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Distinguishing Comorbidity and Successful Management of Adult ADHD

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Abstract

Objective: Given high rates of comorbidity, lack of awareness and global acceptance, and varying guidelines for its management, adult ADHD may be an especially difficult condition to diagnose and treat. The objective of this review was to explore and characterize similarities and differences among comorbidities associated with adult ADHD. **Method:** A review of the literature over the past 10 years was performed using Ovid. **Results:** A myriad of comorbid conditions such as impulse-control/personality, anxiety, mood, substance use, learning, and sleep disorders overlap with adult ADHD. Furthermore, a number of such conditions have symptoms that can mimic those of ADHD, including hyperactivity, impulsivity, inattention, and disruption of circadian rhythms, adding to the complexity of recognition and diagnosis of ADHD in adults. Extensive research shows that adults with ADHD appear to benefit from treatment with stimulant medications in similar ways as children, including significant improvements on driving performance. However, fear surrounding the abuse of stimulants is an important issue. Nevertheless, evidence suggests that children with ADHD who are treated with stimulant medication are less likely to develop a substance use disorder in adolescence and adulthood. **Conclusion:** There are a wide range of comorbidities with adult ADHD with many having overlapping symptoms. The benefits observed with ADHD treatment, however, emphasize the importance of recognition and treatment of adult ADHD. *(J. of Att. Dis. 2012; 16(5S) 3S-19S)*

Keywords

adult ADHD, comorbidity, clinical management

Successful management of adult ADHD involves not only awareness but also recognition of key barriers that may hinder the diagnosis and treatment of ADHD among adults. Some of these barriers include perceptions of gender differences in occurrence, high comorbidity, a lack of diagnosis in childhood, those with ADHD having compensatory mechanisms in place, and negative views of stimulant medication for the treatment of ADHD. Given these challenges and the lack of widespread detailed diagnostic guidelines, prevalence estimates often are incorrect and contribute to the underdiagnosis of adult ADHD. It has been estimated that approximately 4% to 5% of the adult population is impaired by ADHD; however, less than one third of these adults have been diagnosed as having ADHD, likely due to the wide range of barriers to accurate diagnosis (Feifel & MacDonald, 2008). Outside the United States, the number of patients treated for adult ADHD is negligible (Fayyad et al., 2007).

Cultural and societal influences play a large role in how ADHD is viewed and consequently affect the recognition and management of the disorder. Today, it seems that there still are racial and gender discrepancies in representation of ADHD in the media, where individuals with ADHD typically are described as primarily White, middle class, preadolescent boys, thus implying that young children, women, minorities, and older adults generally are less likely to be affected by this disorder (Conrad & Potter, 2000). In the past 20 years, there has been a push in the media to shine light on the neurobiological and genetic causes of ADHD, thus shifting from an emphasis on nonbiological factors such as parenting and diet (Schmitdt, Filippone, & Edelman,

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2003). ADHD has been demonstrated to have a neurobiological basis with 60% to 90% heritability (Faraone & Mick, 2010). Studies comparing ADHD patients with controls show differences in brain volume and deficits in brain functioning (Bekker et al., 2005; Castellanos et al., 2002; Castellanos, Kelly, & Milham, 2009; Lou, Henriksen, Bruhn, Børner, & Nielsen, 1989; Plichta et al., 2009; Snyder & Hall, 2006; T. J. Spencer, Biederman, et al., 2007; Wolf et al., 2009; Zametkin et al., 1990).

The high prevalence of comorbid disorders, estimated at 50% to 75% (Kessler et al., 2006), poses a barrier to proper recognition and treatment of adult ADHD, as many core ADHD symptoms can be nonspecific symptoms of other psychological disorders (Wasserstein, 2005). Moreover, comorbid conditions can affect an individual's treatment pathway for ADHD. Often if substance use disorder (SUD) is present, many fear using a stimulant medication to treat ADHD because they believe it will exacerbate the SUD. However, research has shown that stimulant medication is effective in treating ADHD and does not need to negatively affect treatment of SUD. Furthermore, stimulant medication has shown to have a protective effect in children and adolescents with respect to later substance use problems (Wilens, Faraone, Biederman, & Gunawardene, 2003).

This article discusses factors that should be considered in successfully identifying adult ADHD, including gender differences in presentation and distinguishing among comorbid conditions. It also summarizes research to date on treatment effectiveness in adult ADHD and provides insight into clinical management of patients.

Gender Differences in Presentation

Gender often may not be considered in adult ADHD, but it can affect diagnosis and treatment. Waite and Ivey (2009) explained that because research guidelines currently used in the assessment and diagnosis of ADHD largely are based on Caucasian males, women and those from minority backgrounds may be falling through diagnostic cracks. Furthermore, Caucasian men with ADHD often are referred for any level of impairment, regardless of the level of severity, whereas female or minority adults who are referred to clinics and to clinicians are those usually with significant impairment, which leads to clinical samples that may not be truly representative of those with ADHD. Research suggests that referral bias continues to lead to the underidentification of ADHD in females, specifically those who are younger (Rucklidge, 2008). In a study performed in the United Kingdom, McCarthy et al. (2009) found that among patients with ADHD from ages 15 to 21 years, 89% of prescriptions were issued to male patients.

A retrospective analysis of two placebo-controlled, multicenter studies of adults with ADHD showed significant sex differences in clinical presentation of symptoms, with females more impaired on all measures, including two measures of ADHD, multiple psychological measures, general physical symptoms, and treatment response (Robison et al., 2008). Women were more often given a combined ADHD diagnosis, whereas men were diagnosed more often with inattentive-type ADHD. In addition, women were more likely to have sleep problems, depressive episodes, somatic complaints, and emotional dysregulation than were men.

Table 1. Summary of Sex Differences Across Psychosocial, Cognitive, and Psychiatric Symptoms

Condition	Boys vs. girls	Men vs. women
Hyperactivity/ impulsivity	M > F	M > F
Inattention	F > M	F > M
Poorer coping skills	F > M	F = M
Anxiety	F > M[a]	F = M
Depression	F > M	F = M
Substance abuse	F > M	Inconclusive
Adult psychiatric admissions	NA	F > M
Childhood history of sexual abuse	NA	F > M

Note: Table modified from Rucklidge (2008).
[a]Specifically likely to be separation anxiety disorder.

Recent research also contradicts perceptions that females with ADHD are not as impaired as males with ADHD. Specifically, females with ADHD struggle significantly in all areas of functioning relative to females without ADHD, and with similar rates as ADHD males (Rucklidge, 2008, 2010). Table 1 reports how the occurrence of psychosocial, cognitive, and psychiatric symptoms varies by sex among children and adults. It is noteworthy that females, regardless of age, experience higher levels of inattention than males. In addition, girls are more impaired than boys in areas such as coping skills, anxiety, and depression, whereas in adulthood, females are equally impaired in these areas when compared with men (Rucklidge, 2008).

Comorbidity

A key challenge in newly diagnosing ADHD in adulthood is the high prevalence of comorbidity. The National Comorbidity Survey Replication (NCS-R), conducted in the United States, was the first epidemiological survey that evaluated ADHD among adults in the context of other psychiatric illnesses and disabilities, that is, *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*; American Psychiatric Association, 1994) disorders (Kessler et al., 2006). The likelihood of comorbidity with adult ADHD ranged from 2.7 to 7.5 for mood disorders, 1.5 to 5.5 for anxiety disorders, 1.5 to 7.9 for SUDs, and 3.7 for intermittent explosive disorders (Kessler et al., 2006).

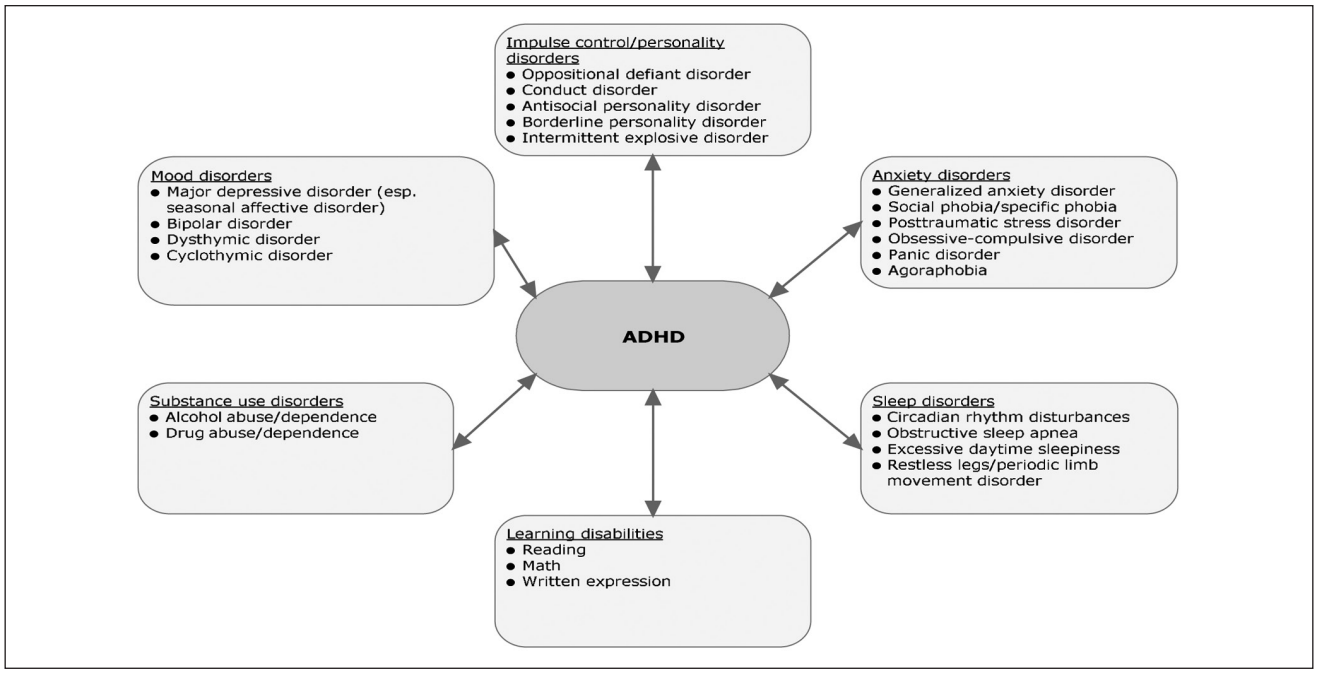

Figure 1. Main comorbid disorders in adult ADHD

Having three or more comorbid disorders was associated with an odds ratio of 7.2 for also having ADHD (Fayyad et al., 2007). The more severe ADHD is, the more likely that the individual will experience comorbidity (Adler, Spencer, Stein, & Newcorn, 2008). Approximately 50% to 87% of individuals with ADHD have at least one other comorbid disorder (Adler, Spencer, et al., 2008; Biederman et al., 1993), and approximately 33% having two or more other comorbid disorders (Adler, Spencer, et al., 2008).

