supplementation with highly unsaturated fatty acids on ADHD-related symptoms in children with specific learning difficulties. Prog Neuropsychopharmacol Biol Psychiatry *26*: 233–239

Rosler M, Retz W, Retz-Junginger P, Hengesch G, Schneider M, Supprian T, Schwitzgebel P, Pinhard K, Dovi-Akue N, Wender P, Thome J (2004) Prevalence of attention-deficit/hyperactivity disorder (ADHD) and comorbid disorders in young male prison inmates. Eur Arch Psychiatry Clin Neurosci *254*: 365–371

Rowe K S, Rowe K J (1994) Synthetic food coloring and behaviour: a dose response effect in a double-blind, placebo-controlled, repeated measures study. J Pediatr *125*: 691–698

Rowland A S, Lesesne C A, Abramowitz A J (2002) The epidemiology of attention-deficit/hyperactivity disorder (ADHD): a public health view. Ment Retard Dev Disabil Res Rev *8*: 162–170

Safren S A, Sprich S, Perlman C A, Otto M W (2005a) Mastering Your Adult ADHD. Guilford Press, New York

Safren S A, Otto M W, Sprich S, Winett C L, Wilens T E, Biederman J (2005b) Cognitive-behavioral therapy for ADHD in medication-treated adults with continued symptoms. Behav Res Ther *43*: 831–842

Santosh P J, Taylor E (2000) Stimulant drugs. Eur Child Adolesc Psychiatry *9* (Suppl. 1): I27–43

Satterfield J H, Hoppe C M, Schell A M (1982) A prospective study of delinquency in 110 adolescent boys with attention deficit disorder and 88 normal adolescent boys. Am J Psychiatry *139*: 795–798

Satterfield T, Swanson J, Schell A, Lee F (1994) Prediction of anti-social behaviour in attention-deficit hyperactivity disorder boys from aggression/defiance scores. J Am Acad Child Adolesc Psychiatry *33*: 185–190

Schachter H M, Pham B, King J, Langford S, Moher D (2001) How efficacious and safe is short-acting methylphenidate for the treatment of attention-deficit disorder in children and adolescents? A meta-analysis. CMAJ *165*: 1475–1488

Schmidt M H, Mocks P, Lay B, Eisert H G, Fojkar R, Fritz-Sigmund D, Marcus A, Musaeus B (1997) Does oligoantigenic diet influence hyperactive/conduct-disordered children – a controlled trial. Eur Child Adolesc Psychiatry *6*: 88–95

Schoechlin C, Engel R R (2005) Neuropsychological performance in adult attention-deficit hyperactivity disorder: meta-analysis of empirical data. Arch Clin Neuropsychol *20*: 727–744

Seager M C, O'Brien G (2003) Attention deficit hyperactivity disorder: a review in learning disability: the Diagnostic Criteria for Psychiatric Disorders for Use with Adults with Learning Disabilities /Mental Retardation [DC/LD] criteria for diagnosis. J Intellectual Disability Res *475* (suppl. 1): 26–31

Secnik K, Swensen A, Lage M J (2005) Comorbidities and costs of adult patients diagnosed with attention-deficit hyperactivity disorder. Pharmacoeconomics *23*: 93–102

Seidman L, Doyle A, Fried R, Valera E, Crum K, Matthews L (2004) Neuropsychological function in adults with attention deficit disorder. Psychiatric Clinics of North America *27*: 261–282

Seidman L J, Valera E M, Makris N (2005) Structural brain imaging of attention-deficit/hyperactivity disorder. Biol Psychiatry *57*: 1263–1272

Sergeant J A (2005) Modeling attention-deficit/hyperactivity disorder: a critical appraisal of the cognitive-energetic model. Biol Psychiatry *57*: 1248–1255

Shaffer D, Gould M S, Brasic J, Ambrosini P, Fisher P, Bird H, Aluwahlia S (1983) A children's global assessment scale (CGAS). Arch Gen Psychiatry *40*: 1228–1231

Sharma V, Halperin J H, Newcorn J N, Wolf L E (1991) The dimension of focussed attention: relationship to behavior and cognitive functioning in children. Percept Mot Skills *72*: 787–793

