

# Developmental Course of Attention Deficit Hyperactivity Disorder and its Predictors

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## Abstract

**Objective:** To outline the key features of the developmental progression of ADHD and to consider the most prominent influences on its developmental course and outcomes. **Methods:** This is a selective review focusing primarily on prospective follow-up studies. Relevant publications were selected by searching the MEDLINE and PubMed databases using keywords: ADHD, development, preschool, adolescent, adult, follow up, outcome, long-term, predictors, and treatment. Reference lists of the resulting articles were then reviewed for additional publications. **Results:** Presentation of ADHD and associated impairments evolve across development, as do outcome predictors. In early development, in addition to genetics, some forms of prenatal adversity increase the risk for ADHD. In preschool years, symptom severity, cognitive function, and family factors become significant predictors of school age outcomes. These continue to predict long-term outcomes in school aged children, and comorbidity emerges as another significant long-term outcome predictor at this stage. **Conclusions:** Presentation of ADHD and risk factors for later adversity evolve across development, which calls for developmentally-informed clinical practices.

**Key Words:** *attention deficit hyperactivity disorder, development, outcomes, predictors*

## Résumé

**Objectif:** Cette revue entend présenter les principales caractéristiques de la progression développementale du trouble de déficit de l'attention avec hyperactivité (TDAH) et examiner les influences les plus dominantes du cours développemental et des résultats du TDAH. **Méthodes:** Cette revue sélective porte principalement sur les études prospectives de suivi. Les publications pertinentes ont été choisies par une recherche dans les bases de données MEDLINE et PubMed, à l'aide des mots clés: TDAH, développement, préscolaire, adolescent, adulte, suivi, résultat, long terme, prédicteurs, et traitement. Des publications additionnelles ont ensuite été repérées dans les bibliographies des articles sélectionnés. **Résultats:** La présentation du TDAH et les déficiences qui y sont associées évoluent durant le développement, tout comme les prédicteurs de résultat. En début de développement, outre la génétique, certaines formes d'adversité prénatale accroissent le risque du TDAH. Dans les années préscolaires, la gravité des symptômes, la fonction cognitive, et les facteurs familiaux deviennent des prédicteurs significatifs des résultats à l'âge scolaire. Ces facteurs continuent de prédire les résultats à long terme des enfants d'âge scolaire; la comorbidité apparaît comme étant un autre prédicteur significatif des résultats à long terme à ce stade. **Conclusions:** La présentation du TDAH et les facteurs de risque d'adversité ultérieure évoluent au cours du développement, ce qui requiert des pratiques cliniques éclairées en matière de développement.

**Mots clés:** *trouble de déficit de l'attention avec hyperactivité, développement, résultats, prédicteurs*

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Submitted: July 9, 2012; Accepted: December 12, 2012

## Introduction

Attention deficit hyperactivity disorder (ADHD) is a common psychiatric disorder with a childhood onset, defined by age-inappropriate symptoms of inattention and/or hyperactivity and impulsivity. Its clinical presentation evolves across the lifespan, and the individual's developmental stage largely determines the disorder's impact on his/her everyday functioning. The current review highlights the key features of the presentation of ADHD across development, explores predictors of its developmental course at different stages in life, and discusses some clinical implications of a developmental view of this disorder. We focus selectively on the findings of controlled prospective follow-up studies, which provide the most robust evidence.

## Presentation of ADHD across development

### Early life

Although ADHD is most typically diagnosed during school years, there is an increasing tendency for it to be identified in preschoolers (Egger, Kondo, & Angold, 2006; Posner et al., 2007). Behavioral manifestations of ADHD, such as high activity levels, poor inhibitory control, and short attention span, are normative in healthy preschool children. However, in clinical cases, they are more pronounced and result in high rates of precarious behavior and physical injury, unmanageable conduct across many settings, including home and classroom, and poor performance in preschool. Preschoolers with ADHD often suffer from other comorbid conditions, most commonly, oppositional defiant disorder (ODD), communication disorders, and anxiety disorders, and those with comorbidities are more impaired than those with ADHD alone (Egger, et al., 2006; Posner, et al., 2007).