The data from the NCS-R and other studies also examined reverse ADHD in adults with other psychiatric disorders. Findings indicated that a significant number of patients with substance abuse, mood or anxiety disorders, and obesity, and up to 50% of prison inmates also have ADHD (Altfas, 2002; Edvinsson, Bingefors, Lindström, & Lewander, 2010; Fuemmeler, Ostbye, Yang, McClernon, & Kollins, 2011; Ginsberg, Hirvikoski, & Lindefors, 2010; Kessler et al., 2006; Newcorn, Weiss, & Stein, 2007). However, even though a considerable number of patients in specialized treatment programs screened positive for ADHD, less than 10% of patients with another diagnosis had been diagnosed with ADHD, according to the NCS-R (Kessler et al., 2006; Newcorn et al., 2007). ADHD seems to be rarely diagnosed in these at-risk populations, thus questioning whether those treating these populations are screening for or treating this condition (Kooij, 2010; Newcorn et al., 2007).

Figure 1 shows key comorbid conditions associated with adult ADHD. Not only does comorbidity significantly affect the diagnosis of ADHD, but it also affects treatment pathways, treatment persistence, treatment response, insight, self-regulation, and attendance (Newcorn et al., 2007). It is important that clinicians and mental health providers are aware of the comorbid disorders associated with ADHD and are willing and able to detect these conditions. Moreover, it is important to understand the substantial complexity in the relationships among the comorbid conditions, given symptom overlap and the various possible causal pathways among the symptoms. When examining the relationship between ADHD and comorbid disorders, it is not clear whether ADHD and the comorbid disorder represent different facets of the same disorder or whether they are truly independent of each other (Adler, Spencer, et al., 2008). Some comorbid conditions may be a manifestation of ADHD symptoms and their impacts. For example, if an individual with ADHD continued to perform badly at work or school, this could lead to feelings of failure or depression. In addition, some comorbid disorders are possibly genetic variants of ADHD. For example, affective dysregulation or the mood swings that often occur among individuals with ADHD may help explain the relationship between mood, bipolar disorder, and ADHD (Adler, Spencer, et al., 2008; Kooij, Middelkoop, van Gils, & Buitelaar, 2001; Kooij et al., 2010; Reimherr et al., 2005).

Discussed in greater detail the following are mood disorders, anxiety disorders, impulse-control/personality disorders, substance abuse, learning disabilities, and sleep disorders associated with ADHD. Table 2 shows the overlap in symptoms between ADHD and these comorbid conditions.

Table 2. Symptom Overlap Among ADHD and Comorbid Disorders

	ADHD symptoms						ADHD-related symptoms	Non-ADHD symptoms
	Hyperactivity		Impulsivity		Inattention			
	Excessive talkativeness	Restlessness/ psychomotor agitation	Racing thoughts	Impulsive behaviors	Difficulty concentrating	Decreased attention/ distractibility	Mood swings/anger outbursts	
Mood disorders								
Major depressive disorder		√			√	√		Depressed mood, weight loss, diminished interest in activities, suicidal thoughts
Bipolar disorder								Episodic symptoms, fluctuating between major depressive and (hypo) manic symptoms
Euthymic								
Hypomanic	√	√	√	√	√	√	√	
Depressed		√			√	√		
Anxiety disorders								
Generalized anxiety disorder		√			√	√	√	Fatigue, muscle tension, sleep disturbance
Impulse-control/personality disorders								
Antisocial personality disorder				√			√	Delinquent behavior, deceitfulness, disregard for self and others, lack of remorse
Borderline personality disorder				√			√	Abandonment fears, unstable relationships and self-image, suicidal thoughts, paranoid
Substance abuse/ dependence	√	√		√	√			Excessive use of a substance, even when there are serious consequences Dependence: excessive use to the point of dependence on the drug; very difficult to stop using
Sleep disorders		√			√	√		Sleepiness, tiredness

Mood Disorders

Mood disorders are one of the most common disorders comorbid with ADHD (Moss, Nair, Vallarino, & Wang, 2007). According to data from the NCS-R, 38.3% of adult ADHD patients have a comorbid mood disorder, with a lifetime prevalence of 45% (Adler, Spencer, et al., 2008; Kessler et al., 2006). Rates of major depressive disorder among adult patients with ADHD range from 11.5% to 53.5% and dysthymia rates range from 11.5% to 25% (Moss et al., 2007). In clinical samples, the rates of the seasonal affective disorder are up to 10-fold increased in adults with ADHD compared with controls (Amons, Kooij, Haffmans, Hoffman, & Hoencamp, 2006; Levitan, Jain, & Katzman, 1999). Rates of bipolar disorder and cyclothymia are 19.4% and 25%, respectively. When examining reverse comorbidity, 13.1% of adults with a mood disorder have ADHD (Adler, Spencer, et al., 2008; Kessler et al., 2006). This is 3 times the prevalence observed in the general adult population. Major depressive disorder and ADHD share similar symptoms, such as decreased attention, memory,

and concentration. However, major depressive disorder is characterized by a low mood and neuro-vegetative symptoms such as anhedonia and appetite disturbance, whereas ADHD is not (Moss et al., 2007).

Bipolar disorder and ADHD are two distinct disorders that may coexist together, especially bipolar II disorder (Wilens, Biederman, et al., 2003). Both disorders are associated with hyperactivity, racing thoughts, distractibility, impulsivity, and talkativeness although these symptoms are limited to the (hypo)manic episodes in bipolar patients, and they are chronically persistent in ADHD. However, bipolar disorder can be differentiated by the prominence of episodic mood symptoms. Grandiosity, decreased need for sleep, hypersexuality, and racing thoughts are more specific to bipolar disorder. Conversely, adults with ADHD show a chronic pattern of high energy, shortened hours of sleep, "scattered minds," and often cannot slow down or turn off their racing thoughts to attain cognitive relaxation. In addition, patients with ADHD may also have episodic-like deterioration in functioning because ADHD is characterized by variable performance, reactivity, and developmental hurdles. Wilens, Biederman et al., (2003) found that adults with ADHD and bipolar disorder have prototypic symptoms of both disorders, suggesting that both disorders can be distinguished clinically.

Anxiety Disorders

In anxiety disorder patients, it has been shown that approximately 25% also have (subthreshold) ADHD (Fones, Pollack, Susswein, & Otto, 2000; Van Ameringen, Mancini, Simpson, & Patterson, 2010). Rates of generalized anxiety disorder range from 8% to 53% among adult ADHD patients relative to those without ADHD (Moss et al., 2007). Data from the NCS-R show that 47.1% of adults with ADHD had comorbid anxiety disorder, with a lifetime prevalence rate of 59% (Adler, Spencer, et al., 2008; Kessler et al., 2006). When NCS-R examined reverse comorbidity, results indicated that 9.5% of adults with anxiety disorders also have ADHD. Anxiety disorders share symptoms with ADHD such as attention and concentration deficits (Moss et al., 2007). However, with anxiety disorders, there usually are symptoms of psychic and somatic anxiety present, whereas for ADHD these symptoms are not typical. Other anxiety disorders that are more prevalent among ADHD patients as compared with non-ADHD patients include panic disorder, agoraphobia, posttraumatic stress disorder, social phobia, and specific phobia (Moss et al., 2007).

Impulse-Control/Personality Disorders

Impulse-control disorders include disorders such as antisocial and borderline personality disorder, oppositional defiant disorder, conduct disorder, and intermittent explosive disorder (Moss et al., 2007). Data from the NCS-R study found that 19.6% of ADHD patients had impulse-control disorders, with a lifetime prevalence rate of 70% (Adler, Spencer, et al., 2008; Kessler et al., 2006). Among the adults with impulse-control disorders, 12.3% had ADHD. Antisocial and borderline personality disorder share symptoms such as impulsivity and affective lability with ADHD; however, antisocial personality disorder is also characterized by an arrest history and lack of insight and remorse regarding behaviors, and borderline personality by chronic instability in interpersonal relationships and self-esteem (Moss et al., 2007). Longitudinal studies suggest that the prevalence of comorbid antisocial and borderline personality disorder in adults with ADHD is 10- to 13-fold compared with adults without ADHD (Mannuzza, Klein, Bessler, Malloy, & LaPadula, 1993; Miller et al., 2008). In clinical samples of borderline and antisocial personality disorder, 38% to 65% had ADHD in childhood and/or still met criteria for ADHD (Ferrer et al., 2010; Fossati, Novella, Donati, Donini, & Maffei, 2002; Philipsen, Heblinger, & Van Elst, 2008; Semiz et al., 2008). To differentiate ADHD from borderline personality disorder, it is important to know that borderline personality disorder is not characterized by lifetime inattention and hyperactivity but by abandonment fears, self-injurious behavior, and dichotomous thinking: behaviors not typical for ADHD (Kooij, 2010; Moss et al., 2007).

Substance Abuse

Substance abuse and dependence are more common in adults with ADHD than adults without ADHD (Biederman, 2004). Results from the NCS-R indicated that 15.2% of patients with ADHD also have SUDs, with a lifetime prevalence rate of 36% (Adler, Spencer, et al., 2008; Kessler et al., 2006). One study found that adults with ADHD are at 5 times greater risk for substance abuse than adults without ADHD (see Moss et al., 2007, for a review). More specifically, there appears to be a specific relationship between ADHD and nicotine abuse, with a prevalence rate of nicotine use in adults with ADHD twice that of the general population (Adler, Spencer, et al., 2008). Moreover, a relationship has been shown between the number of ADHD symptoms and the chance of smoking in adolescents (Kollins, McClernon, & Fuemmeler, 2005). In addition, the lifetime risk for SUD is approximately 50% in patients whose childhood ADHD persists into adulthood (Biederman et al., 1995). Patients with ADHD are more likely to develop substance abuse problems and at an earlier age than those patients without ADHD (Wilens, Gignac, Swezey, Monuteaux, & Biederman, 2006). However, the relationship between ADHD and substance abuse should be examined more closely, as research has shown that individuals who have been diagnosed and treated properly for ADHD are not at a higher risk for developing a SUD, but

prevalence rates often do not reflect this finding (Faraone, Biederman, Wilens, & Adamson, 2007; Huss, Poustka, Lehmkuhl, & Lehmkuhl, 2008).

