

# ADULT ADHD

## When Comorbid Depression Enters In



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# Adult ADHD: When Comorbid Depression Enters In

## NEEDS ASSESSMENT

Approximately 19% of adults with attention-deficit/hyperactivity disorder (ADHD) have comorbid depression, a prevalence rate more than double that found in non-ADHD adults.<sup>1</sup> ADHD individuals lead disorganized, often chaotic lives, and experience significant functional impairments in multiple domains of life.<sup>2</sup> Comorbid depression further compounds their misery and disability and adds a risk for suicidal ideation and suicidality.<sup>3</sup> Diagnosis of coexisting depression and ADHD is challenging because some symptoms and impairments may appear similar and obscure the clinical picture.<sup>1</sup> In addition, the symptoms of depression are more visible than those of ADHD in an adult presentation, and it is common for the former to be diagnosed while the latter is overlooked. If that occurs, not only will the ADHD symptoms fail to be controlled, but treatment for depression may be subverted as well. Clinicians should learn to distinguish these serious, highly prevalent disorders separately and together, and develop management strategies to treat all relevant conditions.

### References:

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2. Biederman J, Faraone SV, Spencer TJ, et al. Functional impairments in adults with self-reports of diagnosed ADHD: a controlled study of 1001 adults in the community. *J Clin Psychiatry*. 2006;67:524-540.
3. Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA*. 2003;289:3095-3105.

## TARGET AUDIENCE

Psychiatrists, neurologists, primary-care physicians

## LEARNING OBJECTIVES

- After taking part in this educational activity, participants should be able to:
1. Compare the prevalence of depression in adults with attention-deficit/hyperactivity disorder (ADHD) and the prevalence of ADHD in adults with depression
  2. Explain how substance abuse disorder (SUD) can complicate a dual diagnosis
  3. Distinguish the symptoms of adult ADHD and depression
  4. Identify the pharmacotherapy options for treating adult ADHD and depression
  5. Discuss the psychotherapies that are most effective for treating for each disorder.

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Dear Colleague,

For more than a decade, evidence has been accruing to suggest that attention-deficit/hyperactivity disorder (ADHD) is not a condition limited to childhood but that, in a majority of cases, it persists across the life span. The 2006 National Comorbidity Survey Replication found that 4.4% of adults in the United States, more than 8 million people, have current ADHD; 75% are undiagnosed and only 11% receive treatment.

A major reason why adult ADHD goes undiagnosed and untreated most of the time is that the incidence of psychiatric comorbidity, in particular mood disorders, anxiety disorders, and substance use disorders, is very high, ranging from 50% to 90%. When one of these disorders coexists with ADHD, it typically presents with more observable symptoms that obscure the subtler but still seriously impairing ones of ADHD. In addition, mood, anxiety, and substance use disorders each have some symptoms overlapping those of ADHD, further disguising what should be multiple diagnosis. Overlooking ADHD will not only fail to control the debilitating symptoms of that disorder, however; it may also compromise other treatments.

In December 2006, the Adult ADHD and Comorbid Disorders Academic Council, a group of recognized experts who are engaged in different areas of ADHD research, met to discuss the current state of clinical knowledge about this serious condition, which affects one in 20 Americans, with a focus on the wide range of psychiatric comorbidities.

This monograph, the first in a three-part CME series, has been developed from those discussions. Its purpose is to share with you compelling evidence that a very high percentage of adults with ADHD also have comorbid depression, and that a very high percentage of adults with depression also have comorbid ADHD. You will learn how to distinguish these two disorders in adults, as well as the treatment options that appear most effective for addressing each condition, including pharmacotherapy and psychotherapy.

The second monograph in this series will discuss the diagnostic and treatment challenges of adult ADHD and another highly comorbid condition: bipolar disorder.

The final monograph in the series will examine adult ADHD and anxiety disorders, which commonly co-occur as well.

We hope you find these educational activities of practical and immediate value, and we welcome your questions, comments, and suggestions.

Many thanks for your time and attention, and for the care you provide to adults with ADHD!

Sincerely,

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Comments? Questions?

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# ADULT ADHD: When Comorbid Depression Enters In

When depression coexists with ADHD, its more easily detected symptoms may cause an ADHD diagnosis to be missed. That some symptoms of depression and ADHD resemble each other adds to the challenges of diagnosis and treatment.

BY THOMAS J. SPENCER, MD

Major depressive disorder and attention-deficit/hyperactivity disorder (ADHD) are two highly prevalent and debilitating psychiatric conditions. Two recent replications of the landmark 1990–1992 National Comorbidity Survey, one published in 2003,<sup>1</sup> the other published in 2006,<sup>2</sup> added much new knowledge to our understanding of the nature and prevalence of these disorders separately and together.

The 2003 National Comorbidity Survey Replication (NCS-R) found that the lifetime prevalence of depression among adults in the United States exceeds 16%.<sup>1</sup> More than half of the NCS-R respondents with depression defined their symptoms as being “severe” or “very severe.” The mean duration of a depressive episode was 16 weeks. Approximately one in two adults with depression receives treatment for the condition.

Until the mid-1990s, ADHD was thought to be primarily a pediatric condition, although numerous studies conducted since then have found ADHD to be lifelong in many pediatric cases. A 2006 iteration of the NCS-R found that 4.4% of adults, more than 8 million individuals, have current ADHD.<sup>2</sup> An estimated 75% have never been diagnosed; approximately 11% have received treatment.

While ADHD symptoms in adults are not usually as pronounced as they are in children, ADHD is a debilitating condi-



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tion regardless of age, with significant impact on academic, occupational, psychosocial, and other important domains of life.<sup>3</sup> Adults with ADHD evince significantly less educational attainment, career advancement, and earning potential, and significantly higher rates of divorce, driving accidents, arrests, emergency room visits, and substance use disorders (SUDs) than non-ADHD adults.<sup>3</sup>

In addition, the 2006 NCS-R found adult ADHD to be highly comorbid with other psychiatric conditions, especially mood and anxiety disorders and SUDs.<sup>2</sup> Yet because the symptoms of these disorders may be more visible than those of ADHD, a multiple diagnosis is often missed. Even when depression is treated, if co-occurring ADHD is overlooked, not only will ADHD symptoms continue, and continue to impair, but treatment for depression may be compromised.

## HERITABLE INDIVIDUALLY AND TOGETHER

Abundant evidence supports the heritability of lifetime depression. The largest twin study to date, published in 2006, included 42,161 twins and 15,493 complete pairs.<sup>4</sup> Lifetime depression

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was assessed via personal interviews using modified criteria in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, Text Revision (*DSM-IV-TR*). The data indicate that the heritability of depression is high for both sexes, but it is significantly higher for women (42%) than for men (29%).