Most ADHD preschoolers present with the combined ADHD subtype (Lahey et al., 2004; Lahey, Pelham, Loney, Lee, & Willcutt, 2005). The predominantly hyperactive-impulsive subtype is more common in preschoolers than in older children, as hyperactivity tends to decrease with age (Galéra et al., 2011; Lahey et al., 1994; Lahey, et al., 2005). The predominantly inattentive subtype, on the other hand, is rare in this age group, and inattention symptoms become more apparent as the child grows older (Egger, et al., 2006; Galéra, et al., 2011); this may reflect either a true developmental pattern or/ and difficulty in measuring inattention in early childhood. Despite the tendency for symptoms of hyperactivity to decrease and for symptoms of inattention to become more evident with age, trajectories of hyperactivity and inattention in early childhood are significantly associated with each other, and higher measures on one predict higher measures on the other (Galéra, et al., 2011).

Preschool ADHD persists into school age in 60-80% of cases, with the combined subtype showing most persistence;

however ADHD subtypes tend to be unstable over time, with many children shifting between them (Lahey, et al., 2005).

### School age

Most ADHD diagnoses are made in school-aged children, as cases are usually identified and referred because of classroom disruptiveness and/or academic difficulties. Most current knowledge regarding ADHD derives from research on this age group. Briefly, school aged children with ADHD tend to be impaired in terms of academic achievement, family interactions and peer relationships, and have elevated rates of psychiatric comorbidity (Barkley, 2006). About 70% of children with ADHD have at least one other comorbid disorder, the most common comorbidities being ODD, anxiety disorders, and learning disorders (Barkley, 2006; Jensen et al., 2001). The prevalence of symptoms of inattention continues to increase, as prevalence of hyperactivity symptoms continues to decrease during school years (Lahey, et al., 1994; Lahey, et al., 2004).

### Adolescence and adulthood

Our current understanding of ADHD beyond childhood derives chiefly from several large prospective long-term follow up studies that followed cohorts of children with ADHD and healthy control children into adolescence and adulthood. Overall, these studies have suggested that roughly 1/3 of children with ADHD show remission by adulthood, while the rest continue to have either the full syndrome or significant symptoms that fall short of the diagnostic criteria (Cherkasova, Ponde, & Hechtman, 2012). Studies have not used uniform criteria to determine the diagnosis and rates of persistence and remission, which poses a challenge to ascertaining the exact rates. The most recent meta-analysis of prospective long-term follow up studies estimated that the rate of persistence of ADHD as a syndrome by age 25 is ~ 15%, but the rate of persistence of residual impairing symptoms by this age is ~ 65% (Faraone, Biederman, & Mick, 2006). Studies published later generally agree with these estimates. The lower rate of syndrome persistence may in part reflect sub-optimal suitability of the DSM-IV criteria to adults, as they were validated using field trials of children. Symptoms of inattention show greater persistence and slower decline with age than symptoms of hyperactivity and impulsivity (Biederman, Mick, & Faraone, 2000; Molina et al., 2009).

Functional adult outcomes are also not uniform. About 1/3 of children with ADHD have relatively unimpaired functioning in adulthood. However, as a group, adults grown up with ADHD have poorer long-term outcomes than controls in terms of academic achievement and attainment, occupational rank and job performance, risky sexual practices and early unwanted pregnancies, relationship and marital problems, traffic violations and car accidents, and psychiatric comorbidities (Barkley, Murphy, & Firscher, 2008;

**Table 1. Estimated effect sizes for adult outcomes of children with ADHD versus controls from controlled prospective follow-up studies**

