Journal of Attention Disorders http://jad.sagepub.com/

Long-Term Outcomes of ADHD: A Systematic Review of Self-Esteem and Social Function

Val Harpin, Luigi Mazzone, Jean-Phillipe Raynaud, Jennifer Kahle and Paul Hodgkins Journal of Attention Disorders published online 22 May 2013 DOI: 10.1177/1087054713486516

> The online version of this article can be found at: http://jad.sagepub.com/content/early/2013/05/21/1087054713486516

Published by: **\$**SAGE

http://www.sagepublications.com

Additional services and information for Journal of Attention Disorders can be found at:

Email Alerts: http://jad.sagepub.com/cgi/alerts

Subscriptions: http://jad.sagepub.com/subscriptions

Reprints: http://www.sagepub.com/journalsReprints.nav

Permissions: http://www.sagepub.com/journalsPermissions.nav

>> OnlineFirst Version of Record - May 22, 2013 What is This?

Long-Term Outcomes of ADHD: A Systematic Review of Self-Esteem and Social Function

Journal of Attention Disorders XX(X) 1–11 © 2013 SAGE Publications Reprints and permissions: sagepub.com/journalsPermissions.nav DOI: 10.1177/1087054713486516 jad.sagepub.com



V. Harpin¹, L. Mazzone², J. P. Raynaud³, J. Kahle⁴ and P. Hodgkins⁵

Abstract

Objective: To compare the long-term self-esteem and social function outcomes of individuals with untreated and treated ADHD across childhood, adolescence, and adulthood. Method: A systematic search of 12 databases was performed to identify peer-reviewed, primary research articles, published January 1980 to December 2011, reporting long-term self-esteem and/or social function outcomes (≥2 years; life consequences distinct from symptoms) of individuals with untreated or treated ADHD. Results: Overall, 127 studies reported 150 outcomes. Most outcomes were poorer in individuals with untreated ADHD versus non-ADHD controls (57% [13/23] for self-esteem; 73% [52/71] for social function). A beneficial response to treatment (pharmacological, nonpharmacological, and multimodal treatments) was reported for the majority of self-esteem (89% [8/9]) and social function (77% [17/22]) outcomes. Conclusion: Untreated ADHD was associated with poorer long-term self-esteem and social function outcomes compared with non-ADHD controls. Treatment for ADHD was associated with improvement in outcomes; however, further long-term outcome studies are needed. (J. of Att. Dis. 2013; XX(X) 1-XX)

Keywords

ADHD, long-term outcomes, self-esteem, social functioning, treatment

Background

The impact of disease and the effect of treatment can be assessed using outcome measures of health status, functional impairment, and health-related quality of life (HRQoL; Coghill, Danckaerts, Sonuga-Barke, & Sergeant, 2009). HRQoL, defined by the World Health Organization (WHO) as "the individual's perception of their position in life, in the context of culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns" (WHO, 1997), is becoming an ever more important outcome parameter in psychiatry, especially in cases when medication management can be accompanied by negative long-term outcomes that reduce the overall quality of life (Coghill, 2010). Instruments to measure HRQoL are increasingly being used to assist clinicians to identify areas of life that are particularly difficult for an individual, to tailor support provided, and in the estimation of treatment cost-effectiveness and reimbursement decisions (Coghill, 2010; Coghill et al., 2009).

ADHD, the most common childhood-onset psychological disorder, estimated to affect 5% to 7% of children worldwide (Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007; Willcutt, 2012), has been shown to have a significant

impact on multiple domains of HRQoL in children and adolescents (Coghill, 2010; Klassen, Miller, & Fine, 2004). Two HRQoL domains, self-esteem and social function, were identified among nine categories of outcome measures most commonly used to examine the long-term impact of ADHD (Hodgkins et al., 2011). Self-esteem outcomes include increased negative beliefs about the self that can lead to individuals developing maladaptive coping strategies, including avoidance and procrastination, and untreated ADHD has been associated with decreased social functioning skills, including poor peer or familial relationships, riskier sexual activity, and increased peer victimization/bullying (Asherson et al., 2012; Hosain, Berenson, Tennen, Bauer, & Wu, 2012; Mrug et al., 2012; Newark & Stieglitz,

¹Sheffield Children's NHS Foundation Trust, UK

²I.R.C.C.S. Children's Hospital Bambino Gesù, Rome, Italy

³CHU de Toulouse, France

⁴BPS International, San Diego, CA, USA

⁵Shire Development, LLC, Wayne, PA, USA

Corresponding Author:

V. Harpin, Ryegate Children's Centre, Sheffield Children's NHS Foundation Trust, Sheffield, UK. Email: val.harpin@sch.nhs.uk

2010; Sciberras, Ohan, & Anderson, 2012). Outcome measures such as self-esteem and social function are valuable as they provide an assessment of functional impairment, which is a requirement for ADHD diagnosis, in addition to the characteristic symptoms of inattention, impulsivity, and hyperactivity (American Psychiatric Association [APA], 2000; WHO, 1992). Impairments associated with ADHD include those in social, emotional, academic, and behavioral functioning (DuPaul, McGoey, Eckert, & VanBrakle, 2001; Wilson & Marcotte, 1996). ADHD-related symptoms and impairments continue through adolescence into adulthood in some individuals (Biederman, Mick, & Faraone, 2000; Faraone, Biederman, & Mick, 2006), with estimates for the prevalence of ADHD in adults ranging from 1.2% to 4.4% (Faraone et al., 2006; Kessler et al., 2006).

While the cost-effectiveness of current ADHD pharmacotherapy has been established (Wu et al., 2012), the longterm benefits of therapy have not been readily acknowledged by Health Technology Assessment Agencies (Canadian Agency for Drugs and Technologies in Health, 2011; National Institute for Health and Clinical Excellence, 2009; Nutt et al., 2007; Scottish Collegiate Guidelines Network, 2009). Recent systematic reviews described improvement in HRQoL associated with effective treatment in children, adolescents, and adults with ADHD; however, these reviews focused predominantly on clinical studies, introducing the possibility of bias and reducing the generalizability of findings (Coghill, 2010; Danckaerts et al., 2010). Nonnarrative reviews that provide a comprehensive assessment and understanding of long-term outcomes, in general and for self-esteem and social function outcomes in particular, in individuals with treated or untreated ADHD are lacking.