Twin studies of childhood behavior problems suggest that individual differences in impulsivity, hyperactivity, and inattention—the three symptom clusters of ADHD—are also largely due to genetic influences. In one large longitudinal study, mothers completed the Child Behavior Checklist, a standard assessment instrument, for their twin offspring when the children were 3 years of age ( $n=11,938$ ), 7 years of age ( $n=10,657$ ), 10 years of age ( $n=6192$ ), and 12 years of age ( $n=3124$ ).<sup>5</sup> The results indicate heritability of overactivity and attention problems to be nearly 75% at each age.

The heritability of ADHD and depression together appears to be high as well. A 1991 study used diagnostic criteria in the 3rd edition of the *DSM* and blinded raters to examine patterns of familial association between ADHD and mood disorders among first-degree relatives of clinically referred children and adolescents with ADHD (73 probands, 264 relatives) and normal controls (26 probands, 92 relatives).<sup>6</sup> Among the 73 ADHD probands, 33% met criteria for mood disorders (major depression, 21%; bipolar disorder, 11%; dysthymia, 1%). The investigators then stratified the ADHD subjects into those with mood disorders and those without them. Familial risk analyses revealed that the relatives of each ADHD proband subgroup were at significantly greater risk for ADHD than were relatives of normal controls. While the morbidity risk for ADHD was not significantly different between relatives of ADHD-only individuals and relatives of individuals with ADHD plus a mood disorder, these two risks were significantly greater than the risk to relatives of normal controls.

### HIGH PREVALENCE, HIGH COMORBIDITY

The 2006 NCS-R produced what many consider to be the most authoritative data available on comorbidity of ADHD and mood, anxiety, SUD, and other psychiatric disorders.<sup>2</sup> Among the NCS-R findings:

- 38% of adults with ADHD had a coexisting mood disorder, compared with 11% of adults without ADHD
- 19% of adults with ADHD had comorbid major depressive disorder, compared with 8% of those without ADHD
- 13% of adults with ADHD had comorbid dysthymia, compared with 2% of those without ADHD
- 9.4% of adults with major depression had comorbid ADHD, compared with 4% of those without depression
- 23% of adults with dysthymia had comorbid ADHD,

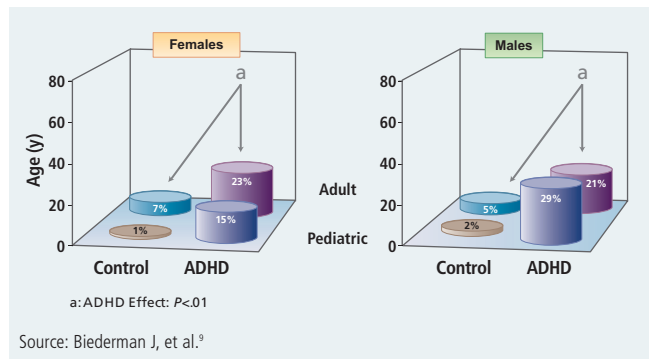


FIGURE 1. Lifetime comorbidity of severe major depression in ADHD: adult vs pediatric subjects.

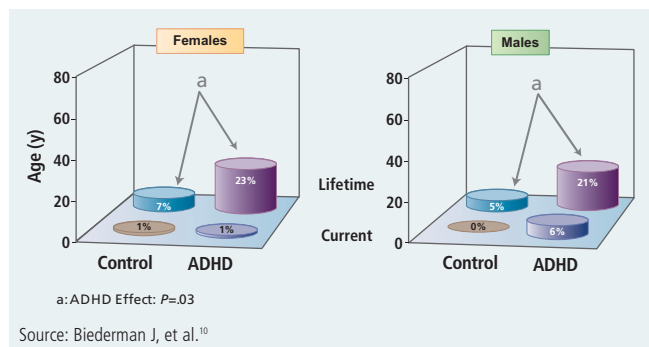


FIGURE 2. Comorbidity of severe major depression in adult ADHD: lifetime vs current disorders.

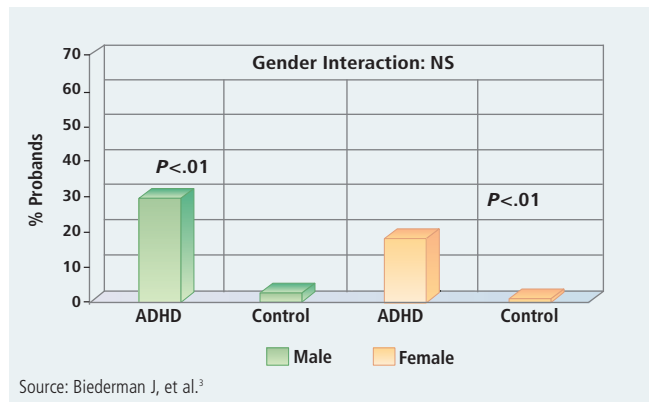


FIGURE 3. Severe major depression in ADHD probands in the Massachusetts General Hospital study of ADHD (2006).

compared with 4% of those without dysthymia.

The high prevalence of comorbid ADHD and depression in NCS-R respondents supports earlier evidence. One study examined ADHD and mood disorders in mid-adolescence. It found a significantly higher and more prolonged incidence of depression at  $>14$  years of age in individuals with a diagnosis of ADHD than in a control group ( $P \leq .01$ ).<sup>7</sup> Over the study's 4-year follow-up period, depressive symptoms increased by

approximately 50% between baseline and year 4.

Another study examined the prevalence of ADHD with childhood onset in depressed adults.<sup>8</sup> Included were 116 patients, aged 18 to 65 years, who were consecutively enrolled for treatment of depressive symptoms. Sixteen percent met full or subthreshold criteria for a *DSM* diagnosis of childhood ADHD; 12% experienced ADHD symptoms as adults.

In a study published in 2002, investigators at Massachusetts General Hospital examined the influence of gender on ADHD in children referred to a psychiatric clinic.<sup>9</sup> Included were 140 boys and 140 girls with ADHD, as well as 120 boys and 122 girls without ADHD, who served as controls. In a subsequent study, published in 2004, gender effects on ADHD were revisited, this time in 219 adults with ADHD who were referred to an outpatient psychiatric clinic over the previous 7 years, compared with 215 non-ADHD control subjects.<sup>10</sup> When data from the two studies were pooled to compare the lifetime comorbidity of ADHD in adult and pediatric subjects with severe major depression, it was found that 15% of girls and 23% of women with ADHD had lifetime depression (compared with 1% of control girls and 7% of control women, respectively), and 29% of boys and 21% of men with ADHD had lifetime depression (compared with 2% of control boys and 5% of control men, respectively) (**Figure 1**). In comparing lifetime vs current disorders, the investigators found that the prevalence of ADHD in depressed adults was similarly high for both females and males (**Figure 2**).

A third Massachusetts General study then examined functional impairments in 500 adults with diagnosed ADHD.<sup>3</sup> Published in 2006, it found that both male and female subjects had significantly more severe depression ( $P < .01$ ) than 501 non-ADHD control subjects. Approximately 28% of the male ADHD probands and 17% of the female ADHD probands had depressive symptoms (**Figure 3**).

