

Impact of Comorbidity in Adults With Attention-Deficit/Hyperactivity Disorder

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Persistence of attention-deficit/hyperactivity disorder (ADHD) into adulthood and male-to-female ratios of this disorder in childhood and adulthood have been controversial issues in the ADHD diagnosis in adults. Research has resolved these controversies and in turn provided support for the validity of the diagnosis in adults. Support for the diagnosis can also be found in data that show the lifetime prevalence rate for comorbid conditions such as antisocial disorders, mood and anxiety disorders, and substance abuse disorders to be consistent across pediatric and adult populations with ADHD. These co-existing conditions add not only to the impairment associated with ADHD in adults but also to the disorder's economic burden, the extent of which is currently unknown. However, adults with the disorder, like children, probably have higher health care use and costs than people without the disorder. Little, too, is known about the social cost of ADHD, but if left untreated, the impact may be substantial. Research to determine the occupational costs associated with ADHD is ongoing, but until that and other cost-of-illness data are available, studies on the economic costs of the comorbid conditions depression, anxiety, and substance abuse and dependence may be used to make suppositions about the economic impact of ADHD in adults. More studies are needed on the outcomes of adults with this disorder, especially cost-of-illness studies. *(J Clin Psychiatry 2004;65[suppl 3]:3-7)*

Despite receiving more attention in recent years, the diagnosis of adult attention-deficit/hyperactivity disorder (ADHD) has continued to be surrounded by controversies. Fortunately, careful research has resolved most of the contended issues and has led to the diagnosis of ADHD in adults being validated as a clinical entity. Data suggest that the comorbid conditions that often coexist in childhood ADHD continue into adulthood, leading to a costly medical and economic burden to society, and although the extent of the burden of ADHD is unknown, it worsens when the disorder and comorbid disorders go untreated.

PERSISTENCE OF ADHD IN MALES AND FEMALES INTO ADULTHOOD

A dominant issue up for debate is the marked differences that have been observed in the male-to-female ratio

between pediatric and adult samples. In pediatric populations, the ratio ranges from 3:1 in community samples to 10:1 in clinic-referred samples,^{1,2} while in adult populations, the ratio is about 3:2.³ To address this discrepancy by way of examining the influence of gender on ADHD, my colleagues and I⁴ studied boys and girls, aged 6 to 17 years, with and without DSM-III-R ADHD criteria. We found that boys and girls had similar patterns of comorbidity but that boys were almost twice as likely as girls to have behavior disorders. Disruptive behavior disorders are often the reason children are referred for treatment, and therefore the high male-to-female ratios in pediatric populations may be due to underidentification because of a gender-based referral bias. Meanwhile, adults typically refer themselves for treatment when they have problems functioning at work or home and suspect these problems are ADHD related.

Another source of controversy and uncertainty in adult ADHD is that of the persistence of the disorder into adulthood. Although follow-up studies have consistently documented the continuation of ADHD into adulthood,⁵⁻⁷ the magnitude of this persistence has been inconsistent across studies, ranging from 8%⁶ to 30%.⁵ As a result of the findings of their nonlinear regression analysis of 9 studies, which included references 1 to 3, Hill and Schoener⁸ went so far as to suggest that almost all people diagnosed with ADHD in childhood will improve over time.

Such discrepancies in persistence are likely the result of variable definitions of remission. My coworkers and I

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sought to explicate persistence as it relates to definitions of remission by looking at the rates of remission in 128 male subjects with ADHD at 1-year and 4-year follow-ups.⁹ In our study, remission had 3 classifications: *syndromatic remission* required that subjects fail to meet full diagnostic DSM-III-R criteria for ADHD (having fewer than 8 of 14 possible symptoms), *symptomatic remission* required that subjects fail to meet subthreshold diagnosis (having fewer than 5 symptoms) regardless of impairment, and *functional remission* required subjects to have fewer than 5 symptoms and no impairment. By the age of 20 years, approximately 60% of the subjects that we followed were classified as having syndromatic remission, but only 10% were classified as having functional remission. On the basis of these results, we concluded that remission rates are highly sensitive to remission definitions and are inconsistent across studies because of various definitions rather than the natural history of ADHD. Further, we found that despite not meeting full diagnostic criteria for ADHD, a majority of subjects struggled with ADHD symptoms and had high levels of dysfunction.