Objectives

The objectives of this systematic review were to assess how self-esteem and social function are impaired in ADHD; to compare the long-term outcomes of untreated and treated ADHD in childhood, adolescence, and adulthood; and to identify any factors (e.g., the effect of treatment, geographic region, age, reporter, and gender) that affect self-esteem and social function.

Method

Search Method

Long-term outcomes of children, adolescents, and adults with ADHD, who were either receiving or had received treatment of some kind (pharmacological, nonpharmacological, or multimodal treatment [MMT]), or were untreated (no documented past or present treatment), were identified through an extensive, systematic literature search of 12 databases. Long-term outcomes were defined as those ≥2

years (MTA Cooperative Group, 2004) and were distinct from the reporting of symptoms.

Eligibility Criteria and Search Strategy

Inclusion Criteria. Peer-reviewed, primary research articles published in English between January 1980 and December 2011 for which full text was available were identified from 12 databases using the electronic search engines and search strategy described in online Appendix 1. Studies were selected using criteria adapted from Hodgkins et al., 2011. Studies were eligible for inclusion if they involved individuals with a diagnosis of ADHD, or presenting with ADHD symptomatology, using any diagnostic criteria as reported by the authors of each study; if the primary disorder under investigation was ADHD, and if the study used a comparator group (e.g., non-ADHD controls) or comparison measure (e.g., pretreatment baseline assessments). Longitudinal studies were eligible for inclusion if prospective follow-up or retrospective measures were for ≥2 years. Cross-sectional studies of individuals aged ≥10 years were also eligible for inclusion. The minimum age for cross-sectional studies was set at 10 years based on the Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.; DSM-IV-TR; APA, 2000) diagnostic criterion that symptoms are present before the child is 7 years old. Assessing outcomes at ≥10 years of age allowed a minimum of 2 years to elapse, in line with the definition of "long-term" being ≥ 2 years. Only studies reporting self-esteem and/or social function outcomes were included in this systematic review.

Exclusion Criteria. Studies examining symptoms only and not self-esteem or social function outcomes, studies in which ADHD was not a primary condition of the study participants but was secondary to another condition (e.g., Down's syndrome or autism), meta-analyses and literature review studies, and studies reporting results for an instrument (e.g., instrument validation studies) were excluded from the analysis.

Search Strategy for Study Identification. The search strategy for study identification and study protocol has been previously published (Hodgkins et al., 2011) and details are provided in Appendix 1.

Data Analysis

Definition of Outcomes. This review focuses on self-esteem and social function outcomes as measured using the assessments listed in Appendix 2. Broad themes for self-esteem outcomes included measures of self-perception, self-concept, psychological well-being, self-worth, and self-image. Broad themes for social function outcomes included measures of social and familial relationships, work and school

relationships, social skills, participation in social activities, living arrangements, dating and marital history, and sexual behavior.

Results reported in each study were summarized as a single self-esteem or social function outcome and were dichotomized as being similar to or poorer than the comparator (e.g., non-ADHD control group). Data were then analyzed by outcome; a single study may have reported results for self-esteem and social function, and would therefore contribute both a self-esteem and a social function outcome to this analysis. Results were categorized as "poorer" outcomes if they were statistically significantly worse than the comparator, or if they were recorded by the authors as worse than the comparator without the need for statistical comparison (e.g., a Norwegian study found that 80% of the male study population with ADHD was unemployed, compared with a concurrent unemployment rate for males of 3.5%; Rasmussen & Levander, 2009). Results that were not statistically significantly different from the comparator were categorized as "similar" outcomes. Outcomes that were statistically significantly better than the comparator were grouped with the "similar" outcomes in this analysis due to the small number of outcomes of this type.

A comparison of treated ADHD versus untreated ADHD was conducted in which "untreated ADHD" comparators included pretreatment baseline assessments and a group of individuals with untreated ADHD. Treatment was considered beneficial if there was a statistically significant improvement compared with untreated ADHD comparators. Treatment was considered of no benefit if there was no statistically significant difference compared with untreated ADHD comparators, or if there were poorer outcomes compared with untreated ADHD comparators. Analysis of the studies that reported only results with treatment compared with non-ADHD controls was performed separately. Treatment types included pharmacological treatment, nonpharmacological treatment (e.g., cognitive behavioral therapy), or MMT (i.e., a combination of drug and nondrug treatment). No minimum therapy duration was required for classification as treatment.

The extent of treatment benefit was examined using effect sizes that were either reported in the study or were derivable based on the information provided. Cohen's d was calculated for continuous measures for which the mean and standard deviation (SD) were reported, such as scores on a social function scale. Cohen's w was calculated for discrete measures of incidence, such as the number of people who were married, often derived from the related reported chisquare statistic.

Treatment outcomes vary considerably by age; therefore, data were analyzed by age group. The categorization of each study by age group (children 6-12 years; adolescents 13-17 years; young adults 18-24 years; adults ≥25 years) was primarily based on the midrange age of study

participants at follow-up. The majority of studies reported participant age ranges; mean age was used for studies that did not report age range.

For geographic location, studies were grouped according to the UN Geoscheme (United Nations Statistics Division, 2012) and placed into the following categories: Northern America (United States and Canada excluding Mexico), Europe, Eastern Asia, Western Asia, Australasia (New Zealand and Australia), and Latin America (including Mexico), and the Caribbean.

Statistical Analyses

Effect sizes were calculated using Cohen's d (from the difference between means divided by the pooled SD of the means) and Cohen's w (from the square root of the reported χ^2 divided by the study population or from a 2×2 contingency table; Cohen, 1988). Effect sizes reported or derivable as Cohen's d index compared with pretreatment baseline were statistically compared among treatment modalities using SYSTAT 12 (Systat Software, Inc., Chicago, Illinois, USA). Two-sample, two-tailed t tests with separate variance, which does not assume homoscedasticity, were used to compare groups. A Type 1 error adjustment for multiple comparisons was used and the alpha level was set at .017.