### DIAGNOSING ADHD AND DEPRESSION

**ADHD.** ADHD is a clinical diagnosis based on a careful patient evaluation, including taking a longitudinal history. *DSM-IV-TR* diagnostic criteria for ADHD state that the patient must have six of nine symptoms of inattention and/or six of nine symptoms of hyperactivity/impulsivity.<sup>11</sup> Symptoms must have persisted for at least 6 months, cause significant functional impairment, and must not be better accounted for by another psychiatric condition. In addition, symptoms should typically occur prior to 7 years of age (**Table 1**).

Because these criteria were developed from pediatric trials, however, clinical judgment must be used when applying them to the assessment of adult patients. Pediatric symptoms of

ADHD do “migrate” with age and will tend to present somewhat differently in adults.<sup>12</sup> The ADHD child’s inability to listen, for example, may present in an adult as a tendency to be distracted and forgetful. The excessive running and climbing of the ADHD child may migrate to a frequent feeling of being overwhelmed in the ADHD adult (**Table 2**).

In another diagnostic challenge, hyperactivity, the predominant ADHD symptom cluster in children, is readily observed. However, the main symptom cluster in ADHD adults, inattention, may not be evident unless the clinician maintains a high index of suspicion, questions the patient, and perhaps asks the patient to complete a brief questionnaire to assess the nature and extent of ADHD symptoms.<sup>12</sup>

This shift in predominant ADHD symptom cluster from childhood to adulthood was documented in a study published in 2000.<sup>13</sup> It measured ADHD symptoms in 128 boys five times over 4 years. The prevalence rates of syndromic (less than full syndrome) remission, symptomatic remission (less than subthreshold diagnosis), and functional remission (full recovery) were estimated as a function of age employing multivariate logistic symptom regression. The investigators found that age was significantly associated with decline in total ADHD symptoms and symptoms of hyperactivity, impulsivity, and inattention. Symptoms of inattention, however, remitted for fewer subjects than did symptoms of hyperactivity and impulsivity. The investigators concluded that inattention symptoms tended to be more enduring across the life span.

A number of diagnostic and symptom assessment scales for adult ADHD, while not diagnostic in themselves, can assist the clinician in confirming an ADHD diagnosis.<sup>12</sup> The Adult ADHD Clinical Diagnostic Scale v1.2 (ACDS) and the Conners Adult ADHD Diagnostic Interview for the *DSM-IV* (CAADID) are useful in diagnostic evaluations. The Adult ADHD Investigator Symptom Rating Scale (AISRS) and the Attention-Deficit/Hyperactivity Disorder Rating Scale (ADHD-RS) can aid in assessing symptoms and treatment progress. The ACDS and AISRS include modular probes and prompts to help the clinician discern the scope and degree of impairment of adult ADHD symptomatology. Convenient self-report scales include the Adult ADHD Self-Report Scale (ASRS) and the Conners Adult ADHD Rating Scale (CAARS).

**Depression.** For a diagnosis of depression, *DSM-IV* criteria require that a major depressive episode is not better accounted for by another psychiatric condition.<sup>11</sup> The patient should also have had no prior manic, mixed (mania and depression), or hypomanic (milder manic) episode, hallmark symptoms of bipolar disorder, a condition that is commonly mistaken for unipolar depression. In addition, the depressive episode should

A. Symptoms must occur often and have persisted for at least 6 months.

At least six of nine symptoms of inattention (ADHD, predominantly inattentive type), hyperactivity/impulsivity (ADHD, predominantly hyperactive/impulsive type), or both (ADHD, combined type) are required for a classic diagnosis of full ADHD.

### Symptom Checklist

Inattention	Hyperactivity/impulsivity
<ul style="list-style-type: none"> <li>• Makes careless mistakes</li> <li>• Has difficulty sustaining attention</li> <li>• Appears not to listen</li> <li>• Fails to finish tasks (frequently shifts activities)</li> <li>• Has difficulty organizing</li> <li>• Avoids tasks requiring sustained attention</li> <li>• Loses things</li> <li>• Is easily distracted</li> <li>• Is forgetful</li> </ul>	<ul style="list-style-type: none"> <li>• Fidgets</li> <li>• Inability to stay seated</li> <li>• Excessive movement (internal restlessness)</li> <li>• Difficulty relaxing</li> <li>• Is always on the go/acts as though driven by a motor</li> <li>• Talks excessively</li> <li>• Blurts out answers</li> <li>• Has difficulty waiting turn (impatience)</li> <li>• Interrupts or intrudes</li> </ul>

B. Some impairing symptoms were present before 7 years of age.

C. Some impairment from symptoms is present in two or more settings (eg, work, school, or home).

D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning.

E. Symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder (such as a mood disorder, anxiety disorder, dissociative disorder, or a personality disorder).

*DSM-IV-TR= Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision. Source: American Psychiatric Association.<sup>11</sup>*

**Table 1. DSM-IV-TR Diagnostic Criteria for ADHD**

be continuous and all-encompassing in its saddening effects during the same 2-week period. The disorder is characterized by other signature symptoms as well (**Table 3**).

The presence of some symptoms of depression should not, however, lead the clinician to automatically conclude that a diagnosis of clinical depression is warranted. While the 2003 NCS-R estimated that one in six adults would have clinical depression at some point in their lives, a 2007 community-based epidemiologic study, which utilized NCS-R participants 15 to 54 years of age (N=8098), came to a different conclusion: that the prevalence rate for depression may be inflated by a large number of diagnoses of depression that are not, in fact,

DSM-IV-TR childhood inattention symptoms	Inattention symptom migration to adulthood
Has difficulty sustaining attention	Has difficulty sustaining attention in reading or paperwork
Does not listen	Is easily distracted/forgetful
Does not follow through	Has poor concentration
Cannot organize	Manages time poorly
Loses or misplaces things	Loses or misplaces things
Is easily distracted/forgetful	Has difficulty finishing tasks
DSM-IV-TR childhood hyperactivity symptoms	Hyperactivity symptom migration to adulthood
Squirms and fidgets	Feels inner restlessness
Runs or climbs excessively	Feels overwhelmed
Cannot play or work quietly	Self-selects active jobs
Seems "on the go" or "driven by a motor"	Talks excessively

*DSM-IV-TR= Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision. Source: Adler LA, et al.<sup>12</sup>*

**Table 2. ADHD Symptom Migration**

clinical depression.<sup>14</sup> The investigators cited as an example sadness caused by "simple bereavement" of brief duration and modest severity. This, they pointed out, is an appropriate response to personal catastrophe, not necessarily a sign of pharmaceutically treatable pathology, although psychotherapy may be beneficial. The authors found that as many as 25% of depression diagnoses may be unwarranted.