The research conducted by my group on the male-to-female ratios in childhood⁴ and adulthood³ and the persistence of ADHD into adulthood⁹ offers explanations for these controversy-causing issues and in turn provides support for the validity of the diagnosis of adult ADHD. We also wanted to further validate this diagnosis through research into the comorbidity and dysfunction of adults with ADHD, reasoning that if ADHD persists into adulthood then its clinical features should be similar in children and adults. We have found that, like children, adults with ADHD generally have a high rate of comorbid conditions that add not only to the impairment associated with ADHD but also to the disorder's economic burden.

LIFETIME COMORBIDITY OF ADULTS WITH ADHD

In the 1990s, my colleagues and I published several articles on the comorbidity of adults with ADHD. One³ examined the clinical, cognitive, and functional characteristics of 128 adults with a clinical diagnosis of childhood-onset ADHD. The adults in the study were identified as having either full or residual ADHD. Subjects were assigned a full diagnosis of adult ADHD if they met full DSM-III-R criteria, i.e., at least 8 of 14 symptoms, for a diagnosis of ADHD by both age 7 years as well as at the time of assessment and described a chronic course of ADHD symptomatology from childhood to adulthood. Subjects were assigned a diagnosis of adult ADHD-residual type if they met full DSM-III-R criteria by age 7 years, had at least 5 symptoms at the time of assessment, and described a chronic course of ADHD symptomatology from childhood to adulthood. Of the 128

subjects with ADHD, 78 (61%) were men and 50 (39%) were women. The control group comprised age- and sex-matched adults without ADHD. Data presented herein are only for subjects with full ADHD (N = 59 for men, mean age = 37 years, and N = 42 for women, mean age = 39 years). Unsure as to whether data from this early study³ may have been misinformed by imprecise diagnostic criteria for adult ADHD, my group wanted to be certain our findings for the next generation of adults with ADHD, i.e., a new cohort of patients that we have seen over the last 7 years, were similar to those of the cohort of patients from the early 1990s. Using subjects from the Massachusetts General Hospital outpatient psychiatric clinic, we hoped to replicate our earlier findings (J.B.; S. V. Faraone, Ph.D.; T. J. Spencer, M.D.; et al., manuscript submitted). The sample included 219 adults (62% were men), with a mean age of 38 years, who had DSM-IV childhood-onset ADHD with a persistence of symptoms into adult life. When we compared data from this study with that from the earlier study,³ we found, in general, little difference in the prevalence of comorbid conditions in the groups, which confirmed the validity of our earlier study.

An important conceptual issue in the diagnosis of adult ADHD is that of syndromatic continuity, because it establishes certainty for clinicians and researchers that they are seeing the same disease entity in both children and adults. Comparing comorbidity data from the early 1990s study with adults³ with comorbidity data from a more recent study we conducted in children with ADHD⁴ illustrates the syndromatic continuity between the pediatric diagnosis and the adult syndrome of the disorder.

Academic underachievement is frequently associated with ADHD, and unsurprisingly, people diagnosed with ADHD as adults report having had problems in school similar to those of children with ADHD.^{3,4} In our adult study, 32% of men had repeated a grade, while in our children's study, 30% of boys had done so. The results for repeating a grade were 17% for women and 19% for girls. Compared with controls without ADHD, adults and children with ADHD also reported that they were frequently placed in special classes and required extra help because of their academic difficulties.

Several psychiatric conditions are significantly more common in individuals with ADHD than in control subjects (Table 1). The similar lifetime rates of these disorders in adults and children with ADHD indicate that many of these conditions begin in early childhood.

Antisocial Disorders

Overall, people with ADHD have a higher lifetime prevalence of conduct disorder, oppositional defiant disorder, and antisocial personality disorder than people without ADHD. However, disorders characterized by aggression and disruptiveness are clearly more problematic for males than females with ADHD. Conduct disorder is

Table 1. Lifetime Prevalence of Comorbid Conditions in Pediatric and Adult Populations With ADHD and Controls by Gender^a

Condition	Pediatric (%)				Adult (%)			
	Female		Male		Female		Male	
	Control (N = 122)	ADHD (N = 140)	Control (N = 140)	ADHD (N = 140)	Control (N = 110)	ADHD (N = 50)	Control (N = 97)	ADHD (N = 78)
Conduct disorder	0	8	3	21	2	7	6	34
Oppositional defiant disorder	4	35	11	66	2	27	3	32
Antisocial personality disorder	2	7	4	17
Major depression (severe)	1	15	2	29	6	36	4	27
Bipolar disorder	0	11	0	11	3	10	4	14
Multiple (> 2) anxiety disorders	5	33	4	28	15	52	10	46
Enuresis	6	25	14	32	3	29	14	28

^aData from Biederman et al.^{3,4}

Abbreviation: ADHD = attention-deficit/hyperactivity disorder.