Results

Details of studies included in this systematic review and reasons for exclusion are provided in Figure 1. A complete list of references reporting social function and/or self-esteem outcomes is provided in Appendix 3.

Of the 127 studies included in the analysis, the sample size ranged from 12 to 8,158 individuals; longitudinal study duration ranged from 2 to 25 years, with a mean (median) duration of 7.4 (5) years.

The publication rate of articles on self-esteem and/or social function in ADHD has risen relatively steadily since 1980, with a total of 127 studies reporting 150 outcomes (the total number of outcomes is greater than the total number of studies because some studies reported self-esteem and social function outcomes; Figure 2).

There was a higher proportion of publications reporting self-esteem versus social function outcomes in Eastern Asia compared with Northern America, Europe, and "Other" regions (Table 1); however, the number of studies in Eastern Asia was low. The number of studies from "Other" regions (Turkey, Israel, Australia, and New Zealand) was also low, but the proportion of studies reporting self-esteem versus social function outcomes was similar to that of Northern America and Europe.

There were two social function outcomes for individuals with untreated ADHD that were reported to be significantly

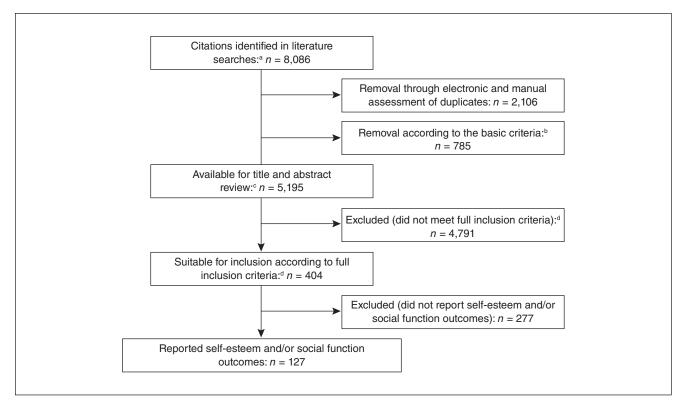


Figure 1. Flow diagram of screened and included studies.

^dFull inclusion criteria comprised studies that included participants with ADHD, reported long-term outcomes and/or sequelae, and included a comparator measure or group.

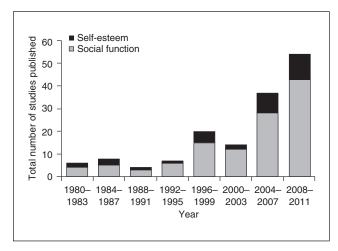


Figure 2. Total studies reporting self-esteem and social function outcomes published within 4-year spans.

better than non-ADHD controls, and were included in the "similar" outcome group. These included one study that reported better social relationships at work in individuals with untreated ADHD compared with non-ADHD controls (Ercan, Coskunol, Varan, & Toksoz, 2003), and another

study that reported significantly more social milestones gained for individuals with treated ADHD compared with non-ADHD controls (Canu & Carlson, 2007). Regression analysis demonstrated that there were no notable medication effects in this study, implying that untreated and treated individuals were functioning equally well and that the type of medication had no impact on this outcome. A third study reported that college students with treated ADHD were more likely to belong to collegiate Greek social organizations than non-ADHD controls (a result presented by the authors as a positive indicator of social function; Advokat, Lane, & Luo, 2011).

Untreated ADHD Outcomes

Figure 3 shows the self-esteem and social function outcomes for individuals with untreated ADHD compared with non-ADHD controls. Individuals with untreated ADHD had a higher percentage of self-esteem and social function outcomes that were poorer compared with non-ADHD controls (57% and 73%, respectively) than outcomes that were similar to non-ADHD controls (43% and 27%, respectively). The number of reported self-esteem outcomes was low and

^aFinal search performed on March 1, 2012.

^bBasic criteria included exclusion of reviews, supplements, case studies, animal studies, editorials, non-peer-reviewed articles, not English language. ^cFull text was reviewed for 720 studies.

Table I. Number	r of Self-Esteem and	d Social Function Out	tcomes Reported by	y World Region.
-----------------	----------------------	-----------------------	--------------------	-----------------

Outcomes, n (%) ^a	Northern America	Europe	Eastern Asia	Other ^b	Total
Self-esteem	26 (23)	4 (16)	3 (50)	I (I7)	34 (23) ^c
Social function	87 (77)	21 (84)	3 (50)	5 (83)	116 (77) ^c

^aPercentage of total number of outcomes for each region.

^cPercentage of total number of self-esteem and social function outcomes.

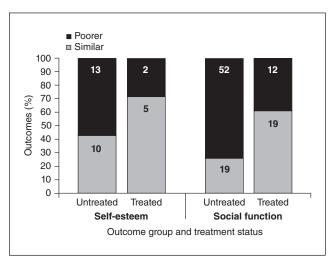


Figure 3. Self-esteem and social function outcomes for individuals with untreated and treated ADHD, compared with non-ADHD individuals.

Note: Outcomes for untreated and treated ADHD were reported in separate studies. Outcomes are shown as a percentage per outcome group (self-esteem or social function), stratified by treatment status. Numbers in bars are numbers of outcomes represented.

all were self-reported, except for one study in which parents reported a poorer outcome for untreated ADHD compared with non-ADHD controls.

Whereas self-esteem outcomes were measured using questionnaires assessing the individual's feelings about himself or herself, social function outcomes were generated from many different domains and instruments/reporters. Studies often measured more than one aspect of social functioning, and four main domains (relationships, social skills, living arrangements, and activities/hobbies) were identified within the social function outcome group. The majority of outcomes relating to activities/hobbies (8/11; 73%), relationships (41/58; 71%), and social skills (17/26; 65%) were poorer compared with non-ADHD controls, and these areas were the main drivers of the overall negative effect of untreated ADHD on social function. In contrast, fewer poorer outcomes were reported for living arrangements (2/6; 33%).