In longitudinal studies, the onset of ADHD appears to precede SUDs, lending to the belief that the psychopathology of ADHD is not secondary to SUDs in most patients (Wilens et al., 2006). There are several theories posed to explain the increased risk for SUD among ADHD patients. One theory has proposed that genetically mediated personality traits, novelty seeking, and impulsivity, common to ADHD and SUD, may result from shared neurological substrates (Chambers, Taylor, & Potenza, 2003). Another theory has suggested that ADHD patients self-medicate to relieve symptoms of ADHD, and the impulsivity and poor judgment lead to the dependence on substances (Khantzian, 1975). Last, some believe that ADHD patients use substances to gain social acceptance (Moss et al., 2007).

Learning Disabilities

A learning disability can significantly affect one's ability to excel in school but even more so among those with ADHD. Learning disabilities also often co-occur with ADHD (Knivsberg & Andreassen, 2008). Adults with ADHD report having had problems in school similar to those in children with ADHD (Biederman, 2004). ADHD and learning disabilities result in an increased risk for poorer grades, grade repetition, school dropout, and working below one's ability (Adler, Spencer, et al., 2008). Biederman and colleagues (1994) found that 32% of men and 17% of women with ADHD had repeated a grade. Adults also reported that they were frequently placed in special classes or received extra help because of academic difficulties, compared with adults without ADHD. Difficulties when assessing a comorbid learning disability are distinguishing between inattention as part of ADHD versus reading difficulties and between an individual's capacities versus achievement (Adler, Spencer, et al., 2008).

Sleep Disorders

Given that the same anatomical and functional central nervous system regions that are responsible for sleep regulation are also involved in presentation of symptoms associated with ADHD, the relationship between the two disorders is perhaps not surprising (Owens, 2005). Still, it is only relatively recently that the relationship has been directly studied, and many gaps remain regarding the exact mechanisms by which sleep is disturbed by ADHD and the role of treatment in improving or exasperating sleep disturbance (Adler, Shaw, Sitt, Maya, & Morrill, 2009). The focus of the research has typically been on children and adolescents, where associations between ADHD and sleep problems such as restless sleep, excessive daytime sleepiness, sleep apnea, periodic leg movement, and sleep onset insomnia related to a delayed onset of melatonin have been documented (Adler, Goodman, Weisler, Hamdani, & Roth, 2009; Chervin et al., 1997; 2002; Cortese et al., 2006; Crabtree et al., 2003; Picchietti et al., 1999; Van der Heijden, Smits, Van Someren, & Gunning, 2005).

Further complicating the comprehension of this relationship is the fact that it is bidirectional; ADHD is thought to affect sleep, and sleep disturbances are thought to affect ADHD symptoms (Adler, Goodman, et al., 2009). In addition, other behaviors known to contribute to sleep disturbances, such as cigarette use, caffeine intake, and obesity tend to appear in higher levels in adults with ADHD and thus it is increasingly difficult to tease out the exact role of ADHD symptoms in the sleep disorder (Adler, Goodman, et al., 2009; Altfas, 2002; Dalby, 1985; Wolk & Somers, 2007). In a study of adults with ADHD, Kooij et al. (2001) found that adults had detriments in sleep quality and experienced higher levels of nocturnal motor activity compared with matched controls. Furthermore, Philipsen and colleagues (2005) found that adults with ADHD had higher levels of nocturnal motor activity and more frequent arousals compared with controls. Recent studies in adults with ADHD found a delayed onset of dim light melatonin (DLMO) and a delayed 24-hr activity pattern as well as a relationship between seasonality scores and circadian preference (Rybak, McNeely, Mackenzie, Jain, & Levitan, 2007; Van Veen, Kooij, Boonstra, Gordijn, & Van Someren, 2010). These findings with respect to circadian disturbances in adults with ADHD are comparable with those in children and need further study.

Clinical Management

Treatment options for adult ADHD can include a variety of modalities, such as psycho-education, pharmacotherapy, cognitive-behavioral therapy (CBT), academic support, ADHD coaching, and so on. In general, a combination of CBT and pharmacotherapy is currently the first choice of treatment for adult ADHD and is considered superior to medication alone (Ramsay, 2007; Safren et al., 2005). CBT's emphasis on self-control strategies is deemed especially useful in the treatment of problems with impulsiveness (Kolar et al., 2008). CBT's efficacy has been demonstrated in multiple studies (Hesslinger et al., 2002; Rostain & Ramsay, 2006; Safren, 2006), though small sample sizes and lack of an adequate control group are often limiting factors (Kolar et al., 2008). There have been no studies to date assessing the efficacy of psychotherapy compared with pharmacotherapy on a randomized, double-blind basis (Philipsen et al., 2008).

Often, treatment with stimulants (methylphenidates [MPH] and amphetamines) is the first-line medication of

choice (Kolar et al., 2008; Kooij et al., 2010; Meijer, Faber, van den Ban, & Tobi, 2009). Research has shown that adults seem to respond to stimulant medications in similar ways as children, thus supporting the validity of ADHD in adults (Coghill, 2004; Krause, Krause, Dresel, La Fougere, & Ackenheil, 2006). Despite what some critics say, stimulants are still considered the most effective medications for the treatment of adult ADHD (R. M. Spencer, Ivry, & Zelaznik, 2005). MPH, commonly the first-line treatment in Europe, is available as (a) short acting (immediate release), (b) intermediate acting (sustained release), and (c) long acting (extended release), with short-acting MPH considered useful as a supplement to once-daily medication or to allow more flexibility for the patient (Kolar et al., 2008). Dextroamphetamines, mixed amphetamine salts (extended release), and lisdexamfetamine (prodrug and long-acting formulation) are other classes of stimulants, which are also commonly used in the treatment of adult ADHD.

Nonstimulants are also used, particularly in the 10% to 30% of patients who do not respond to stimulants and who cannot tolerate their side effects or in certain comorbidities like anxiety and SUDs (Kolar et al., 2008; T. Spencer, Biederman, & Wilens, 2004). More specifically, the noradrenaline reuptake inhibitor, atomoxetine, has also been shown to be efficacious in adults with ADHD. Atomoxetine is the primary nonstimulant used in the treatment of adult ADHD and, though its onset of action is slower than that of stimulants, it has a 24-hr duration of action, and has no abuse potential which can be important when treating adults with comorbid substance abuse problems (M. D. Weiss & Weiss, 2004). Two randomized, double blind, placebo-controlled multicenter studies demonstrated that atomoxetine was superior to placebo in the improvement of adult ADHD symptoms (Michelson et al., 2003).

One qualitative study focused on the psychological impacts of receiving a diagnosis of ADHD in adulthood and treatment with medication (Young, Chesney, Sperlinger, Misch, & Collins, 2009). All participants described an initial sense of relief that they finally had an explanation for their difficulties. This was followed by some anxiety and an adjustment process. Participants reported positive influence of stimulant medication, explaining that the tablet made them feel a sense of normality as opposed to feeling different from others, and that it also had a positive impact on their ability to function more successfully in their daily lives. The medication made them feel more directed and improved their interpersonal interactions in that they did not interrupt others so often. With medication, the participants felt positive about the future and that they could complete tasks and achieve their goals.

Even though pharmacotherapy has been shown to be effective in adults with ADHD, research has indicated that the prevalence of prescribing by physicians to patients with ADHD drops significantly from age 15 to 21 (McCarthy et al., 2009). This decrease is greater than the reported age-related decline in symptoms, suggesting that treatment may be prematurely discontinued in some young adults who continue to experience ADHD symptoms.

Pharmacotherapy Efficacy

Krause and Krause (as cited in Trott, 2006) reported that across a number of double-blind, placebo-controlled studies of pharmacotherapy treatment in adult ADHD (Bouffard, Hechtman, Minde, Laboni-Kassab, 2003; Kooij et al., 2004; Paterson, Douglas, Hallmayer, Hagan, & Krupenia, 1999; T. Spencer, Biederman, et al., 2005; T. Spencer, Biederman, & Wilens, 1998; T. Spencer et al., 1995; Wilens, Spencer, & Biederman, 2002), response rates ranged from 50% to 78%. This range is consistent with more recent studies (e.g., Adler, Goodman, et al., 2008; Wigal et al., 2010). Torgersen, Gjervan, and Rasmussen (2008) conducted a comprehensive review of available treatments. They identified 18 randomized, placebo-controlled studies of MPH in adult ADHD, where 11 of the studies found a significant improvement in symptoms as compared with placebo (Biederman, Mick, et al., 2006; Bouffard et al., 2003; Carpentier, de Jong, Dijkstra, Verbrugge, & Krabbe, 2005; Gualtieri, Ondrusek, & Finley, 1985; Kooij et al., 2004; Kuperman et al., 2001; E. D. Levin, Conners, Silva, Canu, & March, 2001; F. R. Levin, Evans, Brooks, & Garawi, 2007; F. R. Levin, Evans, et al., 2006; Mattes, Boswell, & Oliver, 1984; Reimherr et al., 2007; Schubiner et al., 2002; T. Spencer, Biederman, et al., 2005; T. Spencer et al., 1995; Tenenbaum, Paull, Sparrow, Dodd, & Green, 2002; Wender, Reimherr, Wood, & Ward, 1985; Wood, Reimherr, Wender, Glen, & Johnson, 1976); 6 randomized, placebo-controlled trials with amphetamines, which all found a significant improvement in symptoms compared with placebo (Paterson et al., 1999; T. Spencer et al., 2001; Taylor & Russo, 2000, 2001; Weisler et al., 2006; M. Weiss & Hechtman, 2006); 8 randomized, placebo-controlled studies of nonstimulants in adult ADHD (including bupropion, atomoxetine/tomoxetine, and desipramine) in which 3 of the studies found significant improvement as compared with placebo; and 3 randomized, controlled studies of psychotherapy in adult ADHD, which all showed an improvement, when combined with pharmacotherapy, in ADHD symptoms (Safren et al., 2005; Stevenson, Whitmont, Bornholt, Livesey, & Stevenson, 2002; Stevenson, Stevenson, & Whitmont, 2003).