Table 2. Lifetime Prevalence of Substance Abuse and Dependence in Adults With and Without ADHD by Gender^a

Condition	Female		Male	
	Control (N = 110)	ADHD (N = 50)	Control (N = 97)	ADHD (N = 78)
Alcohol abuse	4	17	14	19
Alcohol dependence	6	19	22	34
Drug abuse	3	7	9	22
Drug dependence	4	19	8	28

^aData from Biederman et al.³

Abbreviation: ADHD = attention-deficit/hyperactivity disorder.

overrepresented in males, such that gender appears to have some effect in the disorder. A similar gender effect is seen in antisocial personality disorder, which is an adult diagnosis, with men with ADHD being diagnosed more frequently than women with ADHD. Meanwhile, in pediatric and adult samples for females, the comorbidity rates of oppositional defiant disorder are almost identical, but the rate for boys is much more robust than it is for men.

Mood and Anxiety Disorders

The recognition that children with ADHD often have comorbid depression is a relatively new insight. Like the diagnosis of bipolar disorder in children today, depression was at one time dismissed as a pediatric diagnosis. The overrepresentation of depression in male and female pediatric and adult samples (Table 1), however, suggests that the condition emerges for the first time in childhood. Conversely, clinicians who diagnose adult patients with depression may overlook ADHD as a comorbid condition because it's considered a pediatric disorder, although Alpert et al.¹⁰ found 16% of adult patients with major depressive disorder met full or subthreshold criteria for a DSM-III-R diagnosis of childhood ADHD. The study, which included 116 adults, aged 18 to 65 years, also reported that 12% of the depressed patients had clinically meaningful persistence of ADHD symptoms into adulthood.

Bipolar disorder has been a controversial diagnosis in children, but the lifetime comorbidity rates in pediatric

and adult samples with ADHD are almost identical (Table 1). Children and adults with ADHD also have much higher rates of anxiety disorders than do controls.

Other Disorders

Although enuresis is not psychopathologically important, the condition is a developmental problem commonly seen in children with ADHD. Therefore it can function as a pattern marker to document that adults with ADHD also have lifetime histories of developmental disorders (Table 1).

Alcohol and drug abuse and dependence are more common in adults with ADHD than in adults without ADHD (Table 2).³ The higher rate in men with ADHD indicates a gender effect. The article by Timothy Wilens¹¹ in this supplement addresses some of the issues surrounding comorbid substance abuse with ADHD in adults.

THE COST OF ADHD AND ITS COMORBID CONDITIONS

Although researchers have examined the health care use and costs of children and adolescents with ADHD,¹²⁻¹⁴ data for adults in this area are lacking. The persistent nature of ADHD would suggest, however, that adults with the disorder, like children, have a higher health care use and costs than people without the disorder.

Little, too, is known about the social cost of ADHD, but if left untreated, the impact of the disorder may be substantial. For example, the prevalence of ADHD in male prisoners has been estimated to be 25%, which is 5 times that of the general population.¹⁵ Barkley has reported that research has begun to determine the occupational costs associated with ADHD,¹⁶ and he and his colleagues have found that people with ADHD frequently get fired, change jobs, and have lower job performance evaluations than people without ADHD. Until cost-of-illness data are available for adults with ADHD, research on the economic costs of disorders comorbid with ADHD may be used to make suppositions about the economic impact of ADHD in adults.

Antisocial Disorders

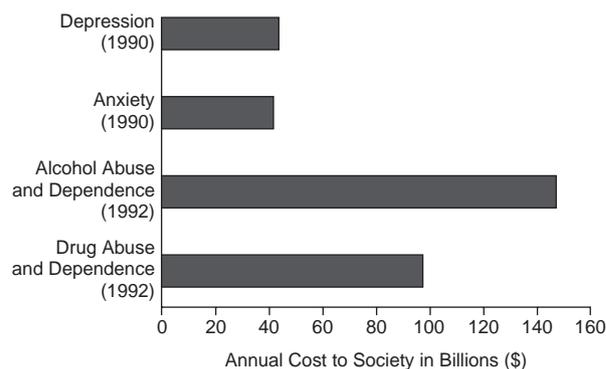
Although antisocial personality disorder is a diagnosis limited to adults, antisocial behaviors often emerge in adolescence. In a study comparing clinic-referred adolescents with ADHD (N = 76 for boys and N = 5 for girls) with controls without ADHD (N = 63 for boys and N = 14 for girls), Barkley et al.¹⁷ reported that adolescents with ADHD had already begun to participate in antisocial acts such as theft (43%), assault (27%), vandalism (21%), and disorderly conduct (12%); all acts were significantly more common in the ADHD group than in the control group.