Untreated ADHD Outcomes: Effect of Age Group. A high proportion of poorer outcomes was reported for individuals with untreated ADHD compared with non-ADHD controls

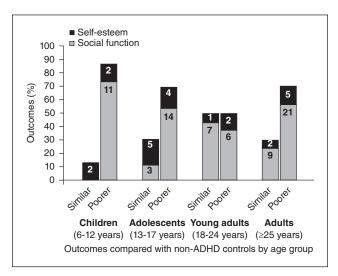


Figure 4. Self-esteem and social function outcomes for individuals with untreated ADHD compared with non-ADHD controls by age group.

Note: Outcomes are shown as a percentage of outcomes per age group. Numbers in bars are numbers of outcomes represented.

across all age ranges (Figure 4). The overall proportion of poorer outcomes was highest for children (87%) followed by adults (aged ≥25 years; 70%), adolescents (69%), and young adults (aged 18-24 years; 50%). Overall proportions were largely driven by social function outcomes, for which all (100%) reported outcomes for children were poorer compared with non-ADHD controls (Figure 4). A lower proportion of reported social function outcomes was poorer for adolescents (82%), adults (70%), and young adults (46%; Figure 4). In contrast, the proportion of poorer self-esteem outcomes was highest in adults (71%) and young adults (67%), and lowest in children (50%) and adolescents (44%).

Untreated ADHD Outcomes: Effect of Reporter. Differences in outcomes between individuals with untreated ADHD and non-ADHD controls were apparent according to the reporter (Table 2). As stated above, all self-esteem outcomes were self-reported, except for one parent-reported outcome. For social function, self-reported outcomes were most common (n = 57), of which 65% were poorer compared with

^bTurkey, Israel (two studies), Australia, and New Zealand (two studies).

Table 2. Social Function Outcomes for Individuals With Untreated ADHD and Treated ADHD, by Reporter.

	Social function o	Social function outcomes, n (%) ^a		
	Similar	Poorer outcomes		
Untreated ADHD	Outcomes	Outcomes		
Individuals with untreated	ADHD vs. non-ADH	ID controls		
Peer report	0 (0)	10 (100)		
Teacher report	L (LI)	8 (89)		
Parent report	2 (22)	7 (78)		
Self-report	20 (35)	37 (65)		
Researcher report	I (33)	2 (67)		
Treated ADHD				
Individuals with treated Al	DHD vs. non-ADHD	controls		
Peer report	0 (0)	I (100)		
Teacher report	2 (22)	7 (78)		
Parent report	8 (40)	12 (60)		
Self-report	18 (75)	6 (25)		
Researcher report	2 (67)	I (33)		

Treated ADHD vs. untreated ADHD	Treatment benefit	No treatment benefit
Peer report	I (50)	I (50)
Teacher report	3 (100)	0 (0)
Parent report	6 (86)	l (l4)
Self-report	4 (80)	I (20)
Researcher report	I (I00)	0 (0)
Employer report	I (I00)	0 (0)

^aPercentage of total number of outcomes per reporter group.

non-ADHD controls (Table 2). All outcomes reported by peers (100%), and the majority of teacher-reported (89%) and parent-reported (78%) outcomes, were poorer compared with non-ADHD controls.

Untreated ADHD Outcomes: Effect of Gender. The majority of self-esteem outcomes reported for males (4/6; 67%) and females (5/7; 71%) with untreated ADHD were poorer compared with non-ADHD controls. Poorer social function outcomes were also more commonly reported for males (13/20; 65%) and females (10/14; 71%) with untreated ADHD. Results were in keeping with the overall results for untreated ADHD versus non-ADHD controls (Figure 3), and no gender effects were observed.

Untreated ADHD Outcomes: Effect of Region. Compared with non-ADHD controls, outcomes for social function and self-esteem in individuals with untreated ADHD in Northern America (Canada and USA; United Nations Statistics Division, 2012) and Europe were similar to the overall results shown in Figure 3.

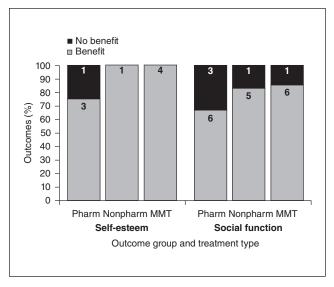


Figure 5. Benefit of treatment by treatment type for selfesteem and social function outcomes.

Note: nonpharm = nonpharmacological treatment; pharm = pharmacological treatment; MMT = multimodal treatment. Within-study comparisons of outcomes for individuals with treated ADHD versus individuals with untreated ADHD. Outcomes are shown as a percentage of outcomes per treatment type within each outcome group (self-esteem or social function). Numbers in bars are numbers of outcomes represented.

Effect of Treatment on Outcomes

The effects of treatment were reported in 52 studies (64 outcomes reported in total; 15 self-esteem outcomes and 49 social function outcomes); all self-esteem outcomes were self-reported.

A beneficial treatment response was evident in the majority of self-esteem (8/9; 89%) and social function outcomes (17/22; 77%) reported for individuals with treated ADHD versus those with untreated ADHD (Figure 5). Effect sizes indicating the degree of treatment benefit were reported in, or derivable for, 12 studies (26 effect sizes were Cohen's d, 3 were Cohen's w; 26 were improvements compared with pretreatment baseline; 3 were improvements compared with untreated individuals with ADHD; 6 were for self-esteem measures; and 23 were for social function measures). Overall, effect sizes ranged from small (d = 0.3) to large (d = 1.7). There were 25 Cohen's d effect sizes for improvement in outcomes compared with pretreatment baseline, of which 4 were for self-esteem measures (mean d = 1.3, SD = 0.2), and 21 were for social function measures (mean d = 0.9, SD = 0.4). Mean Cohen's d values for improvement above pretreatment baseline did not differ statistically by any comparison (all $p \ge .095$) when analyzed separately for different treatment modalities; however, the possibility of a Type 2 error must be acknowledged because of the small sample sizes (n = 8, mean d = 0.9, SD = 0.4, for

pharmacological; n = 4, mean d = 0.7, SD = 0.3, for non-pharmacological; and n = 13, mean d = 1.0, SD = 0.4, for MMT). There were only three Cohen's w values and three effect sizes for improvement compared with untreated individuals, so these were not evaluated further.