Shekelle P G, Woolf S H, Eccles M, Grimshaw J (1999) Clinical guidelines: developing guidelines. BMJ *318*: 593–596

Smalley S L, Kustanovich V, Minassian S L, Stone J L, Ogdie M N, McGough J J, McCracken J T, MacPhie I L, Francks C, Fisher S E, Cantor R M, Monaco A P, Nelson S F (2002) Genetic linkage of attention-deficit/hyperactivity disorder on chromosome 16p13, in a region implicated in autism. Am J Hum Genet *71*: 959–963

Smith B H, Waschbusch D A, Willoughby M T, Evans S (2000) The efficacy, safety, and practicality of treatments for adolescents with attention-deficit/hyperactivity disorder (ADHD). Clin Child Fam Psychol Rev *3*: 243–267

Sonuga-Barke E J (2002) Psychological heterogeneity in AD/HD – a dual pathway model of behaviour and cognition. Behav Brain Res *130*: 29–36

Sonuga-Barke E J (2003) The dual pathway model of AD/HD: an elaboration of neuro-developmental characteristics. Neurosci Biobehav Rev *27*: 593–604

Sonuga-Barke E J (2005) Causal models of attention-deficit/hyperactivity disorder: from common simple deficits to multiple developmental pathways. Biol Psychiatry *57*: 1231–1238

Sonuga-Barke E J, Elgie S, Hall M (2005) More to ADHD than meets the eye: observable abnormalities in search behaviour do not account for performance deficits on a discrimination task. Behav Brain Funct *20*: 10

Sonuga-Barke E J, Swanson J M, Coghill D, DeCory H H, Hatch S J

(2004) Efficacy of two once-daily methylphenidate formulations compared across dose levels at different times of the day: preliminary indications from a secondary analysis of the COMACS study data. BMC Psychiatry *4*: 28

Spencer T, Biederman J, Wilens T Harding M, O'Donnell D, Griffin S (1996) Pharmacotherapy of attention-deficit/hyperactivity disorder across the life cycle. J Am Acad Child Adolesc Psychiatry *35*: 409–432

Spencer T J, Biederman J, Madras B K, Faraone S V, Dougherty D D, Bonab A A, Fischman A J (2005a) In vivo neuroreceptor imaging in attention-deficit/hyperactivity disorder: a focus on the dopamine transporter. Biol Psychiatry *57*: 1293–1300

Spencer T, Biederman J, Wilens T, Faraone S, Prince J, Gerard K, Doyle R, Parekh A, Kagan J, Bearman S K (2001) Efficacy of a mixed amphetamine salts compound in adults with attention-deficit/hyperactivity disorder. Arch Gen Psychiatry *58*: 775–782

Spencer T, Biederman J, Wilens T, Doyle R, Surman C, Prince J, Mick E, Aleardi M, Herzig K, Faraone S (2005b) A large, double-blind, randomized clinical trial of methylphenidate in the treatment of adults with attention-deficit/hyperactivity disorder. Biol Psychiatry *57*: 456–463

Steele M, Weiss M D, Swanson J M, Wang J, Prinzo R S, Binder C E (2006) A randomized, controlled, effectiveness trial of OROS methylphenidate compared to usual care with immediate release methylphenidate in attention deficit-hyperactivity disorder. Can J Clin Pharmacol *13*: e50–62

Stein M A, Waldman I D, Sarampote C S, Seymour K E, Robb A S, Conlon C, Kim S J, Cook E H (2005) Dopamine transporter genotype and methylphenidate dose response in children with ADHD. Neuropsychopharmacology *30*: 1374–1382

Stevenson C S, Whitmont S, Bornholt L, Livesey D, Stevenson R J (2002) A cognitive remediation programme for adults with attention deficit hyperactivity disorder. Aust N Z J Psychiatry *36*: 610–616

Swanson C J, Perry K W, Koch-Krueger S, Katner J, Svensson K A, Bymaster F P (2006) Effect of the attention deficit/hyperactivity disorder drug atomoxetine on extracellular concentrations of norepinephrine and dopamine in several brain regions of the rat. Neuropharmacology *50*: 755–760