Psychiatric treatment recommendations often are based on evidence from systematic reviews (Cornforth et al., 2010; Koesters, Becker, Kilian, Fegert, & Weinmann, 2009). Current guidelines for the treatment of adult ADHD recommend MPH as first-line treatment (Koesters et al., 2009; National Institute for Health and Clinical Excellence [NICE], 2009). To date, there have been five systematic reviews of ADHD treatment that include adult populations:

Faraone, Spencer, Aleardi, Pagano, and Biederman (2004); Faraone and Glatt (2010); Jadad, Boyle, Cunningham, Kim, and Schachar (1999); McDonagh and Peterson (2006); and Castells, Ramos-Quiroga, Bosch, Nogueira, and Casas (2011); of these, only the Faraone studies used meta-analytic methods. Given the methodological limitations in the Faraone et al., (2004) study, Faraone and Glatt (2010) updated the respective analyses. The findings, based on 19 trials that studied 13 drugs, showed that stimulant and nonstimulant medications are effective for treating ADHD in adults; however, stimulant medications showed greater efficacy (effects sizes = 0.73 vs. 0.39, respectively).

Koesters and colleagues (2009) also updated the Faraone et al. (2004) meta-analysis through a systematic review of randomized controlled trials (RCT's) evaluating MPH in the treatment of adult ADHD. They identified 18 studies that met the inclusion criteria for their review, of which 16 were included in their final meta-analysis. Koesters et al., similar to Faraone et al, found a significant effect of MPH compared with placebo on the symptoms of adult ADHD. However, they found an effect size of $d = 0.42$ (95% confidence interval = [0.20, 0.63]).

Koesters and colleagues (2009) noted that these results may challenge the current guideline recommendations and that it is reasonable to suggest that other treatment options for adult ADHD must be evaluated prior to continuing to recommend stimulants as first-line treatment. They further note that although other treatments such as psychotherapeutic interventions have demonstrated efficacy in two trials (Hesslinger et al., 2002; Stevenson et al., 2002), there is a dearth of published research in this area. Most recently, Castells et al. (2011) completed a Cochrane-based meta-analysis of amphetamines in adult ADHD. The analysis was based on seven studies, which enrolled 1,091 participants; all studies were placebo-controlled and three included an active comparator. The findings showed that amphetamines were more efficacious than placebo for reducing ADHD symptoms irrespective of the efficacy definition used.

With respect to driving impairment, simulation studies provide evidence that stimulant treatment may help individuals with ADHD. Cox and colleagues performed a series of randomized, crossover studies involving driving simulator tests or on-road testing that examined the potential benefits of MPH on driving performance (Cox et al., 2006; Cox, Humphrey, Merkel, Penberthy, & Kovatchev, 2004; Cox, Merkel, Kovatchev, & Seward, 2000). Although the sample sizes were small, the findings showed that MPH improved driving performance of individuals with ADHD in areas including inattentive driving errors for on-road performance, speeding, inappropriate braking, and percentage of missed stops (Barkley & Cox, 2007). Furthermore, a separate study found a positive correlation between the dosage of treatment, controlled-release MPH, and improvement in driving performance (Cox et al., 2004). Kay, Michaels, and Pakull (2009) conducted a 6-week, randomized, single-center, double-blind, placebo-controlled, crossover study in which the effect of extended-release mixed amphetamine salts on driving performance was evaluated and found to reduce negative driving behaviors, including tailgating, driving-out-of-lane demarcations, and citation rates compared with placebo.

Managing Comorbidity

With respect to adults with ADHD and depression, positive outcomes have been reported for patients who do not respond to the stimulant monotherapy when an additional medication to treat depression is added to the treatment plan (Krause et al., 2006). Several authors recommend treating comorbid disorders such as depression and anxiety first, and then reassessing the degree of ADHD-caused impairments to create an effective treatment plan (Kooij et al., 2010; Philipsen et al., 2008).

It is noteworthy to mention that very few studies focus on treatment in patients with ADHD and comorbid SUDs (Bukstein, 2008; Carpenter et al., 2005). Nevertheless, most of the literature supports the use of multimodal therapy, although the role of stimulant medication is less clear (Bukstein, 2008). Research has yielded mixed results with respect to treating ADHD with stimulants when the patient has a SUD. One study that examined CBT, MPH, and placebo as treatment options for adult cocaine-dependent ADHD patients found that there were no significant differences in the two treatment groups in terms of mean improvement in ADHD symptoms (F. R. Levin et al., 2007). However, those treated with MPH, who showed improvement in ADHD symptoms, were more likely to have a reduction in cocaine abuse.

Research has shown that treatment with stimulants improves sleep problems associated with ADHD. In a randomized study, Adler, Goodman, et al. (2009) assessed the impact of lisdexamfetamine dimesylate (LDX) on sleep quality in adults with ADHD and found that for most of their participants on dosages of LDX varying from 30 ($n = 119$), 50 ($n = 117$), or 70 ($n = 122$) mg compared with those on placebo ($n = 62$), LDX improved the daytime functioning of adults with ADHD without worsening their sleep quality. Sobanski, Schredl, Kettler, and Alm (2008) assessed the role of MPH on sleep problems and found in a two-group comparison and open-label treatment study that untreated ADHD patients exhibited more nocturnal awakenings, lower rates of rapid eye movement (REM) sleep, higher nocturnal activity, and reduced sleep efficiency when compared with controls, as measured by polysomnographic recordings and subjective reports. Patients treated with MPH showed improvements in increased sleep efficiency and self-reported feelings of enhanced sleep quality. This study contrasts with earlier work by Philipsen et al. (2005) who reported no

polysomnographic differences when comparing adults with ADHD with healthy controls. Similar results as in Sobanski's study were found for untreated adults with ADHD compared with controls in a small actigraphy study by Kooij et al. (2001). Patients reported better sleep quality after treatment with MPH and actigraphy measures supported less nocturnal awakenings compared with baseline.

Consequences of Untreated Versus Treated ADHD

Untreated ADHD in childhood and adulthood has various consequences. Asherson, Chen, Craddock, and Taylor (2007) noted that adults with untreated ADHD may be currently using more medical resources than they would if treated, given the links between ADHD and smoking, substance abuse, obesity, and serious accidents. A major concern is substance abuse. Research has shown that treatment of ADHD may decrease the likelihood of a future SUD (Huss et al., 2008; Wilens, Faraone, et al., 2003). Pinkhardt et al. (2009) indicated that in untreated adults with ADHD, comorbidity is rather the rule than the exception.

Research suggests that those treated properly for their ADHD have better long-term outcomes. In a 2008 Norwegian study, Goksøyr and Nøttestad examined adults with a current diagnosis of ADHD who had been treated with stimulants during childhood and adolescence, and those who had not. Although there are methodological difficulties in designing a study that would be able to definitively link differences in substance abuse, functioning, and quality of life to childhood/adolescent stimulant use, the study did show a link between lower "Index of Burden" scores, which measured variables including alcohol and substance abuse, criminality, functioning, and quality of life, and childhood/adolescent stimulant use. In addition, they found that relative to those treated with stimulants, untreated adults with ADHD had a higher degree of psychological strain and more difficulties with managing important areas in life.

In another similar study, researchers in Norway conducted a retrospective study of 414 adult ADHD and 357 population-based controls. They found that early recognition and treatment of ADHD was a strong predictor of being in work as an adult, independent of comorbidity, substance abuse, and current treatment (Halmoy, Fasmer, Gillberg, & Haavik, 2009). They found that 24% of the adults with ADHD reported being in work compared with 79% in the control group. Combined subtype of ADHD, substance abuse, and reported history of depression or anxiety were correlated with being out of work. Current and past medical treatment of ADHD was correlated with being in work; logistic regression analyses showed that stimulant therapy during childhood was the strongest predictor for being in work as adults (odds ratio = 3.2; $p = .014$).

Concerns Regarding Treatment Abuse

A major factor contributing to variability in diagnosis and treatment across countries is the attitude toward the use and fears surrounding the abuse of stimulants specifically among SUDs. The relationship between ADHD and SUD is unclear because although an association has been identified, studies on the issue have been naturalistic rather than randomized, controlled trials (Wilens, 2004). Although there have been more than 200 controlled studies on the efficacy and safety of stimulants in children (Schachter, Pham, King, Langford, & Moher, 2001; T. J. Spencer et al., 1996) and evidence for safety and efficacy among adults with ADHD (Faraone et al., 2004), these fears still persist (Asherson, 2004). Furthermore, the evidence shows that rates of drug addiction and abuse are reduced by up to 50% for ADHD patients who are treated for their symptoms with stimulants (Huss & Lehmkuhl, 2002). In the United Kingdom, people tend to worry about the abuse of stimulants, especially short-acting dexamphetamine. In the Netherlands, there is less concern about abuse of stimulants, as other drugs available on the street are more potent to obtain their "high."

Several studies indicate that ADHD children treated with medication are less likely to develop a SUD in adolescence and adulthood (Table 3). Biederman and colleagues (2008) investigated the association between stimulant treatment in children and adolescents and subsequent SUDs in the young adult years through a prospective follow-up study of 112 Caucasian children with ADHD. Participants were assessed at baseline and then at a 10-year follow-up. Results showed that there was no evidence that stimulant treatment in childhood or adolescence increases or decreases the risk for subsequent SUDs in young adulthood. With similar findings, Faraone et al. (2007) found that the use of pharmacotherapy does not cause subsequent SUDs. Faraone and colleagues used retrospective data to assess the impact of prior ADHD pharmacotherapy on SUDs in 206 adults with ADHD.