Response to treatment across treatment types (pharmacological, nonpharmacological, and MMT) for self-esteem and social function outcomes was similar, with benefit from treatment in self-esteem reported for all but one outcome (75%-100% across all treatment types), and in social function reported for 67% to 86% of outcomes (Figure 5). The number of outcomes reported was low when stratified by treatment type, however, with only one self-esteem outcome reported for nonpharmacological treatment.

Individuals With Treated ADHD Compared With Non-ADHD Controls. The reported outcomes of individuals with treated ADHD compared with outcomes from non-ADHD controls were examined. For the self-esteem category, 71% of outcomes were similar to the non-ADHD control group following treatment (Figure 3), compared with 43% for individuals with untreated ADHD. Likewise, for the social function category, 61% of the outcomes measured post-treatment were similar to the non-ADHD control group (Figure 3), compared with 26% for individuals with untreated ADHD.

Treated ADHD Outcomes: Effect of Age Group. The majority of studies reporting self-esteem and social function outcomes in individuals with treated ADHD versus untreated ADHD were in children, with fewer studies in adolescents and adults. All self-esteem outcomes in children and adolescents showed improvement following treatment, as did 6/8 social function outcomes in children and 5/5 social function outcomes in adolescents (Table 3). For young adults aged 18 to 24 years, there was one reported outcome of treatment benefit and one of no treatment benefit for self-esteem and social function. There were no studies in adults aged ≥25 years.

Treated ADHD Outcomes: Effect of Reporter. Differences in reported outcomes for individuals with treated ADHD versus non-ADHD controls, and versus individuals with untreated ADHD, were examined by type of reporter. At this level of analysis, study numbers were low for some comparisons and self-esteem outcomes were all self-reported. Most social function outcomes were also self-reported, the majority of which were similar to those of non-ADHD controls (75%; Table 2), and showed benefit with treatment when compared with untreated ADHD (80%; Table 2). Peer-reported, teacher-reported, and parent-reported outcomes for individuals with treated ADHD were more likely to be poorer compared with non-ADHD controls than self-reported or researcher-observed outcomes

Table 3. Treatment Benefit by Age Group: Within-Study Comparisons of Outcomes Reported for Individuals With Treated ADHD Versus Outcomes Reported for Individuals With Untreated ADHD.

	Outcome groups, n (%)		
Category	Self- esteem	Social function	
Treatment benefit			
Children (6-12 years)	5 (63)	6 (40)	
Adolescents (13-17 years)	I (I3)	5 (33)	
Young adults (18-24 years)	I (I3)	I (7)	
Adults (≥25 years)	0 (0)	0 (0)	
No treatment benefit			
Children (6-12 years)	0 (0)	2 (13)	
Adolescents (13-17 years)	0 (0)	0 (0)	
Young adults (18-24 years)	I (I3)	I (7)	
Adults (≥25 years)	0 (0)	0 (0)	

^aPercentage of total number of outcomes for each outcome group. Percentages may total greater than 100% due to rounding.

(Table 2). While the number of outcomes reported for individuals with treated ADHD versus untreated ADHD was low, improvement with treatment was reported for 50% to 100% of social function outcomes, regardless of the reporter of the outcome (Table 2).

Treated ADHD Outcomes: Effect of Gender. For self-esteem, 1 of 2 outcomes were similar compared with non-ADHD controls in males with treated ADHD, and 4 of 5 outcomes were similar for females. For social function, 9 of 11 and 7 of 8 outcomes were similar for males and females with treated ADHD, respectively. While the proportions of similar outcomes tended to be higher for gender-stratified data, results were in keeping with overall data for individuals with treated ADHD versus non-ADHD controls (Figure 3), and no gender effects were observed.

With respect to treatment benefit, the majority of self-esteem (2/3; 67%) and social function (4/6; 67%) outcomes were reported to exhibit treatment benefit for males. This was lower than the percentage of treatment benefit reported overall (8/9, 89% for self-esteem; and 17/22, 77% for social function outcomes; Figure 5). There were no reported self-esteem or social function outcomes of treated versus untreated ADHD specific to females.

Discussion

Our results show that the number of publications on selfesteem and/or social function long-term outcomes in individuals with ADHD has increased over the past three decades. This increase in publications suggests that self-esteem and social function are being recognized as important outcomes for the individual with ADHD. Studies reporting self-esteem and social function outcomes predominantly originated from Northern America followed by Europe, with relatively few studies originating from Eastern Asia or "Other" regions. A higher number of studies reported social function outcomes compared with self-esteem outcomes. Of these, interest in social function predominated in most regions, except Eastern Asia, where there was relatively more interest in self-esteem.

Self-esteem and social function outcomes were often reported to be poorer for individuals with untreated ADHD compared with non-ADHD controls, reflecting the burden of illness associated with ADHD, and the untreated disorder in particular (Brod, Pohlman, Lasser, & Hodgkins, 2012; Goksoyr & Nottestad, 2008); however, nearly a third of outcomes were reported to be similar between the two groups. Examination of the many different domains and instruments/reporters underlying the social function category revealed that poorer outcomes in individuals with untreated ADHD were primarily driven by poor relationships, poor social skills, and less engagement socially or with hobbies during leisure time; in contrast, living arrangements (living alone, with parents, or with a spouse) were not a primary issue.

While the majority (87%) of outcomes in children with untreated ADHD were poorer compared with non-ADHD controls (including all social function outcomes), the overall proportion of poorer outcomes in individuals with untreated ADHD versus non-ADHD controls was lower in older age groups (lowest for young adults aged 18-24 years), despite these being untreated populations. While this may indicate that problems with self-esteem and social function may ameliorate somewhat with maturity during the natural course of ADHD, the greater proportion of poorer versus similar outcomes suggests that they do not always improve over time, in agreement with findings that adults with ADHD continue to experience considerable impairments in daily life (Biederman et al., 2012; Brod et al., 2012; Hinshaw et al., 2012).