As adults, people who participate in these behaviors may be sentenced to prison, which adds to the social costs associated with ADHD. Eyestone and Howell¹⁵ conducted an epidemiologic study of ADHD in a male prison population (N = 102) and found that 25.5% of the inmates, aged 16 to 64 years, met criteria for ADHD. Diagnostic guidelines from the DSM-III-R and the Utah Criteria developed by Wender et al.¹⁸ as well as clinical judgment were used to diagnose child and adult ADHD. Several subcategories were used to classify the ADHD diagnosis including mild or significant symptoms in childhood only, mild or significant symptoms in adulthood only, varied symptoms (i.e., mild in one stage but significant in another, or mild throughout both stages) in childhood and adulthood, or significant symptoms in childhood and adulthood. The 26 inmates that had significant ADHD symptoms as children and adults were diagnosed with the disorder. The authors also studied the epidemiology of major depression in this same sample. On the basis of their findings, they confirmed that a relationship exists between ADHD and depression and that as the symptoms of one disorder increase, the symptoms of the other disorder are likely to do the same.

Mood and Anxiety Disorders

In the early 1990s, Greenberg et al.¹⁹ published a now well-known study that estimated in dollars the economic burden of depression in the United States for 1990. The authors used cost-of-illness analysis that examined the cost to society in a given year of all people who suffer from all types of depression (major depression, bipolar disorder, and dysthymia) and that considered a person's productive contribution to society as measured by the market wage. The total annual cost of affective disorders was estimated to be about \$44 billion (Figure 1). Of the total, direct costs, such as medical services, counseling, and medication, accounted for 28% of costs. Indirect costs such as mortality accounted for 17% of costs, while reduced work productivity both on the job and due to excessive absenteeism accounted for 55% of costs. More data on reduced productivity in people with depression has recently been published by Stewart et al.²⁰ Study participants were drawn from a telephone interview conducted in the spring of 2002 that captured data on work absence, reduced performance while at work, and health-related causes. Workers with de-

Figure 1. Annual Costs of Conditions Commonly Comorbid With ADHD in the United States^a



^aData from Greenberg et al.^{19,21} and Harwood et al.²²
Abbreviation: ADHD = attention-deficit/hyperactivity disorder.

pression cost employers an estimated \$44 billion per year in lost productive time, which is \$31 billion more per year than workers without depression.

Using the same analytical framework as the depression study¹⁹ and data from the National Comorbidity Study and a large health maintenance organization, Greenberg et al.²¹ later estimated the economic burden for anxiety disorders. In 1990 in the United States, the annual cost of anxiety disorders was \$42.3 billion (Figure 1). The largest area of societal cost associated with anxiety disorders was non-psychiatric medical treatment, which accounted for 54% of the total costs. Psychiatric costs accounted for 31%, indirect workplace costs 10%, mortality costs 3%, and prescription costs 2%. The authors noted that in 1998 dollars, the annual economic burden of anxiety was estimated to be \$63.1 billion.

Alcohol and Drug Abuse and Dependence

The National Institute on Alcohol Abuse and Alcoholism and the National Institute on Drug Abuse asked the health care and human services consulting firm The Lewin Group to develop estimates for the cost of drug and alcohol abuse in the early 1990s.²² The economic cost of alcohol abuse and dependence was estimated to be \$148 billion in 1992 and drug abuse and dependence, \$98 billion (Figure 1). The estimated costs for alcohol problems were \$18.8 billion for health care services and \$67.7 billion for lost potential productivity, which was measured in terms of lost earnings and household productivity. Meanwhile, the estimated costs for drug problems were \$9.9 billion for health care services and \$14.2 billion for lost potential productivity.

CONCLUSION

A strong body of evidence, including the comorbidity data on pediatric and adult populations with ADHD pre-

sented here, supports the validity of adult ADHD as a clinical entity. Although the economic cost of ADHD itself is unknown, the medical and societal expenses associated with some symptoms and comorbid conditions, especially when left untreated, are extensive. Research on the treatment of adults with ADHD is growing, but more is needed on the outcomes of adults with ADHD, especially cost-of-illness studies.

Disclosure of off-label usage: The author of this article has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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