Furthermore, a few studies have shown that stimulant use for the treatment of childhood ADHD can help reduce the risk of future substance use problems. Wilens, Faraone, et al. (2003) performed a meta-analytic review of the literature regarding long-term studies in which youths treated with pharmacotherapy and untreated youths with ADHD were examined for later SUDs. Six studies were included in the analysis, and the results indicated that stimulant therapy in childhood is associated with a reduced risk for subsequent alcohol and drug use disorders. Similarly, Huss and colleagues (2008) examined the long-term effects of MPH treatment in ADHD children with regard to future development of nicotine use disorders. Results showed that there was no negative long-term effect of stimulant medication on nicotine use disorders. In addition, the findings supported the idea that long-term treatment of children with

Table 3. Substance Use Disorder Outcomes in Treated Versus Untreated Childhood ADHD

Authors	Design	*n*	Outcome	Results
Wilens, Faraone, Biederman, and Gunawardene (2003)	Data from six prospective and retrospective studies used in a meta-analysis	1,034	Subsequent SUD	Stimulant therapy in childhood associated with reduction in SUD risk
Faraone, Biederman, Wilens, and Adamson (2007)	Naturalistic design; adult participants grouped into no treatment, past pharmacologic treatment, and current and past pharmacologic treatment	206	*DSM-IV* (SCID); drug use screening inventory (DUSI)	Pharmacotherapy did not cause subsequent SUDs; did not provide protective effect either
Biederman (2008)	10-year naturalistic follow-up study evaluating male Caucasian children with ADHD	112	Subsequent SUD	No statistically significant associations between stimulant treatment and alcohol, drug, or nicotine use disorders
Huss, Poustka, Lehmkuhl, and Lehmkuhl (2008)	Multisite retrospective nonrandomized longitudinal study with ADHD children (diagnosis at 9.2 years of age; reassessment for SUD-N at 21.9 years of age) looking at MPH treated children and drug naïve children	215	Nicotine	MPH did not induce nicotine use disorders and may in fact delay onset for continuous nicotine consumption in ADHD patients

Note: SUD = substance use disorder; *DSM-IV* = *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.); SCID = Structured Clinical Interview for *DSM-IV*; MPH = methylphenidates

MPH starting in the early years may have some protective effect on the consumption of nicotine (Huss et al., 2008).

There is concern regarding misuse of stimulants by patients with ADHD who share their prescribed medication with family or peers, or by obtaining stimulants without prescription via the Internet (Rabiner et al., 2009). Recent prevalence estimates of misuse, however, do not exceed the prevalence rate of ADHD (Lord et al., 2009). One segment of the population particularly prone to suspicions of abuse of ADHD medications is college students. Wilens et al. (2006), in the United States, found, in a sample of older adolescents and adults who were receiving psychotropic drugs and were comorbid for ADHD, that 11% reported having sold their medications and twice as many patients with ADHD (10%), compared with controls (5%), admitted to having gotten "high" on their prescribed medication. Still, one factor that must be taken into account is whether these students who are "abusing" the stimulants are simply undiagnosed ADHD patients who need the medication to focus and perform at the level of their peers academically. Rostain and Ramsay (2007) discussed how many students who request help for ADHD symptoms have self-diagnosed themselves after trying a friend's stimulant medication and finding that it helped improve focus.

Conclusion

In summary, given the breadth and overlap of symptoms with other disorders, as well as differences in presentation by age and gender, adult ADHD may be a difficult disorder to detect and effectively manage for the untrained professional. Kooij and colleagues (2010) have developed a new diagnostic interview for ADHD in adults (DIVA 2.0; available for free at www.divacenter.eu) that may be used to better elucidate the presence of ADHD in psychiatric populations. Increasing awareness of this condition and introducing standardized clinical management guidelines will help to limit the development of chronicity in adult ADHD and comorbidity (Kooij et al., 2010). Just as behavioral and medical treatment are effective with childhood ADHD, they can be just as effective in adults given accurate diagnosis of ADHD and comorbid conditions in this life phase. Clinicians can improve health outcomes in their patients with a comprehensive understanding of the complex profile of ADHD in adulthood, and ultimately, society may benefit from less health care costs, increased work performance, and fewer days of sick leave in treated patients.

Declaration of Conflicting Interests

Dr. Asherson has been a member of advisory boards to Shire, Janssen-Cilag, Eli Lilly, and Flynn Pharma, and taken part in educational meetings sponsored by these companies. He has received recent financial support for research and educational activities on ADHD from the National Institute of Health Research (UK NIHR), Action Medical Research, the Wellcome Trust, Vifor, Shire, and Janssen-Cilag. Dr. Akehurst has received consultancy fees from Shire on numerous occasions in the past, but he has no other conflicts of interest. Dr. Kooij has been a speaker for

Janssen-Cilag, Eli Lilly BV, and Shire, and has received unrestricted research grants from Janssen-Cilag and Shire. Dr. Huss serves as a speaker and consultant and on advisory boards for Eli Lilly, Engelhardt, Janssen-Cilag, Medice, Novartis, Shire, and Steiner-Arzneimittel. Ms. Beusterien is an employee of Oxford Outcomes, an ICON plc company, which provides consulting services to Shire. Dr. Sasané has no current conflicts of interest. Ms. French has no current conflicts of interest. Dr. Hodgkins is employed by Shire Pharmaceuticals and owns stock/stock options in the company. Shire develops and markets drugs to treat central nervous system (CNS) disorders including ADHD.

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References

Adler, L. A., Goodman, D. W., Kollins, S. H., Weisler, R. H., Krishnan, S., Zhang, Y., & Biederman, J. (2008). Double-blind, placebo-controlled study of the efficacy and safety of lisdexamfetamine dimesylate in adults with attention-deficit/hyperactivity disorder. *Journal of Clinical Psychiatry, 69*, 1364-1373.

Adler, L. A., Goodman, D., Weisler, R., Hamdani, M., & Roth, T. (2009). Effect of lisdexamfetamine dimesylate on sleep in adults with attention-deficit/hyperactivity disorder. *Behavioral and Brain Function, 5*, 34.

Adler, L. A., Shaw, D., Sitt, D., Maya, E., & Morrill, M. (2009). Issues in the diagnosis and treatment of adult ADHD by primary care physicians. *Primary Psychiatry, 16*, 57-63.

Adler, L. A., Spencer, T. J., Stein, M. A., & Newcorn, J. H. (2008). Best practices in adult ADHD: Epidemiology, impairments, and differential diagnosis. *CNS Spectrums, 13*, 1-19.

Altfas, J. R. (2002). Prevalence of attention deficit/hyperactivity disorder among adults in obesity treatment. *BMC Psychiatry, 2*, 9.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

Amons, P. J., Kooij, J. J., Haffmans, P. M., Hoffman, T. O., & Hoencamp, E. (2006). Seasonality of mood disorders in adults with lifetime attention-deficit/hyperactivity disorder (ADHD). *Journal of Affective Disorders, 91*, 251-255.

Asherson, P. (2004). Bridging the service gap: Invited commentary on attention-deficit hyperactivity disorder in adults. *Advances in Psychiatric Treatment, 10*, 257-259.

Asherson, P., Chen, W., Craddock, B., & Taylor, E. (2007). Adult attention-deficit hyperactivity disorder: Recognition and treatment in general adult psychiatry. *British Journal of Psychiatry, 190*, 4-5.

Barkley, R. A., & Cox, D. (2007). A review of driving risks and impairments associated with attention-deficit/hyperactivity disorder and the effects of stimulant medication on driving performance. *Journal of Safety Research, 38*, 113-128.

Bekker, E. M., Overtoom, C. C., Kooij, J. J., Buitelaar, J. K., Verbaten, M. N., & Kenemans, J. L. (2005). Disentangling deficits in adults with attention-deficit/hyperactivity disorder. *Archives of General Psychiatry, 62*, 1129-1136.

Biederman, J. (2004). Impact of comorbidity in adults with attention-deficit/hyperactivity disorder. *Journal of Clinical Psychiatry, 65*(Suppl. 3), 3-7.

Biederman, J., Faraone, S. V., Spencer, T. J., Wilens, T., Mick, E., & Lapey, K. A. (1994). Gender differences in a sample of adults with attention deficit hyperactivity disorder. *Psychiatry Research, 53*, 13-29.

Biederman, J., Faraone, S. V., Spencer, T. J., Wilens, T., Norman, D., Lapey, K. A., . . . Doyle, A. (1993). Patterns of psychiatric comorbidity, cognition, and psychosocial functioning in adults with attention deficit hyperactivity disorder. *American Journal of Psychiatry, 150*, 1792-1798.

Biederman, J., Mick, E., Surman, C., Doyle, R., Hammerness, P., Harpold, T., . . . Spencer, T. (2006). A randomized, placebo-controlled trial of OROS methylphenidate in adults with attention-deficit/hyperactivity disorder. *Biological Psychiatry, 59*, 829-835.

Biederman, J., Monuteaux, M. C., Spencer, T., Wilens, T. E., MacPherson, H. A., & Faraone, S. V. (2008). Stimulant therapy and risk for subsequent substance use disorders in male adults with ADHD: A naturalistic controlled 10-year follow-up study. *American Journal of Psychiatry, 165*, 597-603.

Biederman, J., Wilens, T., Mick, E., Milberger, S., Spencer, T. J., & Faraone, S. V. (1995). Psychoactive substance use disorder in adults with attention deficit hyperactivity disorder (ADHD): Effects of ADHD and psychiatric comorbidity. *American Journal of Psychiatry, 152*, 1652-1658.

Bouffard, R., Hechtman, L., Minde, K., Laboni-Kassab, F. (2003). The efficacy of 2 different dosages of methylphenidate in treating adults with attention-deficit hyperactivity disorder. *Canadian Journal of Psychiatry, 48*, 546-554.

Bukstein, O. (2008). Substance abuse in patients with attention-deficit/hyperactivity disorder. *MedGenMed: Medscape General Medicine, 10*, 24.

Carpenter, L. L., Milosavljevic, N., Schecter, J. M., Tyrka, A. R., & Price, L. H. (2005). Augmentation with open-label atomoxetine for partial or nonresponse to antidepressants. *Journal of Clinical Psychiatry, 66*, 1234-1238.

Carpentier, P. J., de Jong, C. A., Dijkstra, B. A., Verbrugge, C. A., & Krabbe, P. F. (2005). A controlled trial of methylphenidate in adults with attention deficit/hyperactivity disorder and substance use disorders. *Addiction, 100*, 1868-1874.