Treatment of ADHD was often reported to result in significant improvement in self-esteem and social function outcomes over pretreatment baseline assessments or compared with individuals with untreated ADHD. While it has been reported that there is a lack of effective treatment for poor social function in ADHD (Sibley, Evans, & Serpell, 2010), we found that many types of treatment were often reported to be associated with significantly improved long-term social function outcomes, often with large effect sizes. Response to treatment across treatment types (pharmacological, nonpharmacological, and MMT) was similar for self-esteem and social function outcomes, and similar between the different treatment types; however, more long-term studies are required. When compared with non-ADHD controls, a higher proportion of similar outcomes was

reported for treated individuals with ADHD than for those who were untreated, demonstrating that in individuals with ADHD, outcomes are more likely to be similar to the general population following treatment for the disorder. The majority of studies for which treatment benefit could be assessed were in children, and most of these studies reported an improvement in self-esteem and social function outcomes with treatment. There were fewer studies overall in adolescents and adults reporting either self-esteem or social function outcomes, but all studies of adolescents reported a treatment benefit.

When stratified by reporter, social function outcomes reported by peers, teachers, and parents were more likely to be poorer than similar compared with non-ADHD controls for the untreated and treated ADHD groups; however, results suggest that parents, teachers, and the patients themselves were able to see improvement in social function outcomes with treatment. It should be noted that teacher- and parent-reported outcomes were observer ratings and not proxy self-reports for young children; children included in these studies tended to be at an age when they could read and write, and answer questions about self-perception. The small number of outcomes in some categories, however, must be taken into consideration when drawing conclusions from these results. Furthermore, no marked effects of gender were observed. While gender differences in brain activity have been reported for self-esteem using functional magnetic resonance imaging, outcome assessment scales may not be sensitive to such differences (Miyamoto & Kikuchi, 2012).

This review of long-term studies suggests that levels of self-esteem and social function may be higher in individuals receiving treatment for ADHD compared with those with untreated ADHD. As two of the core impairments specified in the *DSM-IV-TR* and International Classification of Diseases, Tenth Revision (ICD-10; APA, 2000; WHO, 1992), improvement of self-esteem and social function is an objective of treatment in ADHD. Clinicians may want to consider measuring these parameters as they monitor treatment response, and discuss appropriate goals with patients with ADHD and their families. Further research into the effects of adherence and treatment type (including combination therapy) may be valuable in guiding clinical practice.

Limitations

There are several possible limitations and risks of bias regarding the studies included in this analysis. Only articles published in English were included, which may have resulted in a publication and cultural bias. A search engine and literature database bias may have been introduced by including only articles listed in electronic databases; this was minimized by searching 12 different databases. Some

studies may have been inadvertently excluded by relying on search engines for "peer-reviewed" status, or through strict adherence to the Cochrane systematic review guidelines and including only publications that were identified in the original electronic search. Extensive searching of 12 databases, however, reduced this bias.

Changes in diagnostic criteria over the past three decades or discrepancies between classification systems, in particular, differences between the definition of hyperkinetic disorder (ICD-9 or ICD-10; WHO, 1992) and ADHD (DSM-III/DSM-III-R/DSM-IV/DSM-IV-TR; APA, 1980, 1987, 1994, 2000) may have resulted in further bias; however, studies using all these classification systems were included in this analysis. While only studies in which ADHD was the primary disorder under investigation were included, study participants may have had comorbidities, whether identified in the study or not, which may have affected the outcomes. Whenever possible, the present analysis used reported results that were controlled or adjusted for comorbidities.

Available assessments of self-esteem and social function have innate limitations, and study heterogeneity, in terms of instruments used and measures recorded, makes the creation of summary data challenging. We acknowledge that dichotomizing all results into a binary variable of either "poorer" or "similar" outcomes and, with respect to treatment outcomes, either "benefit" or "no benefit," is a simplification of the data; however, given the vast differences in study design and measurements used, drawing on a binary measure common to all of the included studies ("significantly different" and "not significantly different") enabled us to summarize results from all the included studies in a nonstatistical manner. In accordance with the classification protocol, two publications that reported "better" outcomes were included in the "similar" group.

Despite these limitations, we highlight the need for more long-term studies examining self-esteem and social function outcomes in individuals with ADHD, and emphasize the importance of including optimal measures of self-esteem and social function in such studies.

Conclusion

There was a higher proportion of poorer outcomes in individuals with untreated ADHD compared with non-ADHD controls. Individuals receiving treatment for ADHD had better outcomes compared with pretreatment baseline assessments or individuals with untreated ADHD. Response to treatment across treatment types (pharmacological, nonpharmacological, and MMT) was similar for all treatment types for self-esteem and social function outcomes; however, the number of studies was small, highlighting the need for further long-term studies on the effects of treatment for ADHD.

Acknowledgments

Shire AG, Switzerland, provided funding to Caudex Medical, Oxford, UK, for support in writing and editing this manuscript. Under the direction of the authors, Clare Hall and Alyson Bexfield, employees of Caudex Medical, provided writing assistance for this publication. Editorial assistance in formatting, proofreading, copy-editing, and fact-checking was also provided by Caudex Medical. Anne Thompson from Shire Pharmaceuticals, UK, provided extensive assistance with reference retrieval. Amina Elsner, MD, from Shire AG, Switzerland, reviewed and edited the manuscript for scientific accuracy.

Authors' Note

V.H., L.M., J.P.R., and P.H. contributed to the development of study design, critical editing of the text and figures, and approved the final version of the manuscript; J.K. participated in the design of the study, the literature search and included study identification, data analysis, creation of the figures, editing of the text, and approved the final version of the manuscript. Although Shire was involved in the topic concept and fact checking of information, the content of this manuscript, the ultimate interpretation, and the decision to submit it for publication in the *Journal of Attention Disorders* was made by the authors independently.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: V.H. has an unrestricted research grant awarded by Shire and was sponsored to attend the American Academy of Child and Adolescent Psychiatry (AACAP) congress in Toronto in 2011; L.M. was invited by Shire Italy to attend the AACAP congress in Toronto in 2011; J.P.R. was invited by Shire France to attend the AACAP congress in Toronto in 2011 and San Francisco in 2012; J.K. is the owner of BPS International. BPS International received funding from Shire Development, LLC to perform this analysis and participate in the writing of this manuscript; P.H. is an employee of, and owns stock/stock options in, Shire Development, LLC. Shire develops and markets treatments for psychiatric disorders including ADHD.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was funded by Shire Development, LLC.