Swanson J M, Wigal S B, Wigal T, Sonuga-Barke E, Greenhill L L, Biederman J, Kollins S, Nguven A S, DeCory H H, Hirshe Dirksen S J, Hatch S J, COMACS Study Group (2004) A comparison of once-daily extended-release methylphenidate formulations in children with attention-deficit/hyperactivity disorder in the laboratory school (the Comacs Study). Pediatrics *113*: e206–216

Swensen A, Birnbaum H G, Ben Hamadi R, Greenberg P, Cremieux P Y, Secnik K (2000) Incidence and costs of accidents among attention-deficit/hyperactivity disorder patients. J Adolesc Health *35*: 346–349

Tamm L, Menon V, Ringel J, Reiss A L (2004) Event-related fMRI evidence of frontotemporal involvement in aberrant response inhibition and task switching in attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry *43*: 1430–1440

Tan M, Appleton R (2005) Attention deficit and hyperactivity disorder, methylphenidate, and epilepsy. Arch Dis Child *90*: 57–59

Taylor E, Chadwick O, Heptinstall E, Danckaerts M (1996) Hyperactivity and conduct problems as risk factors for adolescent development. J Am Acad Child Adolesc Psychiatry *35*: 1213–1226

Taylor E, Dopfner M, Sergeant J, Asherson P, Banaschewski T, Buitelaar J, Coghill D, Danckaerts M, Rothenberger A, Sonuga-Barke E, Steinhausen H C, Zuddas A (2004) European clinical guidelines for hyperkinetic disorder – first upgrade. Eur Child Adolesc Psychiatry *13* (suppl. 1): I7–30

Taylor F B, Russo J (2000) Efficacy of modafinil compared to dextroamphetamine for the treatment of attention deficit hyperactivity disorder in adults. J Child Adolesc Psychopharmacol *10*: 311–320

Taylor F B, Russo J (2001) Comparing guanfacine and dextroamphetamine for the treatment of adult attention-deficit/hyperactivity disorder. J Clin Psychopharmacol *21*: 223–228

Thapar A, Harrington R, McGuffin P (2001) Examining the comorbidity of ADHD-related behaviours and conduct problems using a twin study design. Br J Psychiatry *179*: 224–229

Thapar A, O'Donovan M, Owen M J (2005a) The genetics of attention deficit hyperactivity disorder. Hum Mol Genet *14* (Spec No. 2): R275–282

Thapar A, Langley K, Fowler T, Rice F, Turic D, Whittinger N, Aggleton J, Van den Bree M, Owen M, O'Donovan M (2005b) Catechol O-methyltransferase gene variant and birth weight predict early-onset antisocial behavior in children with attention-deficit/hyperactivity disorder. Arch Gen Psychiatry *62*: 1275–1278

Thomason C, Michelson D (2004) Atomoxetine – treatment of attention deficit hyperactivity disorder: beyond stimulants. Drugs Today (Barc) *40*: 465–473

Toplak M E, Dockstader C, Tannock R (2006) Temporal information processing in ADHD: findings to date and new methods *151*(1): 15–29

Torgersen T, Gjervan B, Rasmussen K (2006) ADHD in adults: a study of clinical characteristics, impairment and comorbidity. Nord J Psychiatry *60*: 38–43

Tripp G, Luk S L, Schaughency E A, Singh R (1999) DSM-IV and ICD-10: a comparsion of the correlatoes of ADHD and hyperkinetic disorder. J Am Acad Child Adol Psych *38*: 156–164

van der Feltz-Cornelis C M, Aldenkamp A P (2006) Effectiveness and safety of methylphenidate in adult attention deficit hyperactivity disorder in patients with epilepsy: an open treatment trial. Epilepsy Behav *8*: 659–662

Van Dyck, Quinlan D M, Cretella L M, Staley J K, Malison R T, Baldwin R M, Seibyl J P, Innis R B (2002) Unaltered dopamine transporter availability in adult attention deficit disorder. Am J Psychiatry *159*: 309–312

Vitelli R (1995) Prevalence of childhood conduct and attention-deficit hyperactivity disorders in adult maximum-security inmates. Int J Offender Ther Comp Criminology *40*: 263–271

Volkow N D, Insel T R (2003) What are the long-term effects of methylphenidate treatment? Biol Psychiatry *54*: 1307–1309