Castellanos, F. X., Kelly, C., & Milham, M. P. (2009). The restless brain: Attention-deficit hyperactivity disorder, resting-state functional connectivity, and intrasubject variability. *Canadian Journal of Psychiatry, 54*, 665-672.

Castellanos, F. X., Lee, P. P., Sharp, W., Jeffries, N. O., Greenstein, D. K., Clasen, L. S., . . . Rapoport, J. L. (2002). Developmental trajectories of brain volume abnormalities in children and

adolescents with attention-deficit/hyperactivity disorder. *Journal of the American Medical Association, 288*, 1740-1748.

Castells, X., Ramos-Quiroga, J. A., Bosch, R., Nogueira, M., & Casas, M. (2011). Amphetamines for attention deficit hyperactivity disorder (ADHD) in adults. *Cochrane Database of Systematic Reviews,* Issue 6. Art. No. CD007813. doi:10.1002/14651858.CD007813.pub2

Chambers, R. A., Taylor, J. R., & Potenza, M. N. (2003). Developmental neurocircuitry of motivation in adolescence: A critical period of addiction vulnerability. *American Journal of Psychiatry, 160*, 1041-1052.

Chervin, R. D., Archbold, K. H., Dillon, J. E., Pituch, K. J., Panahi, P., Dahl, R. E., & Guilleminault, C. (2002). Associations between symptoms of inattention, hyperactivity, restless legs, and periodic leg movements. *Sleep, 25*, 213-218.

Chervin, R. D., Dillon, J. E., Bassetti, C., Ganoczy, D. A., & Pituch, K. J. (1997). Symptoms of sleep disorders, inattention, and hyperactivity in children. *Sleep, 20*, 1185-1192.

Coghill, D. (2004). Understudied and underrecognised: Invited commentary on attention-deficit hyperactivity disorder in adults. *Advances in Psychiatric Treatment, 10*, 338-340.

Conrad, P., & Potter, D. (2000). From hyperactive children to ADHD adults: Observations on the expansion of medical categories. *Social Problems, 47*, 559-582.

Cornforth, C., Sonuga-Barke, E., & Coghill, D. (2010). Stimulant drug effects on attention deficit/hyperactivity disorder: A review of the effects of age and sex of patients. *Current Pharmaceutical Design, 16*, 2424-2433.

Cortese, S., Konofal, E., Yateman, N., Mouren, M. C., & Lecendreux, M. (2006). Sleep and alertness in children with attention-deficit/hyperactivity disorder: A systematic review of the literature. *Sleep, 29*, 504-511.

Cox, D. J., Humphrey, J. W., Merkel, R. L., Penberthy, J. K., & Kovatchev, B. (2004). Controlled-release methylphenidate improves attention during on-road driving by adolescents with attention-deficit/hyperactivity disorder. *Journal of American Board Family Practice, 17*, 235-239.

Cox, D. J., Merkel, R. L., Kovatchev, B., & Seward, R. (2000). Effect of stimulant medication on driving performance of young adults with attention-deficit hyperactivity disorder: A preliminary double-blind placebo-controlled trial. *Journal of Nervous and Mental Disease, 188*, 230-234.

Cox, D. J., Merkel, R. L., Moore, M., Thorndike, F., Muller, C., & Kovatchev, B. (2006). Relative benefits of stimulant therapy with OROS methylphenidate versus mixed amphetamine salts extended release in improving the driving performance of adolescent drivers with attention-deficit/hyperactivity disorder. *Pediatrics, 118*, 704-710.

Crabtree, V. M., Ivaneko, A., O'Brien, L. M., & Gozal, D. (2003). Periodic limb movement disorder of sleep in children. *Journal of Sleep Research, 12*, 73-81.

Dalby, J. T. (1985). Will population decreases in caffeine consumption unveil attention deficit disorder in adults. *Medical Hypotheses, 18*, 163-167.

Edvinsson, D., Bingefors, K., Lindström, E., & Lewander, T. (2010). ADHD-related symptoms among adults in out-patient psychiatry and female prison inmates as compared with the general population. *Upsala Journal of Medical Sciences, 115*, 30-40.

Faraone, S. V., Biederman, J., Wilens, T. E., & Adamson, J. (2007). A naturalistic study of the effects of pharmacotherapy on substance use disorders among ADHD adults. *Psychological Medicine, 37*, 1743-1752.

Faraone, S. V., & Glatt, S. J. (2010). A comparison of the efficacy of medications for adult attention-deficit/hyperactivity disorder using meta-analysis of effect sizes. *Journal of Clinical Psychiatry, 71*, 754-763.

Faraone, S. V., & Mick, E. (2010). Molecular genetics of attention deficit hyperactivity disorder. *Psychiatric Clinics of North America, 33*, 159-180.

Faraone, S. V., Spencer, T., Aleardi, M., Pagano, C., & Biederman, J. (2004). Meta-analyses of the efficacy of methylphenidate for treating adult attention-deficit/hyperactivity disorder. *Journal of Clinical Psychopharmacology, 24*, 24-29.

Faraone, S. V., Wilens, T. W., Petty, C., Antshel, S., Spencer, T., & Biederman, J. (2007). Substance use among ADHD adults: Implications of late onset and subthreshold diagnoses. *American Journal on Addictions, 16*, 24-34.

Fayyad, J., De Graaf, R., Kessler, R., Alonso, J., Angermeyer, M., Demyttenaere, K., . . . Zaslavsky, A. M. (2007). Cross national prevalence and correlates of adult attention-deficit hyperactivity disorder. *British Journal of Psychiatry, 190*, 402-409.

Feifel, D., & MacDonald, K. (2008). Attention-deficit/hyperactivity disorder in adults: Recognition and diagnosis of this often-overlooked condition. *Postgraduate Medicine, 120*, 39-47.

Ferrer, M., Andión, O., Matalí, J., Valero, S., Navarro, J. A., Ramos-Quiroga, J. A., . . . Casas, M. (2010). Comorbid attention-deficit/hyperactivity disorder in borderline patients defines an impulsive subtype of borderline personality disorder. *Journal of Personality Disorders, 24*, 812-822.

Fones, C. S., Pollack, M. H., Susswein, L., & Otto, M. (2000). History of childhood attention deficit hyperactivity disorder (ADHD) features among adults with panic disorder. *Journal of Affective Disorders, 58*, 99-106.

Fossati, A., Novella, L., Donati, D., Donini, M., & Maffei, C. (2002). History of childhood attention deficit/hyperactivity disorder symptoms and borderline personality disorder: A controlled study. *Comprehensive Psychiatry, 43*, 369-377.

Fuemmeler, B. F., Ostbye, T., Yang, C., McClernon, F. J., & Kollins, S. H. (2011). Association between attention-deficit/hyperactivity disorder symptoms and obesity and hypertension in early adulthood: A population-based study. *International Journal of Obesity, 35*, 852-862.

Ginsberg, Y., Hirvikoski, T., & Lindefors, N. (2010). Attention deficit hyperactivity disorder (ADHD) among longer-term prison inmates is a prevalent, persistent and disabling disorder. *BMC Psychiatry, 10*, 112.

Goksøyr, P. K., & Nøttestad, J. A. (2008). The burden of untreated ADHD among adults: The role of stimulant medication. *Addictive Behaviors, 33*, 342-346.

Gualtieri, C. T., Ondrusek, M. G., & Finley, C. (1985). Attention deficit disorders in adults. *Clinical Neuropharmacology, 8*, 343-356.

Halmoy, A., Fasmer, O. B., Gillberg, C., & Haavik, J. (2009). Occupational outcome in adult ADHD: Impact of symptom profile, comorbid psychiatric problems, and treatment: A cross-sectional study of 414 clinically diagnosed adult ADHD patients. *Journal of Attention Disorders, 13*, 175-187.

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. *European Archives of Psychiatry & Clinical Neurosciences, 252*, 177-184.

Huss, M., & Lehmkuhl, U. (2002). Methylphenidate and substance abuse: A review of pharmacology, animal and clinical studies. *Journal of Attention Disorders, 6*(Suppl. 1), S65-S71.

Huss, M., Poustka, F., Lehmkuhl, G., & Lehmkuhl, U. (2008). No increase in long-term risk for nicotine use disorders after treatment with methylphenidate in children with attention-deficit/hyperactivity disorder (ADHD): Evidence from a non-randomised retrospective study. *Journal of Neural Transmission, 115*, 335-339.

Jadad, A. R., Boyle, M., Cunningham, C., Kim, M., & Schachar, R. (1999). Treatment of attention-deficit/hyperactivity disorder. *Evidence Report/Technology Assessment (Summ), 11*, 1-341.

Kay, G. C., Michaels, A., & Pakull, B. (2009). Simulated driving changes in young adults with ADHD receiving mixed amphetamine salts extended release and atomoxetine. *Journal of Attention Disorders, 12*, 316-329.

Kessler, R. C., Akiskal, H. S., Ames, M., Birnbaum, H., Greenberg, P., Hirschfeld, M., . . . Wang, P. S. (2006). Prevalence and effects of mood disorders on work performance in a nationally representative sample of U.S. workers. *American Journal of Psychiatry, 163*, 1561-1568.

Khantzian, E. J. (1975). Self-selection and progression in drug dependence. *Psychiatry Digest, 36*, 19-22.

Knivsberg, A. M., & Andreassen, A. B. (2008). Behaviour, attention and cognition in severe dyslexia. *Nordic Journal of Psychiatry, 62,* 59-65.

Koesters, M., Becker, T., Kilian, R., Fegert, J. M., & Weinmann, S. (2009). Limits of meta-analysis: Methylphenidate in the treatment of adult attention-deficit hyperactivity disorder. *Journal of Psychopharmacology, 23*, 733-744.

Kolar, D., Keller, A., Golfinopoulos, M., Cumyn, L., Syer, C., & Hechtman, L. (2008). Treatment of adults with attention-deficit/hyperactivity disorder. *Neuropsychiatric Disease and Treatment, 4*, 389-403.

Kollins, S. H., McClernon, F. J., & Fuemmeler, B. F. (2005). Association between smoking and attention-deficit/hyperactivity disorder symptoms in a population-based sample of young adults. *Archives of General Psychiatry, 62*, 1142-1147.