References

Advokat, C., Lane, S. M., & Luo, C. (2011). College students with and without ADHD: Comparison of self-report of medication usage, study habits, and academic achievement. *Journal of Attention Disorders*, 15, 656-666.

American Psychiatric Association. (1980). *Diagnostic and statistical manual of mental disorders* (3rd ed.). Washington, DC: Author

American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., rev.). Washington, DC: Author.

- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.
- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders*, (4th ed., text rev.). Washington, DC: Author.
- Asherson, P., Akehurst, R., Kooij, J. J., Huss, M., Beusterien, K., Sasane, R., & Hodgkins, P. (2012). Under diagnosis of adult ADHD: Cultural influences and societal burden. *Journal of Attention Disorders*, 16(Suppl. 5), 20S-38S.
- Biederman, J., Mick, E., & Faraone, S. V. (2000). Age-dependent decline of symptoms of attention deficit hyperactivity disorder: Impact of remission definition and symptom type. *American Journal of Psychiatry*, 157, 816-818.
- Biederman, J., Petty, C. R., Woodworth, K. Y., Lomedico, A., Hyder, L. L., & Faraone, S. V. (2012). Adult outcome of attention-deficit/hyperactivity disorder: A controlled 16-year follow-up study. *Journal of Clinical Psychiatry*, 73, 941-950.
- Brod, M., Pohlman, B., Lasser, R., & Hodgkins, P. (2012). Comparison of the burden of illness for adults with ADHD across seven countries: A qualitative study. *Health and Quality of Life Outcomes*, 10, 47.
- Canadian Agency for Drugs and Technologies in Health. (2011). Quality assessment of the Canadian Attention Deficit Hyperactivity Disorder Resource Alliance ADHD Practice Guidelines in Adults With ADHD. Retrieved from http://www.cadth.ca/media/pdf/htis/march-2011/Quality_Assessment_ of Canadian ADHD L2 e.pdf
- Canu, W. H., & Carlson, C. L. (2007). Rejection sensitivity and social outcomes of young adult men with ADHD. *Journal of Attention Disorders*, 10, 261-275.
- Coghill, D. (2010). The impact of medications on quality of life in attention-deficit hyperactivity disorder: A systematic review. *CNS Drugs*, *24*, 843-866.
- Coghill, D., Danckaerts, M., Sonuga-Barke, E., & Sergeant, J. (2009). Practitioner review: Quality of life in child mental health—Conceptual challenges and practical choices. *Journal* of Child Psychology and Psychiatry, 50, 544-561.
- Cohen, J. (1988). Statistical Power Analysis for the Behavioural Sciences. Hillsdale, NJ: Lawrence Erlbaum Associates.
- Danckaerts, M., Sonuga-Barke, E. J., Banaschewski, T., Buitelaar, J., Dopfner, M., Hollis, C., & Coghill, D. (2010). The quality of life of children with attention deficit/hyperactivity disorder: A systematic review. *European Child & Adolescent Psychiatry*, 19, 83-105.
- DuPaul, G. J., McGoey, K. E., Eckert, T. L., & VanBrakle, J. (2001). Preschool children with attention-deficit/hyperactivity disorder: Impairments in behavioral, social, and school functioning. *Journal of the American Academy of Child & Adolescent Psychiatry*, 40, 508-515.
- Ercan, E. S., Coskunol, H., Varan, A., & Toksoz, K. (2003). Childhood attention deficit/hyperactivity disorder and alcohol dependence: A 1-year follow-up. *Alcohol and Alcoholism*, 38, 352-356.
- Faraone, S. V., Biederman, J., & Mick, E. (2006). The age-dependent decline of attention deficit hyperactivity disorder: A meta-analysis of follow-up studies. *Psychological Medicine*, 36, 159-165.
- Goksoyr, P. K., & Nottestad, J. A. (2008). The burden of untreated ADHD among adults: The role of stimulant medication. *Addictive Behaviors*, *33*, 342-346.

- Hinshaw, S. P., Owens, E. B., Zalecki, C., Huggins, S. P., Montenegro-Nevado, A. J., Schrodek, E., & Swanson, E. N. (2012). Prospective follow-up of girls with attention-deficit/ hyperactivity disorder into early adulthood: Continuing impairment includes elevated risk for suicide attempts and self-injury. *Journal of Consulting and Clinical Psychology*, 80, 1041-1051.
- Hodgkins, P., Arnold, L. E., Shaw, M., Caci, H., Kahle, J., Woods, A. G., & Young, S. (2011). A systematic review of global publication trends regarding long-term outcomes of ADHD. Frontiers in Psychiatry, 2, 84.
- Hosain, G. M., Berenson, A. B., Tennen, H., Bauer, L. O., & Wu, Z. H. (2012). Attention deficit hyperactivity symptoms and risky sexual behavior in young adult women. *Journal of Women's Health*, 21, 463-468.
- Kessler, R. C., Adler, L., Barkley, R., Biederman, J., Conners, C. K., Demler, O., & Zaslavsky, A. M. (2006). The prevalence and correlates of adult ADHD in the United States: Results from the National Comorbidity Survey Replication. *American Journal of Psychiatry*, 163, 716-723.
- Klassen, A. F., Miller, A., & Fine, S. (2004). Health-related quality of life in children and adolescents who have a diagnosis of attention-deficit/hyperactivity disorder. *Pediatrics*, 114, e541-e547.
- Miyamoto, R., & Kikuchi, Y. (2012). Gender differences of brain activity in the conflicts based on implicit self-esteem. *PLoS ONE*, 7, e37901.
- Mrug, S., Molina, B. S., Hoza, B., Gerdes, A. C., Hinshaw, S. P., Hechtman, L., & Arnold, L. E. (2012). Peer rejection and friendships in children with attention-deficit/hyperactivity disorder: Contributions to long-term outcomes. *Journal of Abnormal Child Psychology*, 40, 1013-1026.
- MTA Cooperative Group. (2004). National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder. *Pediatrics*, 113, 754-761.
- National Institute for Health and Clinical Excellence. (2009). Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults. Retrieved from http://www.nice.org.uk/nicemedia/live/12061/42060/42060.pdf.
- Newark, P. E., & Stieglitz, R. D. (2010). Therapy-relevant factors in adult ADHD from a cognitive behavioural perspective. *Attention Deficit and Hyperactivity Disorders*, *2*, 59-72.
- Nutt, D. J., Fone, K., Asherson, P., Bramble, D., Hill, P., Matthews, K., & Young, S. (2007). Evidence-based guidelines for management of attention-deficit/hyperactivity disorder in adolescents in transition to adult services and in adults: Recommendations from the British Association for Psychopharmacology. *Journal of Psychopharmacology*, 21, 10-41.
- Polanczyk, G., de Lima, M. S., Horta, B. L., Biederman, J., & Rohde, L. A. (2007). The worldwide prevalence of ADHD: A systematic review and metaregression analysis. *American Journal of Psychiatry*, 164, 942-948.
- Rasmussen, K., & Levander, S. (2009). Untreated ADHD in adults: Are there sex differences in symptoms, comorbidity, and impairment? *Journal of Attention Disorders*, 12, 353-360.