Volkow N D, Wang G J, Fowler J S, Ding Y S (2005) Imaging the effects of methylphenidate on brain dopamine: new model on its therapeutic actions for attention-deficit/hyperactivity disorder. Biol Psychiatry *57*: 1410–1415

Volkow N D, Wang G J, Fowler J S, Gatley S J, Logan J, Ding Y S, Hitzemann R, Pappas N (1998) Dopamine transporter occupancies in the human brain induced by therapeutic doses of oral methylphenidate. Am J Psychiatry *155*: 1325–1331

Volkow N D, Wang G, Fowler J S, Logan J, Gerasimov M, Maynard L, Ding Y, Gatley S J, Gifford A, Franceschi D (2001) Therapeutic doses of oral methylphenidate significantly increase extracellular dopamine in the human brain. J Neurosci *21*: RC121

Volkow N D, Wang G J, Fowler J S, Fischman M, Foltin R, Abumrad N N, Gatley S J, Logan J, Wong C, Gifford A, Ding Y S, Hitzemann R, Pappas N (1999) Methylphenidate and cocaine have a similar in vivo potency to block dopamine transporters in the human brain. Life Sci *65*: PL7–12

Waldman I D (2005) Statistical approaches to complex phenotypes: evaluating neuropsychological endophenotypes for attention-deficit/hyperactivity disorder. Biol Psychiatry *57*: 1347–1356

Ward M F, Wender P H, Reimherr F W (1993) The Wender Utah Rating Scale: an aid in the retrospective diagnosis of childhood attention

deficit hyperactivity disorder. Am J Psychiatry *150*: 885–890. Erratum in: *150*: 1280
Weiss G, Hechtman L T (1993) Hyperactive Children Grown Up, 2nd edn. Guildford, New York
Weiss M, Murray C (2003) Assessment and management of attention-deficit hyperactivity disorder in adults. CMAJ *18*: 715–722
Weiss M D, Murray C (2004) Practice Guideline for the Assessment of ADHD in adults. Canadian ADHD Resource Alliance, Vancouver, Canada
Weiss M D, Weiss J R (2004) A guide to the treatment of adults with ADHD. J Clin Psychiatry *65* (Suppl 3): 27–37
Wender P H (1995) Attention-deficit hyperactivity disorder in adults. Oxford University Press, New York, pp. 122–143
Wender P H, Reimherr F W (1990) Bupropion treatment of attention-deficit hyperactivity disorder in adults. Am J Psychiatry *147*: 1018–1020
Wender P H, Wolf L E, Wasserstein J (2001) Adults with ADHD. An overview. Ann N Y Acad Sci *931*: 1–16
WHO (1992) The ICD-10 classification of mental and behavioural disorders. Geneva, Switzerland
Wiggins D, Singh K, Getz H G, Hutchins D E (1999) Effects of brief group intervention for adults with attention deficit/hyperactivity disorder. J Mental Health Counseling *21*: 82–92
Wilens T E, Faraone S V, Biederman J, Gunawardene S (2003) Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. Pediatrics *111*: 179–185
Wilens T E, McDermott S P, Biederman J, Abrantes A, Hahesy A, Spencer T J (1999a) Cognitive therapy in the treatment of adults with ADHD: A systematic chart review of 26 cases. J Cogn Psychother *13*: 215–226
Wilens T E, Biederman J, Prince J, Spencer T J, Faraone S V, Warburton R, Schleifer D, Harding M, Linehan C, Geller D (1996) Six-week, double-blind, placebo-controlled study of desipramine for adult attention deficit hyperactivity disorder. Am J Psychiatry *153*: 1147–1153
Wilens T E, Spencer T J, Biederman J, Girard K, Doyle R, Prince J, Polisner D, Solhkhah R, Comeau S, Monuteaux M C, Parekh A (2001) A controlled clinical trial of bupropion for attention deficit hyperactivity disorder in adults. Am J Psychiatry *158*: 282–288
Wilens T E, Biederman J, Spencer T J, Frazier J, Prince J, Bostic J, Rater M, Soriano J, Hatch M, Sienna M, Millstein R B, Abrantes A (1999b) Controlled trial of high doses of pemoline for adults with attention-deficit/hyperactivity disorder. J Clin Psychopharmacol *19*: 257–264
Willcutt E G, Pennington B F, DeFries J C (2000) Twin study of the etiology of comorbidity between reading disability and attention-deficit/hyperactivity disorder. Am J Med Genet *96*: 293–301
Willcutt E G, Doyle A E, Nigg J T, Faraone S V, Pennington B F (2005) Validity of the executive function theory of attention-deficit/hyperactivity disorder: a meta-analytic review. Biol Psychiatry *57*: 1336–1346
World Health Organization (1992) The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. World Health Organization, Geneva
Young S, Gudjonsson G, Ball S, Lam J (2003) Attention deficit hyperactivity disorder in personality disordered offenders and the association with disruptive behavioural problems. J Forensic Psychiatry Psychol *14*: 491–505
Young S J, Gudjonsson G (submitted) Growing out of attention-deficit/hyperactivity disorder: the relationship between functioning and symptoms
Young S J, Harty M A (2001) Treatment issues in a personality disordered offender: a case of attention deficit hyperactivity disorder in secure psychiatric services. J Forensic Psychiatry *12*: 158–167
Young S J, Ross R R (2006) R&R2 for ADHD youth and adults. A handbook for teaching prosocial competence. Cognitive Centre of Canada, Ottawa (cogcen@canada.com)
Young S J, Ross R R (in preparation) R&R2 for ADHD children. A handbook for teaching prosocial competence