A diagnosis that is warranted is based on a thorough medical and psychiatric evaluation, as well as a physical exam. Urine drug screening can determine whether the patient's condition is due at least in part to co-occurring SUD. Consider a thyroid stimulating hormone (TSH) test, complete blood count (CBC), and chemistry panel to rule out a non-psychiatric medical condition that might cause depressive symptoms. A history of central neurologic illness, infection, or trauma may also be relevant. All prescription, over-the-counter, herbal, sports-endurance, and vitamin products the patient is taking should be reviewed. Common medications may cause symptoms mimicking those of depression.

As with adult ADHD, the use of diagnostic and symptom assessment scales, while not diagnostic in themselves, can help confirm a depression diagnosis. Among the useful clinician-rated instruments are The Hamilton Rating Scale for

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

*Note: Do not include symptoms that are clearly due to a general medical condition, or mood-congruent delusions or hallucinations.*

- |   |   |
|---|---|
| <ol style="list-style-type: none"> <li>1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (eg, feels sad or empty) or observation made by others (eg, appears tearful)</li> <li>2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)</li> <li>3. Significant weight loss when not dieting or weight gain (eg, a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day</li> <li>4. Insomnia or hypersomnia nearly every day</li> </ol> | <ol style="list-style-type: none"> <li>5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)</li> <li>6. Fatigue or loss of energy nearly every day</li> <li>7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)</li> <li>8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)</li> <li>9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide</li> </ol> |
|---|---|

B. The symptoms do not meet criteria for a mixed episode (depression and mania).

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to the direct physiological effects of a substance (eg, a drug of abuse, a medication) or a general medical condition (eg, hypothyroidism).

E. The symptoms are not better accounted for by bereavement (ie, after the loss of a loved one), and the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

Source: American Psychiatric Association.<sup>11</sup>

**Table 3. DSM-IV-TR Diagnostic Criteria for a Major Depressive Episode**

Depression,<sup>15</sup> the Montgomery-Åsberg Depression Rating Scale,<sup>16</sup> the Geriatric Depression Scale,<sup>17</sup> and the Bech-Rafaelsen Melancholia Scale.<sup>18</sup> Other scales, such as the Major Depression Inventory<sup>19</sup> and the Quick Inventory of Depressive Symptomatology—Self-Rated<sup>20</sup> are convenient self-report forms. Another instrument, the Beck Depression Inventory, can be used as either a clinician- or patient-rated scale.<sup>21</sup>

**Symptom overlap.** ADHD and depressive symptoms do not generally overlap.<sup>11</sup> Some symptoms, however, may initially appear similar. The excessive hyperactivity of ADHD, for example, may be mistaken for the psychomotor agitation of depression, although the former tends to be chronic and not emotionally fraught, whereas the latter tends to be a finite episode of frantic, disturbed restlessness. The only true overlapping symptoms are distractibility (ADHD) and diminished ability to think or concentrate (depression). The very different chronologies of depression (variable age of onset) and ADHD (onset usually prior to age 7) and the very different frequency of symptoms—episodic in the case of depression, chronic in the case of ADHD—can help distinguish these disorders.

It is possible that an adult with ADHD may become depressed because the condition is untreated, rather than

depression being a discrete disorder. Evidence suggests, however, that depressive symptoms in an ADHD adult usually indicate a separate condition.<sup>22</sup> A 1995 study, for example, assessed the extent of symptom overlap between ADHD and depression, bipolar disorder, and generalized anxiety disorder—all common comorbidities—in three groups of subjects: clinically referred children and adolescents, nonreferred adults who were the parents of the subjects in the first group, and clinically referred adults with ADHD.<sup>22</sup> When overlapping symptoms were factored out, 79% of subjects maintained their diagnosis of depression, 56% maintained their diagnosis of bipolar disorder, and 75% maintained their diagnosis of generalized anxiety disorder. The investigators concluded that ADHD is not an artifact of symptoms shared with other psychiatric disorders and that comorbid psychiatric disorders are not artifacts of overlapping ADHD symptoms. Each is a distinct disorder that requires separate diagnosis and separate treatment.

The possibility of comorbid SUD may further complicate diagnosis. Adults with ADHD, depression, or both often attempt to self-medicate with alcohol, tobacco, caffeine, marijuana, and/or other readily available substances with high risk for abuse or addiction.<sup>23,24</sup> The NCS-R found that

ADHD Medications	Depression Medications
<b>Methylphenidate (MPH)</b> Dexmethylphenidate HCl/Focalin™ Methylphenidate HCl/Ritalin® MPH (generic) Methylphenidate HCl/Methylin®	<b>Selective serotonin reuptake inhibitors (SSRIs)</b> Citalopram Escitalopram oxalate Fluoxetine Fluvoxamine maleate Paroxetine Sertraline
<b>MPH-Extended Duration</b> Dexmethylphenidate HCl/Focalin® XR* Methylphenidate HCl/Ritalin SR® Methylphenidate HCl/Metadate® ER Methylphenidate HCl/Ritalin® CD Methylphenidate HCl/Ritalin® LA Methylphenidate HCl/Concerta® Methylphenidate transdermal system/Daytrana™	<b>Serotonin-norepinephrine reuptake inhibitors (SNRIs)</b> Duloxetine Nefazodone Venlafaxine
<b>Amphetamine (AMP)</b> Dextroamphetamine sulfate/Dexedrine® Dextroamphetamine sulfate/Dexrostat® Mixed amphetamine salts /Adderall® Mixed amphetamine salts (generic) Lisdexamfetamine dimesylate/Vyvanse™ (prodrug)	<b>Norepinephrine reuptake inhibitor (NRI)</b> Bupropion
<b>AMP-Extended Duration</b> Dextroamphetamine sulfate/Dexedrine® Spansule Mixed amphetamine salts/Adderall XR®*	<b>Tricyclic antidepressants</b> Amitriptyline      Imipramine Clomipramine      Nortriptyline Desipramine      Protriptyline Doxepin              Trimipramine
<b>Atomoxetine</b> Atomoxetine HCl/Strattera®*	
* FDA-approved for treating adult ADHD	

**Table 4. Pharmacotherapy for ADHD and Depression**

adults with ADHD and a comorbid mood disorder have a nearly threefold greater chance of having coexisting SUD than adults with neither ADHD nor a mood disorder.<sup>2</sup> ADHD, depression, and SUD are all typified by problems with attention, concentration, and memory, as well as by mood swings.<sup>11,12</sup> Symptom overlap can obscure the presence of one or more of the disorders if all three are present, yet all must be addressed, often with different treatments, to resolve or at least control symptoms.