Outcome	Mean effect size <sup>a</sup>	Range of effect sizes <sup>a</sup>	Studies
<b>Education</b>			
Attainment	.63	.23 - 1.1	A, B, C, D, G, J
Achievement	.58	.20 - 1.1	A, B, I, K
Grade retention	.51	.43 - .62	A, B, I, K
Suspension/expulsion	.41	.24 - .57	A, B
Assistance	1.0	.7 - 1.3	B, I
<i>All outcomes</i>	.63	.22 - 1.1	A, B, C, D, G, I, J, K
<b>Occupation</b>			
Occupational rank	.51	.03 - .92	A, B, C, D, G, J
Employment stability	.28	.03 - .59	A, B, C, D, G
Self-rated performance	.63	.46 - .70	B, G
<i>All outcomes</i>	.41	.03 - .92	A, B, C, D, J
<b>Comorbidity<sup>b</sup></b>			
Antisocial PD	.80	.33 - 1.25	A, B, C, E, G, H
ODD/CD	.76	.4 - 1.15	B, G, H, J
Substance-use disorders	.26	.16 - .34	A, B, E, G, H <sup>c</sup>
Mood disorders	.27	-.05 - .74	B, E, G, H <sup>c</sup> , J
Anxiety disorder	.22	-.004 - .97	B, D, E, G, H <sup>c</sup> , K
<i>Overall DSM psychopathology</i>	.56	.24 - 1.11	A, B, D, E
<b>Criminality</b>			
Arrests	.45	.37 - .61	B, F, K
Incarcerations	.92	.79 - .95	B, F, G
<i>All measures of criminality</i>	.77	.21 - 1.94	A, B, F, G, K
<b>Driving</b>			
Traffic violations	1.04	.56 - 1.93	B
Car accidents	1.46		B, A <sup>d</sup>
Relationship/ marital problems	.58	.43 - .85	B, G
<b>Sexual behaviour</b>			
Risky sexual practices	.45		B
Early pregnancies	1.18		B

<sup>a</sup> Effect sizes (ES) were either taken from the original articles, or, where unavailable, estimated from a) means and standard deviations using the formula  $d = (M_1 - M_2) / SD_{\text{pooled}}$ ; or b) chi-square values ( $df = 1$ ) using the formulas  $r_e = \sqrt{(\chi^2/N)}$ ;  $d = 2r/\sqrt{1-r^2}$ ; or c) odds ratios using the formula  $ES = \ln(OR)/(\pi/\sqrt{3})$  (Chinn, 2000).

A. Weiss and Hechtman (1993)

B. Barkely (2008)

C. Mannuzza et al (1993)

D. Mannuzza et al (1997)

E. Mannuzza et al (1998)

F. Mannuzza et al (2008)

G. Klein et al (2012)

H. Biederman et al (2006)

I. Biederman et al (1996)

J. Yan et al (1998)

K. Molina et al (2009)

<sup>b</sup> Results are collapsed across rates of current comorbidity and rates of past or lifetime comorbidity, as the two yield virtually identical effect sizes for differences between probands and controls.

<sup>c</sup> The ES estimates from Biederman et al (2006) study include data on lifetime comorbidities, which are not adjusted for baseline rates of comorbidity in childhood, which were unusually high in the probands. Excluding these data results in little change to overall effect size estimates.

<sup>d</sup> Weiss and Hechtman (1993) noted a significantly increased rate of car accidents in the ADHD probands compared to controls, however, the effect size was not possible to determine based on information provided.

Biederman, Faraone, Milberger, Guite, et al., 1996; Biederman et al., 2006; Klein et al., 2012; Mannuzza, Klein, Bessler, Malloy, & Hynes, 1997; Mannuzza, Klein, Bessler, Malloy, & LaPadula, 1993; Mannuzza, Klein, Bessler, Malloy, & LaPadula, 1998; Mannuzza, Klein, & Moulton III, 2008; Molina, et al., 2009; Weiss & Hechtman, 1993; Yan, 1998). The effect sizes (ES) have been in the medium range for most of these outcomes (see Table 1). In terms of psychiatric comorbidity, prospective studies have uniformly reported elevated rates of antisocial personality disorder (ADHD: 12-28%; Controls: 2-8%), as well as elevated rates of ODD and conduct disorder (CD) (ADHD: 22-62%; Controls: 4-8%) (Barkley, et al., 2008; Biederman, et al., 2006; Klein, et al., 2012; Mannuzza, et al., 1997; Mannuzza, et al., 1998; Molina, et al., 2009; Weiss & Hechtman, 1993). This shows continuity from elevated rates of disruptive behavior disorders in childhood. Furthermore, consistent with elevated rates of antisocial personality disorder, adults grown up with ADHD have higher rates of criminal behavior (Table 1). However, studies have not reliably reported significantly elevated rates of mood, anxiety, or substance use disorders in grownup ADHD probands, which somewhat contradicts the cross-sectional data showing elevated rates of these disorders in adults diagnosed with ADHD (Kessler et al., 2006; Sobanski, 2006). This may be partly explained by:

1. probands with remitted ADHD, who represent a proportion of prospective samples, having better mental health outcomes; and,
2. the majority of cross-sectional studies looking at clinical samples, which might be more pathological than samples in prospective studies (Barkley, et al., 2008).

## Predictors of developmental course and functional outcomes

In this section, we provide an overview of the most prominent predictors of symptom and functional outcomes in ADHD. Hence, the review is not exhaustive, and we do not consider interactions among predictors in yielding particular outcomes or provide an in-depth critique of the studies' methodologies.

ADHD is a highly heritable disorder, with twin studies suggesting a heritability estimate of .76 (Faraone et al., 2005). However, a number of early developmental risk factors have also emerged as significant predictors of ADHD and its symptoms. Prospective studies have repeatedly linked smoking during pregnancy with hyperactivity and inattention in the offspring, reporting small to medium effect sizes (Cornelius & Day, 2009; Galéra, et al., 2011; Linnet et al., 2003). Associations between ADHD and prenatal exposures to other agents, such as alcohol, illicit drugs, and psychotropic medications have been more tenuous (Linnet, et al., 2003; Rodriguez et al., 2009). One large controlled prospective study suggested that premature birth and low

birth weight increased risk for inattention and hyperactivity/ impulsivity, reporting medium effect sizes (Galéra, et al., 2011), a finding which also finds support in uncontrolled and retrospective data (Millichap, 2008). Finally, prospective evidence has suggested contributions of maternal stress and psychosocial adversity during pregnancy, with medium to large effect sizes (Galéra, et al., 2011; Linnet, et al., 2003; Rodriguez, et al., 2009).

In early childhood, ADHD symptom severity and executive functioning have emerged as significant predictors of ADHD symptom scores later in childhood with medium to large ESs (Berlin, Bohlin, & Rydell, 2003; Brocki, Nyberg, Thorell, & Bohlin, 2007; Latimer et al., 2003; LeBlanc et al., 2008; Wahlstedt, Thorell, & Bohlin, 2008). Early ADHD symptom severity also predicted aspects of school age socioemotional maladjustment, such as ODD symptoms, lower levels of social competence, and emotional regulation problems with large ESs (Wahlstedt, et al., 2008). In addition, early parenting practices have been reported to modestly predict emotional and behavioral adjustment and ODD symptoms at school age with medium ESs (Chronis et al., 2007; Latimer, et al., 2003), though, notably, behavioral problems in children and parenting practices appear to be bi-directionally related.

The factors predicting persistence of childhood ADHD into adolescence and adulthood have included: severity of and impairment from childhood ADHD; comorbid childhood CD, ODD, mood, and anxiety disorders; IQ; poor school and social functioning and behavioral problems; and parental psychopathology and conflict (Barkley, et al., 2008; Biederman, Faraone, Milberger, Curtis, et al., 1996; Biederman, Petty, Clarke, Lomedico, & Faraone, 2011; Molina, et al., 2009; Swanson et al., 2007). Notably, family history of ADHD emerged as a significant predictor of ADHD persistence into adolescence (large ES), but was not a predictor of persistence into adulthood in the same sample, suggesting that probands with highly familial ADHD tended to enter remission later than less familial cases (Biederman, Faraone, Milberger, Curtis, et al., 1996; Biederman, et al., 2011). The ESs for these predictors have varied substantially across studies, ranging from small to large.