Appendix

DSM-IV-TR attention-deficit/hyperactivity disorder

I Either A or B:

A Six or more of the following symptoms of inattention have been present for at least 6 months to a point that is disruptive and inappropriate for developmental level.

Inattention

1 Often does not give close attention to details or makes careless mistakes in schoolwork, work, or other activities.
2 Often has trouble keeping attention on tasks or play activities.
3 Often does not seem to listen when spoken to directly.
4 Often does not follow instructions and fails to finish schoolwork, chores or duties in the workplace (not due to oppositional behaviour or failure to understand instructions).
5 Often has trouble organizing activities.
6 Often avoids, dislikes or doesn't want to do things that take a lot of mental effort for a long period of time (such as schoolwork or homework).
7 Often loses things needed for tasks and activities (e.g. toys, school assignments, pencils, books or tools).
8 Is often easily distracted.
9 Is often forgetful in daily activities.

B Six or more of the following symptoms of hyperactivity–impulsivity have been present for at least 6 months to an extent that is disruptive and inappropriate for developmental level.

Hyperactivity

1 Often fidgets with hands or feet or squirms in seat.
2 Often gets up from seat when remaining in seat is expected.
3 Often runs about or climbs when and where it is not appropriate (adolescents or adults may feel very restless).
4 Often has trouble playing or enjoying leisure activities quietly.
5 Is often 'on the go' or often acts as if 'driven by a motor'.
6 Often talks excessively.

Impulsivity

1 Often blurts out answers before questions have been finished.
2 Often has trouble waiting one's turn.
3 Often interrupts or intrudes on others (e.g. butts into conversations or games).

II Some symptoms that cause impairment were present before age 7 years.

III Some impairment from the symptoms is present in two or more settings (e.g. at school/work and at home).

IV There must be clear evidence of significant impairment in social, school or work functioning.

V The symptoms do not happen only during the course of a pervasive developmental disorder, schizophrenia or other psychotic disorder. The symptoms are not better accounted for by another mental disorder (e.g. mood disorder, anxiety disorder, dissociative disorder or a personality disorder).

Based on these criteria, three types of ADHD are identified:

1 ADHD, *Combined Type*: if both criteria 1A and 1B are met for the past 6 months
2 ADHD, *Predominantly Inattentive Type*: if criterion 1A is met but criterion 1B is not met for the past 6 months.
3 ADHD, *Predominantly Hyperactive-Impulsive Type*: if Criterion 1B is met but Criterion 1A is not met for the past 6 months.

Note: for individuals (especially adolescents and adults) who currently have symptoms that no longer meet full criteria, 'In Partial Remission' should be specified.