A diagnosis of ADHD plus co-occurring SUD should prompt a routine evaluation for other psychiatric comorbidity. A study published in 2005 underscored this point.<sup>25</sup> Subjects were adults (n=78) participating in a controlled family study of ADHD and SUD. Four groups were identified based on a diagnosis of ADHD or SUD: ADHD alone, SUD alone, ADHD plus SUD, and neither ADHD nor SUD. Diagnoses were determined by structured clinical interview using *DSM-IV* criteria. Rates of psychiatric comorbidity were lowest in the controls, intermedi-

ate in the ADHD and SUD groups, and highest in the ADHD plus SUD group. Relative to controls, the ADHD, SUD, and ADHD plus SUD groups had higher rates of depression, conduct disorder, antisocial personality disorder, agoraphobia, and social phobia. Higher rates of psychiatric comorbidity, especially mood and anxiety disorders, existed in subjects with SUD plus ADHD relative to subjects with SUD, ADHD, or controls.

#### PHARMACOTHERAPY FOR ADHD AND DEPRESSION

Few studies have assessed pharmacotherapy for adult ADHD and comorbid depression. Although no drug is FDA-approved for both disorders, several medications appear to have efficacy for both. Despite this, the conditions should usually be treated individually with separate medications.

Which disorder to address first depends on symptom severity. The acute nature of a major depressive episode, with its potential risk for suicidal ideation and suicidality, makes it the clear treatment priority. An adult being treated for ADHD

who subsequently presents with depression may also benefit from antidepressant medication.

### FDA-approved Drugs for Adult ADHD

ADHD is treated with a variety of formulations of the psychostimulants methylphenidate and amphetamine, as well as the non-stimulant atomoxetine HCl, a selective noradrenergic reuptake inhibitor. Only three drugs, however, are FDA-approved for adults: extended-release dexamethylphenidate (Focalin XR), extended-release mixed amphetamine salts (Adderall XR), and atomoxetine (Strattera) (**Table 4**).

Psychostimulants are core treatments for ADHD, with approximately 70% of patients responding to treatment.<sup>26</sup> While methylphenidate and amphetamine products are available in immediate-, sustained-, and extended-release formulations, immediate-release formulations of stimulant drugs can cause a “likeability” euphoria that places them at a greater risk of misuse or addiction.<sup>27</sup> This risk is magnified if a non-medication-related SUD already coexists. For this reason, extended-release formulations of psychostimulants with their slower rate of medication delivery appear to reduce the risk of abuse and addiction by reducing their ability to produce an immediate and pleasurable “high.” Similarly, the non-stimulant atomoxetine has a reduced risk of likeability and abuse.<sup>28</sup>

**Dexamethylphenidate extended-release (d-MPH-XR).** d-MPH-XR is a chirally pure *d*-isomer of methylphenidate, which has a greater potency than racemic methylphenidate. Dosing is usually half that of racemic methylphenidate. In the extended-release formulation, capsules provide an initial release of medication immediately after administration; a second release occurs approximately 4 hours later, thus mimicking the twice-daily dosing of d-MPH immediate-release. This design is intended to overcome acute drug tolerance.

A multicenter, randomized, fixed-dose, double-blind, placebo-controlled study, published in 2006, found d-MPH-XR to be safe and effective for adults with ADHD.<sup>29</sup> In the study, 221 randomized adults with ADHD received once-daily extended-release dexamethylphenidate 20 mg, 30 mg, or 40 mg, or placebo, for 5 weeks. The primary efficacy variable was a change from baseline to final visit in *DSM-IV* ADHD-RS total score. The results showed that all extended-release dexamethylphenidate doses were significantly superior to placebo in improving ADHD-RS total scores. Placebo scores improved by 7.9; d-MPH-XR, 20 mg, improved by 13.7 ( $P=.006$ ); d-MPH-XR, 30 mg, improved by 13.4 ( $P=.012$ ); and d-MPH-XR, 40 mg, improved by 16.9 ( $P<.001$ ). Adverse effects were mostly mild to moderate in severity; they included headache, decreased appetite, and dry mouth. The only FDA-approved dose of

d-MPH-XR is 20 mg/day. Some patients, however, may benefit from higher doses.

**Mixed amphetamine salts extended-release (MAS XR).** A number of studies have found treatment efficacy of MAS XR in adult ADHD. A recent, prospective, multisite, randomized, double-blind, placebo-controlled, parallel-group, dose-escalation study, for example, assessed the efficacy, safety, and duration of action of MAS XR in adults with ADHD, combined type (with both hyperactive/impulsive and inattention symptoms).<sup>30</sup> Adults  $\geq 18$  years of age ( $N=255$ ) were given placebo or once-daily MAS XR 20 mg, 40 mg, or 60 mg for 4 weeks. The main outcome measures were the ADHD-RS and the self-report form (short version) of the CAARS (CAARS-S-S). Subjects were then randomly assigned to treatment with MAS XR or placebo. MAS XR treatment was associated with statistically and clinically significant ADHD symptom reduction at study end point. Adults with more severe symptoms (ADHD-RS score  $>32$  at baseline) had significantly greater symptom reduction with the highest MAS XR dose (60 mg/day). This dose-response relationship was, however, determined by post-hoc analysis. Statistically significant ( $P<.05$ ) improvements in the CAARS-S-S ADHD index scores occurred at 4 and 12 hours post-dose for all MAS XR groups, indicating a 12-hour duration of effect. Symptoms improved within the first treatment week. Adverse effects were mostly mild to moderate and common to other stimulant medications as well. Vital signs and ECGs showed no clinically significant cardiovascular changes.

**Atomoxetine.** Atomoxetine was FDA-approved to treat adult ADHD in 2002. Evidence of its efficacy was confirmed in an ongoing, 3-year, open-label study of adults with *DSM-IV* ADHD who were previously enrolled in one of two double-blind, acute-treatment studies of atomoxetine.<sup>31</sup> Results of an interim analysis were derived from the study of 384 patients at 31 sites who had been studied for up to 97 weeks. The primary efficacy measure was the investigator-rated screening version of the CAARS (CAARS—Inv.SV) total ADHD symptom score. Safety, adverse events, and vital sign measurements were also assessed. The results, published in 2005, showed significant improvement with atomoxetine therapy, with mean CAARS—Inv.SV total ADHD symptom scores decreasing 33.2%, from 29.2 (baseline of open-label therapy) to 19.5 (end point of open-label therapy) ( $P<.001$ ). Similar and significant decreases were noted for the secondary efficacy measures as well. Adverse events consisted primarily of pharmacologically (noradrenergic) expected effects, such as increases in heart rate and blood pressure and a slight decrease in weight.