Kooij, J. J. (2010). *Adult ADHD: Diagnostic assessment and treatment*. Amsterdam, Netherlands: Pearson Assessment and Information B. V.

Kooij, J. J., Bejerot, S., Blackwell, A., Caci, H., Casas-Brugué, M., Carpentier, P. J., . . . Asherson, P. (2010). European consensus statement on diagnosis and treatment of adult ADHD: The European Network Adult ADHD. *BMC Psychiatry, 10*, 67.

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. *Psychological Medicine, 34*, 973-982.

Kooij, J. J., Middelkoop, H. A., Van Gils, K., & Buitelaar, J. K. (2001). The effect of stimulants on nocturnal motor activity and sleep quality in adults with ADHD: An open-label case-control study. *Journal of Clinical Psychiatry, 62*, 952-956.

Krause, J., Krause, K. H., Dresel, S. H., La Fougere, C., & Ackenheil, M. (2006). ADHD in adolescence and adulthood, with a special focus on the dopamine transporter and nicotine. *Dialogues in Clinical Neuroscience, 8*, 29-36.

Kuperman, S., Perry, P. J., Gaffney, G. R., Lund, B. C., Bever-Stille, K. A., Arndt, S., . . . Paulsen, J. S. (2001). Bupropion SR vs. methylphenidate vs. placebo for attention deficit hyperactivity disorder in adults. *Annals of Clinical Psychiatry, 13*, 129-134.

Levin, E. D., Conners, C. K., Silva, D., Canu, W., & March, J. (2001). Effects of chronic nicotine and methylphenidate in adults with attention deficit/hyperactivity disorder. *Experimental and Clinical Psychopharmacology, 9*, 83-90.

Levin, F. R., Evans, S. M., Brooks, D. J., & Garawi, F. (2007). Treatment of cocaine dependent treatment seekers with adult ADHD: Double-blind comparison of methylphenidate and placebo. *Drug and Alcohol Dependency, 87*, 20-29.

Levin, F. R., Evans, S. M., Brooks, D. J., Kalbag, A. S., Garawi, F., & Nunes, E. V. (2006). Treatment of methadone-maintained patients with adult ADHD: Double-blind comparison of methylphenidate, bupropion and placebo. *Drug and Alcohol Dependency, 81*, 137-148.

Levitan, R. D., Jain, U. R., & Katzman, M. A. (1999). Seasonal affective symptoms in adults with residual attention-deficit hyperactivity disorder. *Comprehensive Psychiatry, 40*, 261-267.

Lord, S., Downs, G., Furtaw, P., Chaudhuri, A., Silverstein, A., Gammaitoni, A., & Budman, S. (2009). Nonmedical use of prescription opioids and stimulants among student pharmacists. *Journal of the American Pharmacists Association, 49*, 519-528.

Lou, H. C., Henriksen, L., Bruhn, P., Børner, H., & Nielsen, J. B. (1989). Striatal dysfunction in attention deficit and hyperkinetic disorder. *Archives of Neurology, 46*, 48-52.

Mannuzza, S., Klein, R. G., Bessler, A., Malloy, P., & LaPadula, M. (1993). Adult outcome of hyperactive boys: Educational achievement, occupational rank, and psychiatric status. *Archives of General Psychiatry, 50*, 565-576.

Mattes, J. A., Boswell, L., & Oliver, H. (1984). Methylphenidate effects on symptoms of attention deficit disorder in adults. *Archives of General Psychiatry, 41*, 1059-1063.

McCarthy, S., Asherson, P., Coghill, D., Hollis, C., Murray, M., Potts, L., . . . Wong, I. C. (2009). Attention-deficit hyperactivity disorder: Treatment discontinuation in adolescent and young adults. *British Journal of Psychiatry, 194*, 273-277.

McDonagh, M. S., & Peterson, K. (2006). *Drug class review on pharmacologic treatment for ADHD. Final report*. Re-trieved from http://www.ohsu.edu/xd/research/centers-institutes/evidence-based-policy-center/derp/index.cfm/

Meijer, W. M., Faber, A., Van den Ban, E., & Tobi, H. (2009). Current issues around the pharmacotherapy of ADHD in children and adults. *Pharmacy World & Science, 31*, 509-516.

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

Miller, C. J., Flory, J. D., Miller, S. R., Harty, S. C., Newcorn, J. H., Halperin, J. M. (2008). Childhood attention-deficit/hyperactivity disorder and the emergence of personality disorders in adolescence: A prospective follow-up study. *Journal of Clinical Psychiatry, 69*, 1477-1484.

Moss, S. B., Nair, R., Vallarino, A., & Wang, S. (2007). Attention deficit/hyperactivity disorder in adults. *Primary Care: Clinics in Office Practice, 34*, 445-473.

National Institute for Health and Clinical Excellence. (2009). *The NICE guideline on attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults.* Leicester, England, & London, England: The British Psychological Society & The Royal College of Psychiatrists. Retrieved from http://www.nice.org.uk/nicemedia/pdf/ADHDFullGuideline.pdf

Newcorn, J. H., Weiss, M., & Stein, M. A. (2007). The complexity of ADHD: Diagnosis and treatment of the adult patient with comorbidities. *CNS Spectrums, 12*(Suppl. 8), 1-16.

Owens, J. A. (2005). The ADHD and sleep conundrum: A review. *Journal of Developmental and Behavioral Pediatrics, 26*, 312-322.

Paterson, R., Douglas, C., Hallmayer, J., Hagan, M., & Krupenia. (1999). A randomised, double-blind, placebo-controlled trial of dexamphetamine in adults with attention deficit hyperactivity disorder. *Australian and New Zealand Journal of Psychiatry, 33*, 494-502.

Philipsen, A., Feige, B., Hesslinger, B., Ebert, D., Carl, C., Hornyak, M., . . . Riemann, D. (2005). Sleep in adults with attention deficit/hyperactivity disorder: A controlled polysomnographic study including spectral analysis of the sleep EEG. *Sleep, 28*, 877-884.

Philipsen, A., Heblinger, B., & Van Elst, L. T. (2008). Attention deficit hyperactivity disorder in adulthood. *Deutsches Ärzteblatt International, 150*, 311-317.

Picchietti, D. L., Underwood, D. J., Farris, W. A., Walters, A. S., Shah, M. M., Dahl, R. E., . . . Hening, W. A. (1999). Further studies on periodic limb movement disorder and restless legs syndrome, in children with attention-deficit hyperactivity disorder. *Movement Disorders, 14*, 1000-1007.

Pinkhardt, E. H., Kassubek, J., Brummer, D., Koelch, M., Ludolph, A. C., Fegert, J. M., & Ludolph, A. G. (2009). Intensified testing for attention-deficit hyperactivity disorder (ADHD) in girls should reduce depression and smoking in adult females and the prevalence of ADHD in the long term. *Medical Hypotheses, 72*, 409-412.

Plichta, M. M., Vasic, N., Wolf, R. C., Lesch, K. P., Brummer, D., Jacob, C., . . . Gron, G. (2009). Neural hyporesponsiveness and hyperresponsiveness during immediate and delayed reward processing in adult attention-deficit/hyperactivity disorder. *Biological Psychiatry, 65*, 7-14.

Rabiner, D. L., Anastopoulos, A. D., Costello, E. J., Hoyle, R. H., McCabe, S. E., & Swartzwelder, H. S. (2009). The misuse and diversion of prescribed ADHD medications by college students. *Journal of Attention Disorders, 13*, 144-153.

Ramsay, J. R. (2007). Current status of cognitive-behavioral therapy as a psychosocial treatment for adult attention-deficit/hyperactivity disorder. *Current Psychiatry Reports, 9*, 427-433.

Reimherr, F. W., Marchant, B. K., Strong, R. E., Hedges, D. W., Adler, L., Spencer, T. J., . . . Soni, P. (2005). Emotional dysregulation in adult ADHD and response to atomoxetine. *Biological Psychiatry, 58*, 125-131.

Reimherr, F. W., Williams, E. D., Strong, R. E., Mestas, R., Soni, P., & Marchant, B. K. (2007). A double-blind, placebo-controlled, crossover study of osmotic release oral system methylphenidate in adults with ADHD with assessment of oppositional and emotional dimensions of the disorder. *Journal of Clinical Psychiatry, 68*, 93-101.

Robison, R. J., Reimherr, F. W., Marchant, B. K., Faraone, S. V., Adler, L. A., & West, S. A. (2008). Gender differences in 2 clinical trials of adults with attention-deficit/hyperactivity disorder: A retrospective data analysis. *Journal of Clinical Psychiatry, 69*, 213-221.

Rostain, A. L., & Ramsay, J. R. (2006). A combined treatment approach for adults with ADHD: Results of an open study of 43 patients. *Journal of Attention Disorders, 10*, 150-159.

Rostain, A. L., & Ramsay, J. R. (2007). Psychosocial treatments for attention-deficit/hyperactivity disorder in adults: Current evidence and future directions. *Professional Psychology, 38*, 338-346.

Rucklidge, J. J. (2008). Gender differences in ADHD: Implications for psychosocial treatment. *Expert Reviews in Neurotherapeutics, 8*, 643-655.

Rucklidge, J. J. (2010). Gender differences in attention-deficit/hyperactivity disorder. *Psychiatric Clinics of North America, 33*, 357-373.

Rybak, Y. E., McNeely, H. E., Mackenzie, B. E., Jain, U. R., & Levitan, R. D. (2007). Seasonality and circadian preference in adult attention-deficit/hyperactivity disorder: Clinical and neuropsychological correlates. *Comprehensive Psychiatry, 48*, 562-571.

Safren, S. A. (2006). Cognitive-behavioral approaches to ADHD treatment in adulthood. *Journal of Clinical Psychiatry, 67*(Suppl. 8), 46-50.

Safren, S. A., Otto, M. W., Sprich, S., Winett, C. L., Wilens, T. E., & Biederman, J. (2005). Cognitive-behavioral therapy for ADHD in medication-treated adults with continued symptoms. *Behaviour Research and Therapy, 43*, 831-842.

Schachter, H. M., Pham, B., King, J., Langford, S., & Moher, D. (2001). How efficacious and safe is a short-acting methylphenidate for the treatment of attention-deficit disorder in children and adolescents? A meta-analysis. *Canadian Medical Association Journal, 27*, 1475-1488.