ICD-10 DCR hyperkinetic disorders

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

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

1 at least three of the following attention problems:
   a short duration of spontaneous activities;
   b often leaving play activities unfinished;
   c over-frequent changes between activities;
   d undue lack of persistence at tasks set by adults;
   e unduly high distractibility during study e.g. homework or reading assignment;
2 plus at least three of the following activity problems:
   a very often runs about or climbs excessively in situations where it is inappropriate; seems unable to remain still;
   b markedly excessive fidgeting & wriggling during spontaneous activities;
   c markedly excessive activity in situations expecting relative stillness (e.g. mealtimes, travel, visiting, church);
   d often leaves seat in classroom or other situations when remaining seated is expected;
   e often has difficulty playing quietly.
3 plus at least one of the following impulsivity problems:
   a often has difficulty awaiting turns in games or group situations;
   b often interrupts or intrudes on others (e.g. butts in to others' conversations or games);
   c often blurts out answers to questions before questions have been completed.

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

1 at least two of the following attention problems:
   a undue lack of persistence at tasks;
   b unduly high distractibility, i.e. often orienting towards extrinsic stimuli;
   c over-frequent changes between activities when choice is allowed;
   d excessively short duration of play activities;
2 and by at least three of the following activity problems:
   a continuous (or almost continuous) and excessive motor restlessness (running, jumping, etc.) in situations allowing free activity;
   b markedly excessive fidgeting and wriggling in structured situations;
   c excessive levels of off-task activity during tasks;
   d unduly often out of seat when required to be sitting;
   e often has difficulty playing quietly.

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

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

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

G5 Onset before the age of seven years.

G6 Duration of at least six months.

G7 IQ above 50.

F90.0 Disturbance of activity and attention
The general criteria for hyperkinetic disorder (F90) must be met, but not those for conduct disorders (F91).
F90.1 Hyperkinetic conduct disorder

Both the general criteria for hyperkinetic disorder (F90) and conduct disorder (F91) must be met.
F90.8 Other hyperkinetic disorders
F90.9 Hyperkinetic disorder, unspecified
This residual category is not recommended and should be used only when there is a lack of differentiation between F90.0 and F90.1 but the overall criteria for F90.- are fulfilled.

Questions from the adult ADHD self-report scale (ASRS-v1.1) symptom checklist (based on DSM-IV-TR) www.med.nyu.edu/psych/assets/adhdscreen18.pdf

Screening questions

1 How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?
2 How often do you have difficulty getting things in order when you have to do a task that requires organization?
3 How often do you have problems remembering appointments or obligations?
4 When you have a task that requires a lot of thought, how often do you avoid or delay getting started?
5 How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?
6 How often do you feel overly active and compelled to do things, like you were driven by a motor?

Additional questions

7 How often do you make careless mistakes when you have to work on a boring or difficult project?
8 How often do you have difficulty keeping your attention when you are doing boring or repetitive work?
9 How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?
10 How often do you misplace or have difficulty finding things at home or at work?
11 How often are you distracted by activity or noise around you?
12 How often do you leave your seat in meetings or other situations in which you are expected to remain seated?
13 How often do you feel restless or fidgety?
14 How often do you have difficulty unwinding and relaxing when you have time to yourself?
15 How often do you find yourself talking too much when you are in social situations?
16 When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to, before they can finish them themselves?
17 How often do you have difficulty waiting your turn in situations when turn taking is required?
18 How often do you interrupt others when they are busy?

Expert Canadian Consensus: suggested screening questions for ADHD

Questions for parents of school-age patients

1 Compared to other boys/girls of the same age [and ethnic group, if applicable], does your child have more difficulty paying attention or listening?
2 Is he/she more fidgety or hyperactive than boys/girls of the same age [and ethnic group, if applicable]?
3 Does he/she do dangerous, disobedient, or inappropriate/'annoying' things impulsively, without concern for the possible consequences more often than boys/girls of the same age [and ethnic group, if applicable]?
4 Compared to other boys/girls of the same age [and ethnic group, if applicable], does your child have trouble paying attention or being hyperactive both at home *and* at school?
5 Have other people (e.g. teachers) complained about your child not paying attention properly, being hyperactive, or acting impulsively?

Questions for adult patients

1 Do you feel that you get bored, restless, or impatient more easily than most people?
2 Are you more forgetful or more disorganized than the average person?
3 Do you feel you are consistently failing to achieve your own potential?
4 Did you have problems with paying attention or doing dangerous or disobedient things impulsively as a child?