## Other Drugs Studied for Adult ADHD

**Osmotically controlled-release oral system methylphenidate (OROS MPH) (Concerta).** Although OROS MPH is approved for ADHD children and adolescents, it has shown off-label treatment efficacy in adults with the disorder. In a randomized, 6-week, placebo-controlled, parallel-design study, 141 ADHD adults received OROS MPH or placebo initiated at 36 mg/day and titrated to optimal response, depending on efficacy and tolerability, up to 1.3 mg/kg/day.<sup>32</sup> The investigators found that treatment with OROS MPH was associated with clinically and statistically significant reductions in *DSM-IV* symptoms of inattention and hyperactivity/impulsivity relative to subjects treated with placebo. At study end point, 66% of subjects (n=44) receiving OROS MPH and 39% of subjects (n=23) receiving placebo attained the investigators' a priori definition of response of "much improved" or "very much improved" on the Clinical Global Impression-Improvement Scale, a standard assessment instrument, plus a >30% reduction in AISRS score. OROS MPH was associated with small but statistically significant increases in systolic and diastolic blood pressure and in heart rate. While OROS MPH in daily doses of up to 1.3 mg/kg/day was effective in treating adult ADHD, subjects should be monitored for changes in blood pressure while on the drug.

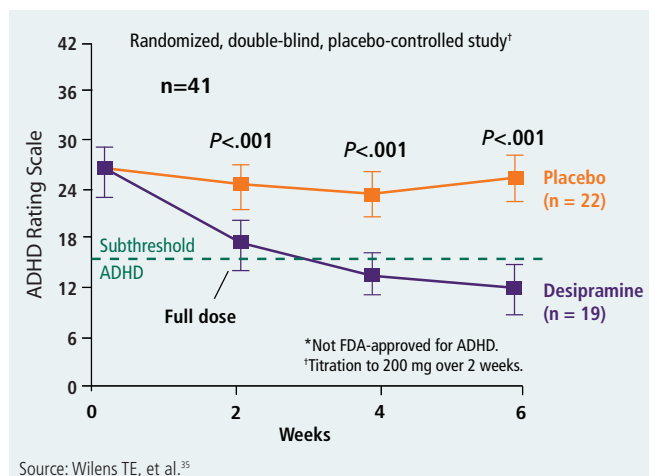
**Lisdexamfetamine dimesylate (Vyvanse).** In February 2007, the FDA approved lisdexamfetamine for treatment of ADHD.<sup>33</sup> A Schedule II compound, lisdexamfetamine is an amphetamine "prodrug" that is therapeutically inactive until converted to dextroamphetamine in the gastrointestinal tract. Although testing in adults has not been completed, studies in children show that the drug has an efficacy similar to that of other stimulants, but its conversion step in the body may translate into a smoother and more consistent rise to maximum plasma concentration.<sup>34</sup> Symptom control lasted approximately 12 hours following dosing. When lisdexamfetamine was administered orally and intravenously to adults in two clinical trials, the drug produced subjective responses on a scale of "Drug Liking Effects" that were less than dextroamphetamine at equivalent doses while at the same time significantly controlling ADHD symptoms.

## TREATING ADHD WITH ANTIDEPRESSANTS

**Desipramine.** One of the original tricyclic antidepressants, desipramine is not FDA-approved for use in ADHD, although it has been used to treat depression and comorbid ADHD in an off-label capacity. Since desipramine was found to be effective in treating ADHD in pediatric groups, a randomized, 6-week, placebo-controlled, parallel-design study was

conducted to test its efficacy in ADHD adults.<sup>35</sup> In the study, 41 adults with *DSM*-defined ADHD received a target daily dose of 200 mg of desipramine. Standard psychiatric instruments were used to diagnose and assess ADHD, depressive, and anxiety symptoms at baseline and at each biweekly visit. The investigators found highly significant differences in the reduction of ADHD symptoms between adults receiving desipramine and placebo (**Figure 4**). Within the desipramine-treated group, there were clinically and statistically significant differences between baseline and the week 6 end point for reduction of 12 of 14 symptoms of ADHD, as well as for decreases in broad categories of hyperactivity, impulsivity, and inattentiveness. Placebo-treated patients, in contrast, showed no differences between baseline and end point for any of the ADHD symptoms assessed. Judged by strict, predefined criteria for response, 68% of desipramine-treated subjects and no subjects in the placebo group were considered positive responders. Response to desipramine was independent of dose, level of impairment, gender, or lifetime psychiatric comorbidity with anxiety or depressive disorders. Based on these results, which were similar to those in ADHD children and adolescents, the investigators concluded that desipramine had efficacy for adult ADHD. Desipramine's safety and tolerability profile, however, especially regarding overdose and cardiovascular effects, limit its usefulness.

**Bupropion.** The norepinephrine-reuptake-inhibiting (NRI) antidepressant bupropion has not been FDA-approved for ADHD treatment, but its efficacy in controlling ADHD symptoms has been studied. A multisite, placebo-controlled, 8-week prospective trial to evaluate the efficacy and safety of an extended-release, once-daily formulation of bupropion (XL), for example, assessed 162 adult patients diagnosed with ADHD



**FIGURE 4.** Desipramine\* efficacy in adults with ADHD.

(combined and inattentive types).<sup>36</sup> Subjects were treated with up to 450 mg/day of bupropion XL. The primary efficacy end point was the proportion of ADHD responders (defined as at least a 30% reduction in investigator-rated ADHD-RS score) at week 8. The results showed that the bupropion XL responders (53%) exceeded placebo responders (31%) ( $P=.004$  at week 8) with a significantly greater proportion of bupropion XL responders as early as week 2 ( $P=.01$ ) (Figure 5). The investigators concluded that bupropion XL appeared to provide sustained benefit throughout the day compared with placebo. The drug was safe and well-tolerated, with no serious or unexpected adverse events and a low rate of drug-related study discontinuation (5%). However, bupropion may worsen tics and decreases the seizure threshold.

A sustained-release (SR) formulation of bupropion was also assessed to determine whether it is effective and well-tolerated in adolescents with comorbid ADHD and depression.<sup>37</sup> After a 2-week, single-blind placebo lead-in, 24 adolescents aged 11 to 16 years were treated for >8 weeks with bupropion SR at doses flexibly titrated up to 3 mg/kg bid (mean final doses: 2.2 mg/kg qam and 1.7 mg/kg qpm). Outcomes were global improvement in ADHD and depression (clinician-rated), with changes in depressive symptomatology (parent- and child-rated), ADHD symptomatology (parent- and teacher-rated), and functional impairment (parent-rated). The investigators rated 14 subjects (58%) responders in both depression and ADHD, 7 (29%) responders in depression only, and 1 (4%) a responder in ADHD only. Compared with post-placebo ratings, final parents' and children's ratings of depressive symptomatology improved significantly ( $P<.0005$  and  $P=.016$ , respectively), as did parents' but not teachers' ratings of ADHD symptomatology ( $P<.0005$

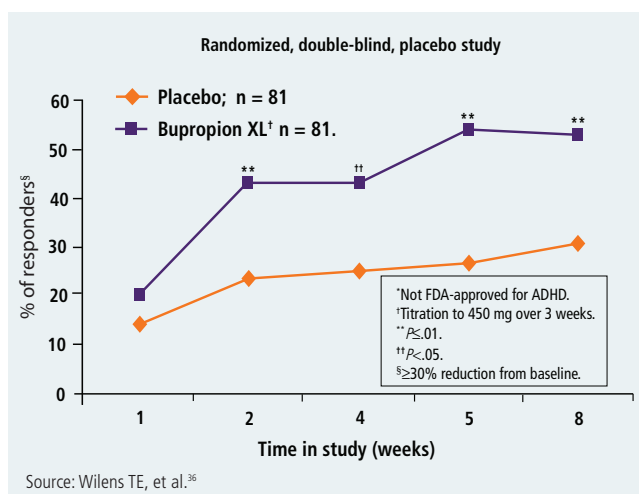


FIGURE 5. Bupropion XL\* efficacy in adults with ADHD.

and  $P=.080$ , respectively). Final ratings of functional impairment improved significantly from enrollment ( $P<.0005$ ). No subject discontinued medication because of side effects. The investigators concluded that bupropion SR may be effective and well-tolerated in adolescents with comorbid ADHD and depressive disorders. They cautioned, however, that more randomized, placebo-controlled studies are needed.