Sciberras, E., Ohan, J., & Anderson, V. (2012). Bullying and peer victimisation in adolescent girls with attention-deficit/hyperactivity disorder. *Child Psychiatry & Human Development*, 43, 254-270.

- Scottish Intercollegiate Guidelines Network. (2009). Management of attention deficit and hyperkinetic disorders in children and young people: A national clinical guideline. Edinburgh, Scotland. Retrieved from http://www.sign.ac.uk/pdf/sign112.pdf
- Sibley, M. H., Evans, S. W., & Serpell, Z. N. (2010). Social cognition and interpersonal impairment in young adolescents with ADHD. *Journal of Psychopathology and Behavioral Assessment*, 32, 193-202.
- United Nations Statistics Division. (2012, August). Composition of macro geographical (continental) regions, geographical sub-regions, and selected economic and other groupings. Retrieved from http://unstats.un.org/unsd/methods/m49/m49regin.htm
- Willcutt, E. G. (2012). The prevalence of DSM-IV attention-deficit/hyperactivity disorder: A meta-analytic review. *Neurotherapeutics*, *9*, 490-499.
- Wilson, J. M., & Marcotte, A. C. (1996). Psychosocial adjustment and educational outcome in adolescents with a childhood diagnosis of attention deficit disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, 35, 579-587.
- World Health Organization. (1992). *International classification of diseases (ICD-10)*. Geneva, Switzerland: Author.
- World Health Organization. (1997). WHOQOL: Measuring Quality of Life. Retrieved from http://www.who.int/mental_health/media/en/68.pdf
- Wu, E. Q., Hodgkins, P., Ben-Hamadi, R., Setyawan, J., Xie, J., Sikirica, V., & Erder, M. H. (2012). Cost effectiveness of pharmacotherapies for attention-deficit hyperactivity disorder: A systematic literature review. CNS Drugs, 26, 581-600.

Author Biographies

V. Harpin trained at Cambridge University, UK, and Middlesex Hospital, UK, before specializing in pediatrics. She is currently a consultant in neurodevelopmental pediatrics in Sheffield, UK. She was Chair of the Royal College of Paediatrics and Child Health Specialty Group for Neurodisability (BACD) from 2004 to 2007 and is now a member of the BACD Strategic Research Group. She is course director for the Sheffield MSc in pediatric neurodisability. Her particular research interests are in ADHD and autism spectrum disorder.

- L. Mazzone investigated the neurobiological substrates underlying psychiatric disorders such as autism spectrum disorders, ADHD, and Tourette's syndrome during a postdoctoral visiting fellowship at the Division of Intramural Research Programs at the National Institute of Mental Health (NIMH), Bethesda, USA. In 2006, he was awarded the "Alexander Bodini" Fellowship at the Italian Academy for Advanced Studies in America at Columbia University to continue his research in this area. He is currently working as a clinical researcher at the Division of Child Psychiatry at Bambino Gesù Hospital in Vatican, Rome, Italy.
- J. P. Raynaud trained at the University of Toulouse and University of Paris. While predominantly working as a clinician, he is also head of department and professor of child and adolescent psychiatry at Toulouse University Hospital. As a member of a research unit at the National Institute for Health and Medical Research (INSERM), he coordinates work on factors of vulnerability among children and adolescents. He is also vice president of the International Association for Child and Adolescent Psychiatry and Allied Professions (IACAPAP) and president of the Scientific Council of the French Society for Child and Adolescent Psychiatry and Allied Disciplines (SFPEADA).
- J. Kahle received her doctorate in neuroscience from the University of California, Irvine, in 1993, focusing on electrophysiological and pharmacological neuroplasticity. In 1995, she founded BPS Intl., a biomedical/scientific consulting company, currently based in San Diego, to work with scientists, physicians, pharmaceutical, and biotechnology companies, and research institutes on projects involving analysis and writing of a broad range of scientific, technical, and medical content. These projects include scientific articles, continuing medical education reviews, internal reports, Food and Drug Administration submissions, product monographs, consumer education web content and video script, and invited chapters.
- P. Hodgkins is the senior director of the Global Health Economics and Outcomes Research Department at Shire Development and also holds an honorary senior lecturer position at the School of Health and Related Research, University of Sheffield, UK. His global drug development experience includes leading teams responsible for regulatory and market-access clinical trials, regulatory approval of drugs, and outcomes research, as well as pharmacoeconomic evaluations and health technology assessments. He graduated with a PhD in neuropharmacology from Aston University, Birmingham, UK, and completed an MSc in health economics and management at the University of Sheffield, UK.