Schmitdt, M. F., Filippone, P., & Edelman, E. M. (2003). Social representations of attention deficit/hyperactivity disorder, 1988-1997. *Culture and Psychology, 9*, 383-406.

Schubiner, H., Saules, K. K., Arfken, C. L., Johanson, C. E., Schuster, C. R., Lockhart, N., . . . Pihlgren, E. (2002). Double-blind placebo-controlled trial of methylphenidate in the treatment of adult ADHD patients with comorbid cocaine dependence. *Expert Clinical Psychopharmacology, 10*, 286-294.

Semiz, U. B., Basoglu, C., Oner, O., Munir, K. M., Ates, A., Algul, A., . . . Cetin, M. (2008). Effects of diagnostic comorbidity and dimensional symptoms of attention-deficit-hyperactivity disorder in men with antisocial personality disorder. *Australian and New Zealand Journal of Psychiatry, 42*, 405-413.

Snyder, S. M., & Hall, J. R. (2006). A meta-analysis of quantitative EEG power associated with attention-deficit hyperactivity disorder. *Journal of Clinical Neurophysiology, 23*, 440-455.

Sobanski, E., Schredl, M., Kettler, N., & Alm, B. (2008). Sleep in adults with attention deficit hyperactivity disorder (ADHD) before and during treatment with methylphenidate: A controlled polysomnographic study. *Sleep, 31*, 375-381.

Spencer, R. M., Ivry, R. B., & Zelaznik, H. N. (2005). Role of the cerebellum in movements: Control of timing or movement transitions? *Experimental Brain Research, 161*, 383-396.

Spencer, T., Biederman, J., & Wilens, T. (1998). Adults with attention-deficit/hyperactivity disorder: A controversial diagnosis. . *Journal of Clinical Psychiatry, 59*(Suppl. 7), 59-68.

Spencer, T., Biederman, J., & Wilens, T. (2004). Nonstimulant treatment of adult attention-deficit/hyperactivity disorder. *Psychiatric Clinics of North America, 27*, 373-383.

Spencer, T., Biederman, J., Wilens, T., Doyle, R., Surman, C., Prince, J., . . . Faraone, S. (2005). A large, double-blind, randomized clinical trial of methylphenidate in the treatment of adults with attention-deficit/hyperactivity disorder. *Biological Psychiatry, 57*, 456-463.

Spencer, T., Biederman, J., Wilens, T., Faraone, S., Prince, J., Gerard, K., . . . Bearman, S. K. (2001). Efficacy of a mixed amphetamine salts compound in adults with attention-deficit/hyperactivity disorder. *Archives of General Psychiatry, 58*, 775-782.

Spencer, T. J., Adler, L. A., McGough, J. J., Muniz, R., Jiang, H., & Pestreich, L. (2007). Efficacy and safety of dexmethylphenidate extended-release capsules in adults with attention-deficit/hyperactivity disorder. *Biological Psychiatry, 15*, 1380-1387.

Spencer, T. J., Biederman, J., Madras, B. K., Dougherty, D. D., Bonab, A. A., Livni, E., . . . Fischman, A. J. (2007). Further evidence of dopamine transporter dysregulation in ADHD: A controlled PET imaging study using altropane. *Biological Psychiatry, 62*, 1059-1061.

Spencer, T. J., Biederman, J., Wilens, T., Harding, M., O'Donnell, D., & Griffin, S. (1996). Pharmacotherapy of attention deficit hyperactivity disorder across life cycle. A literature review. *Journal of the American Academy of Child & Adolescent Psychiatry, 35*, 409-432.

Spencer, T., Wilens, T., Biederman, J., Faraone, S. V., Ablon, J. S., & Lapey, K. (1995). A double-blind, crossover comparison of methylphenidate and placebo in adults with childhood-onset attention-deficit hyperactivity disorder. *Archives of General Psychiatry, 52*, 434-443.

Stevenson, C. S., Stevenson, R. J., & Whitmont, S. (2003). A self-directed psychosocial intervention with minimal therapist contact for adults with attention deficit hyperactivity disorder. *Clinical Psychology and Psychotherapy, 10*, 93-101.

Stevenson, C. S., Whitmont, S., Bornholt, L., Livesey, D., & Stevenson, R. J. (2002). A cognitive remediation programme for adults with attention deficit hyperactivity disorder. *Australian and New Zealand Journal of Psychiatry, 36*, 610-616.

Taylor, F. B., & Russo, J. (2000). Efficacy of modafinil compared to dextroamphetamine for the treatment of attention deficit hyperactivity disorder in adults. *Journal of Child and Adolescent Psychopharmacology, 10*, 311-320.

Taylor, F. B., & Russo, J. (2001). Comparing guanfacine and dextroamphetamine for the treatment of adult attention-deficit/hyperactivity disorder. *Journal of Clinical Psychopharmacology, 21*, 223-228.

Tenenbaum, S., Paull, J. C., Sparrow, E. P., Dodd, D. K., & Green, L. (2002). An experimental comparison of pycnogenol and methylphenidate in adults with attention-deficit/hyperactivity disorder (ADHD). *Journal of Attention Disorders, 6*, 49-60.

Torgersen, T., Gjervan, B., & Rasmussen, K. (2008). Treatment of adult ADHD: Is current knowledge useful to clinicians? *Journal of Neuropsychiatric Disease and Treatment, 4*, 177-186.

Trott, G. E. (2006). Attention-deficit/hyperactivity disorder (ADHD) in the course of life. *European Archives of Psychiatry and Clinical Neurosciences, 256*, 1-22.

Van Ameringen, M., Mancini, C., Simpson, W., & Patterson, B. (2010). Adult attention deficit hyperactivity disorder in an anxiety disorders population. *CNS Neuroscience and Therapeutics, 17*, 221-226.

Van der Heijden, K. B., Smits, M. G., Van Someren, E. J., & Gunning, W. B. (2005). Idiopathic chronic sleep onset insomnia in attention-deficit/hyperactivity disorder: A circadian rhythm sleep disorder. *Chronobiology International, 22*, 559-570.

Van Veen, M. M., Kooij, J. J., Boonstra, A. M., Gordijn, M. C., & Van Someren, E. J. (2010). Delayed circadian rhythm in adults with attention-deficit/hyperactivity disorder and chronic sleep-onset insomnia. *Biological Psychiatry, 67*, 1091-1096.

Waite, R., & Ivey, N. (2009). Unveiling the mystery about adult ADHD: One woman's journey. *Issues in Mental Health Nursing, 30*, 547-553.

Wasserstein, J. (2005). Diagnostic issues for adolescents and adults with ADHD. *Journal of Clinical Psychology, 61*, 535-547.

Weisler, R. H., Biederman, J., Spencer, T. J., Wilens, T. E., Faraone, S. V., Chrisman, A. K., . . . Tulloch, S. J. (2006). Mixed amphetamine salts extended-release in the treatment of adult ADHD: A randomized, controlled trial. *CNS Spectrums, 11*, 625-639.

Weiss, M., & Hechtman, L. (2006). A randomized double-blind trial of paroxetine and/or dextroamphetamine and problem-focused therapy for attention-deficit/hyperactivity disorder in adults. *Journal of Clinical Psychiatry, 67*, 611-619.

Weiss, M. D., & Weiss, J. R. (2004). A guide to the treatment of adults with ADHD. *Journal of Clinical Psychiatry, 65* (Suppl. 3), 27-37.

Wender, P. H., Reimherr, F. W., Wood, D., & Ward, M. (1985). A controlled study of methylphenidate in the treatment of attention deficit disorder, residual type, in adults. *American Journal of Psychiatry, 142*, 547-552.

Wigal, T., Brams, M., Gasior, M., Gao, J., Squires, L., & Giblin, J. (2010). Randomized, double-blind, placebo-controlled, crossover study of the efficacy and safety of lisdexamfetamine dimesylate in adults with attention-deficit/hyperactivity disorder: Novel findings using a simulated adult workplace environment design. *Behavioral and Brain Functions, 6*, 34.

Wilens, T. E. (2004). Impact of ADHD and its treatment on substance abuse in adults. *Journal of Clinical Psychiatry, 65*, 38-45.

Wilens, T. E., Biederman, J., Wozniak, J., Gunawardene, S., Wong, J., & Monuteaux, M. (2003). Can adults with attention-deficit/hyperactivity disorder be distinguished from those with comorbid bipolar disorder? Findings from a sample of clinically referred adults. *Biological Psychiatry, 54*, 1-8.

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., Gignac, M., Swezey, A., Monuteaux, M. C., & Biederman, J. (2006). Characteristics of adolescents and young adults with ADHD who divert or misuse their prescribed medications. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*, 408-414.

Wilens, T. E., Spencer, T., & Biederman, J. (2002). A review of the pharmacotherapy of adults with attention-deficit/hyperactivity disorder. *Journal of Attention Disorders, 5*, 189-202.

Wolf, R. C., Plichta, M. M., Sambataro, F., Fallgatter, A. J., Jacob, C., Lesch, K. P., . . . Vasic, N. (2009). Regional brain activation changes and abnormal functional connectivity of the ventrolateral prefrontal cortex during working memory processing in adults with attention-deficit/hyperactivity disorder. *Human Brain Mapping, 30*, 2252-2266.

Wolk, R., & Somers, V. K. (2007). Sleep and the metabolic syndrome. *Experimental Physiology, 92*, 67-78.

Wood, D. R., Reimherr, F. W., Wender, P. H., Glen, E., & Johnson, M. D. (1976). Diagnosis and treatment of minimal brain dysfunction in adults: A preliminary report. *Archives of Gen Psychiatry, 33*, 1453-1460.

Young, S., Chesney, S., Sperlinger, D., Misch, P., & Collins, P. (2009). A qualitative study exploring the life-course experiences of young offenders with symptoms and signs of ADHD who were detained in a residential care setting. *Criminal Behaviour and Mental Health, 19*, 54-63.

Zametkin, A. J., Nordahl, T. E., Gross, M., King, A. C., Semple, W. E., Rumsey, J., . . . Cohen, R. M. (1990). Cerebral glucose metabolism in adults with hyperactivity of childhood onset. *New England Journal of Medicine, 323*, 1361-1366.

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