**Other antidepressants.** A 1996 literature review of 155 controlled studies of 5768 ADHD children, adolescents, and adults documented the efficacy of stimulants in an estimated 70% of subjects, not only in improving abnormal behaviors but also self-esteem, cognition, and social and family function.<sup>26</sup> In addition, the investigators noted the impressive body of literature attesting to the efficacy of tricyclic antidepressants in treating ADHD in more than 1000 subjects. Studies of other antidepressants, antipsychotics, antihypertensives, and other compounds were also reviewed with less-sanguine but preliminary results.

There is currently no evidence to support the efficacy of selective serotonin reuptake inhibitors (SSRIs) for the core symptoms of ADHD. SSRIs were found to be useful in treating comorbid depression and anxiety, however, and they seem safe to use with stimulants when there is coexisting ADHD. The SSRIs fluoxetine and paroxetine may increase the blood levels of atomoxetine, requiring a dose adjustment.

### PHARMACOTHERAPY FOR DEPRESSION

Depression medications are numerous and better known to clinicians than those for ADHD in adults. They include SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), the NRI bupropion, and the tricyclic antidepressants (Table 4). The variety of available dosages enables treatment to be tailored to the patient's needs. Side-effect profiles and treatment efficacy can vary from patient to patient and drug to drug. The clinician therefore has the latitude to select another agent if the first agent fails therapeutically or causes unacceptable adverse reactions.

### TREATING DEPRESSION WITH ADHD DRUGS

**Psychostimulants.** Stimulants are used off-label to augment therapy for depression in conjunction with standard non-SSRI antidepressants.<sup>38</sup> One study, for example, evaluated the efficacy of methylphenidate in medically ill depressed patients.<sup>39</sup> Hospital charts were reviewed for 29 patients who received trials of methylphenidate for treatment of depressive disorders while admitted to a medical/surgical unit. Of the 29 patients, 16 (55%) had moderate or marked improvement, all within 2 days of starting treatment with the maximum dose. Of the 25 non-delirious patients, 16 (64%) had moder-

ate or marked improvement; the presence of delirium was significantly associated with a decreased response. Therapeutic response was significantly correlated with maximum methylphenidate dose. Side effects were noted in eight patients (28%). Most side effects were mild (tachycardia or agitation), and all reversed after the methylphenidate was discontinued. The investigators concluded that methylphenidate provides a safe, effective alternative to tricyclic antidepressants in medically ill populations but appears to be less effective in the presence of delirium.

When an SSRI produces only a partial response in a depressed patient, adding a stimulant may be a viable therapeutic option, although data are preliminary.<sup>40</sup> Because the two drug classes impact different systems—amphetamines affect the dopamine and norepinephrine systems, while SSRIs affect the serotonin system—an additive effect may occur. When added early in treatment with SSRIs, psychostimulants may also decrease SSRI response latency.<sup>40</sup>

**Atomoxetine.** Atomoxetine is not an antidepressant, has no demonstrated efficacy in treating depression, and is not indicated for depression.<sup>41</sup> While research into its efficacy for depression is scant, a 2005 study assessed the safety and effectiveness of atomoxetine monotherapy compared with combined atomoxetine/fluoxetine therapy in a population of children and adolescents with ADHD and concurrent symptoms of depression or anxiety.<sup>42</sup> Patients were randomized to treatment with fluoxetine (n=127) or placebo (n=46) under double-blind conditions for 8 weeks, with concomitant atomoxetine use the last 5 weeks. At study end point, reductions in ADHD, depressive symptoms, and anxiety symptoms were marked for both treatment groups ( $P<.001$  for the relevant scale for each symptom cluster). Some differences between treatment groups for depressive symptoms were significant, but, in the investigators' estimation, the magnitude of the differences was small and their clinical importance was probably limited. Completion rates for the two groups were similar, as were discontinuation rates for adverse events. The combination group had greater increases in blood pressure and pulse than did the monotherapy group. The investigators concluded that in pediatric patients with ADHD and comorbid symptoms of depression or anxiety, atomoxetine monotherapy appears to be effective for treating ADHD. Anxiety and depressive symptoms also improved, but with the absence of a placebo-only arm, whether these effects were specifically the result of atomoxetine treatment could not be confirmed. Combined atomoxetine/fluoxetine therapy was well-tolerated. As noted previously, because the SSRIs fluoxetine and paroxetine may increase the blood levels of atomoxetine, the dose may require adjustment.<sup>41</sup>

## WHICH NONPHARMACOTHERAPY IS BEST?

**Depression.** Interpersonal psychotherapy is a time-limited therapeutic intervention that has been shown to provide a level of efficacy in depression comparable to that of pharmacotherapy.<sup>43</sup> A 2006 meta-analysis integrated the results of 89 controlled studies of treatments that focused on acute major depression (37 studies) and other depressive disorders (52 studies conducted with mixed diagnostic groups, including patients with major depression, minor depression, and dysthymia).<sup>44</sup> In these studies, 5328 older adults received pharmacotherapy or psychotherapy. The analysis demonstrated that available treatments for depression are efficacious, with effect sizes that are moderate to large.

A 2005 systematic review of research findings on interpersonal therapy for depressive disorders, which included four meta-analyses of 13 studies, found that interpersonal therapy was superior to placebo, similar to medication, and did not increase when combined with medication.<sup>43</sup> Overall, interpersonal therapy was found to be more efficacious than cognitive behavioral therapy (CBT) in treating acute depression.

A recent study of long-term treatment for depression, however, drew a distinction between continuation therapy, which is aimed at suppressing symptoms during a current depressive episode, and maintenance therapy, designed to prevent the development of a new episode.<sup>45</sup> Candidates for the latter include patients who have achieved remission and have had two or more lifetime episodes, especially if they have comorbid disorders, ongoing psychological stressors, poor symptom control, or severe depressive episodes. For these individuals, as an adjunct to antidepressant medication, CBT has demonstrated the greatest efficacy.

**ADHD.** For adult ADHD, CBT appears to be the nonpharmacotherapy of choice, although research is nascent. A 2005 study, for example, examined the potential efficacy, patient acceptability, and feasibility of CBT for adults with ADHD who had been stabilized on medication but still showed clinically significant symptoms.<sup>46</sup> Thirty-one adults with ADHD and stable psychopharmacology for ADHD were randomized for CBT plus continued pharmacotherapy or continued pharmacotherapy alone. Assessments included ADHD severity and associated anxiety and depression rated by an independent evaluator and by self-report. At the outcome assessment, those who were randomized to CBT/psychopharmacology had lower evaluator-rated ADHD symptoms ( $P<.01$ ) and global severity ( $P<.002$ ), as well as self-reported ADHD symptoms ( $P<.0001$ ) than those randomized to continued psychopharmacology alone. Those in the CBT/psychopharmacology group also had lower evaluator-rated depression ( $P<.01$ ), and

a trend toward having lower self-reported depression ( $P=.06$ ). CBT/psychopharmacology continued to demonstrate superiority over continued psychopharmacology alone when statistically controlling levels of depression in analyses of core ADHD symptoms. There were significantly more treatment responders among patients who received CBT/psychopharmacology (56%) compared to those who did not (13%) ( $P<.02$ ).

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On the answer sheet on the next page, please darken the circle of the one answer to each question that is true. Completed answer sheets should be placed in a stamped envelope and returned to the address shown on the form. Credit available through July 25, 2008.

1. Patterns of familial association between ADHD and mood disorders were assessed in first-degree relatives of clinically referred children and adolescents with ADHD. What percentage of the probands met the criteria for depression?
  - a. 4.4%
  - b. 18%
  - c. 21%
  - d. 33%.
2. In the 2006 National Comorbidity Survey Replication, what percentage of adults with depression had comorbid ADHD?
  - a. 4.4%
  - b. 9.4%
  - c. 13.1%
  - d. 22.6%.
3. For a *DSM-IV* diagnosis of ADHD, the patient must have:
  - a. had some impairing ADHD symptoms prior to 7 years of age
  - b. at least 5 inattention and/or at least 5 hyperactivity/impulsivity symptoms
  - c. a pervasive developmental disorder during which ADHD symptoms exclusively occur
  - d. ADHD symptoms that do not necessarily cause clinically significant impairment.
4. Problems with attention, concentration, memory, and mood swings indicate a diagnosis of:
  - a. ADHD but not depression
  - b. depression but not ADHD
  - c. substance use disorder but not ADHD or depression
  - d. it could be any or all of the above.
5. For a *DSM-IV* diagnosis of depression, the patient must present with depressed mood or loss of interest or pleasure for a period of at least:
  - a. 2 consecutive weeks
  - b. 3 consecutive weeks
  - c. 4 consecutive weeks
  - d. 8 consecutive weeks.
6. What do all FDA-approved drugs for adult ADHD have in common?
  - a. they are all stimulant medications
  - b. they are all non-stimulant medications
  - c. they are all available in several approved formulations
  - d. they all are intended to reduce the risk for abuse and addiction.
7. There is an impressive body of literature attesting to the efficacy of which class of antidepressants in treating ADHD?
  - a. selective serotonin reuptake inhibitors (SSRIs)
  - b. serotonin-norepinephrine reuptake inhibitors (SNRIs)
  - c. tricyclics
  - d. monoamine oxidase inhibitors (MAOIs).
8. In a study in which methylphenidate was used to treat 29 medically ill depressed patients, the drug:
  - a. caused the patients to become overly agitated and tachycardic
  - b. had little or no effect on depression in most of the patients
  - c. produced a therapeutic response regardless of the dose
  - d. offered a safe, effective alternative to tricyclic antidepressants provided delirium was not present.
9. For treating acute depression, the most effective nonpharmacotherapy appears to be:
  - a. interpersonal psychotherapy
  - b. cognitive behavioral therapy
  - c. object relations therapy
  - d. group psychotherapy.
10. With ADHD adults, evidence suggests that cognitive behavioral therapy is:
  - a. superior to pharmacotherapy
  - b. inferior to pharmacotherapy
  - c. most effective when paired with pharmacotherapy
  - d. a replacement for pharmacotherapy.



# Program Evaluation and Answer Sheet

Adult ADHD: When Comorbid Depression Enters In

Please darken the circle of the most correct answer for each question and return a copy of this page to: BUSM CME • E.ADHDAHAYDM07 • 715 Albany Street, A305 • Boston, MA 02118 • Fax 617-638-4905.

For questions, please call BUSM CME at 617-638-4605.

CME credit will be awarded if a score of 70% or better is achieved. A certificate of credit will be sent within 6 weeks of receipt of the test answers to those who successfully complete the exam. Credit available through July 25, 2008.

Please type or print clearly.

First name	Middle initial	Last name	Degree	Specialty
Mailing address				
City		State	ZIP + 4-digit code	
Phone		Fax	E-mail	

The amount of time I spent on this activity was \_\_\_\_\_ (max of 60 minutes).

## Exam Answer Form

Darken the circle with the correct answer to each question in the CME activity.

- |                    |                    |                     |
|--------------------|--------------------|---------------------|
| 1. (A) (B) (C) (D) | 5. (A) (B) (C) (D) | 9. (A) (B) (C) (D)  |
| 2. (A) (B) (C) (D) | 6. (A) (B) (C) (D) | 10. (A) (B) (C) (D) |
| 3. (A) (B) (C) (D) | 7. (A) (B) (C) (D) |                     |
| 4. (A) (B) (C) (D) | 8. (A) (B) (C) (D) |                     |

## Program Evaluation

- How would you rate this activity overall?  
(5=excellent, 1=poor; please circle one)    5    4    3    2    1
- Do you feel each of the learning objectives (see page 2) was met?  
Objective 1     Yes     Partially     No     N/A  
Objective 2     Yes     Partially     No     N/A  
Objective 3     Yes     Partially     No     N/A  
Objective 4     Yes     Partially     No     N/A  
Objective 5     Yes     Partially     No     N/A
- In your opinion, did you perceive any commercial bias?  
 Yes     No  
If yes, please specify: \_\_\_\_\_
- Please rate the content of this activity.  
(5 = excellent, 1 = poor; please circle one)  
4a. Timely, up to date?    5    4    3    2    1  
4b. Relevant to your practice?    5    4    3    2    1
- Do you feel that the information in this activity was based on the best evidence available?     Yes     No  
If no, please explain: \_\_\_\_\_
- Do you intend to make changes in your practice as a result of this activity?     Yes     No  
If yes, please explain: \_\_\_\_\_
- Please make suggestions for future programs.  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

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Comments? Questions? Write to [adhd@haymarketmedical.com](mailto:adhd@haymarketmedical.com)