In terms of functional adult outcomes, perhaps the most important determinant is persistence of ADHD. As adults, those with persisting ADHD showed more impairment in major life domains, such as occupation, education, home responsibilities, romantic relationships, social functioning, and community activities, and had higher comorbidity rates than those considered in remission (medium to large effects) (Barkley, et al., 2008; Biederman, Faraone, Milberger, Curtis, et al., 1996; Biederman, Petty, Evans, Small, & Faraone, 2010; Klein, et al., 2012). The latter were indistinguishable from controls in these areas.

Severity of childhood and adolescent ADHD is another factor that has been reported to predict adult impairment in the

above major life domains (small to medium effects) (Barkley, et al., 2008). Persistence and severity of ADHD at every developmental stage were associated with adult antisocial problems and criminality (medium to large effects), while childhood behavioral problems, such as ODD and CD were themselves associated with ADHD persistence into adulthood (medium effects) (Barkley, et al., 2008).

Comorbidity in childhood predicts comorbidity in later life. Childhood behavioural problems, such as CD and ODD, are the most prominent predictors, as they are associated both with continuing behavioural and antisocial problems (medium to large ES) and with other psychopathology, such as substance use disorders, mood disorders, and personality disorders later in life (ES unavailable) (Barkley, et al., 2008; Biederman, Faraone, Milberger, Guite, et al., 1996; Biederman et al., 2008). In addition, CD and ODD symptoms in childhood and adolescence were found to predict academic and occupational outcomes (medium to large ES) (Barkley, et al., 2008). Other childhood psychopathology (e.g. anxiety and mood disorders) was also found to predict adolescent psychopathology and account for some of the variance in adult psychopathology (ES unavailable) (Biederman, Faraone, Milberger, Guite, et al., 1996; Biederman, et al., 2006).

As expected, intellectual functioning in ADHD children has most robustly predicted educational outcomes (medium ES) (Barkley, et al., 2008; Weiss & Hechtman, 1993), though some have suggested that it also predicts non-academic outcomes, such as antisocial behavior, occupational functioning, and substance use (Weiss & Hechtman, 1993).

Finally, one group has identified family parameters, namely parental psychopathology, parenting practices, and socioeconomic status (SES) as predictors of adult antisocial behavior in ADHD probands. Parental psychopathology and parenting practices also predicted emotional adjustment, while parenting and SES predicted academic outcomes, and SES additionally predicted occupational outcomes (ES unavailable) (Weiss & Hechtman, 1993).

Findings are equivocal as to whether stimulant treatment impacts outcomes. The Multimodal Treatment Study of Children with ADHD (MTA), the largest treatment study to date, found that treatment was not a significant determinant of long-term outcome (MTA-Cooperative-Group, 1999). This, however, may have been in part due to the time-limited nature of the treatment, as the initial benefits were short-lived, dissipating after 2 years of follow up. The MTA study identified a subgroup of children who initially benefitted most from medication and also had more favorable long-term outcomes, suggesting that treatment may improve long-term outcomes only in some (Swanson, et al., 2007). On the other hand, two studies have suggested that stimulant medication might protect children with ADHD against subsequent depressive, anxiety, and behavioural disorders, as well as from academic underachievement (Biederman,

Monuteaux, Spencer, Wilens, & Faraone, 2009; Powers, Marks, Miller, Newcorn, & Halperin, 2008). However, treatment in these studies was not randomly assigned, which raises the possibility that participants initially at lower risk for negative outcomes may have preferentially sought out and/or persisted with pharmacological treatment.

## Summary

To summarize, research has identified a variety of predictors of developmental course of ADHD and associated impairments at different developmental stages. In early life, in addition to genetic factors, maternal smoking, low birth weight, premature birth, maternal stress and psychosocial adversity are risk factors for ADHD. In the preschool period, the severity of ADHD symptoms and executive functioning become significant predictors of ADHD persistence and functional impairment, while parenting practices predict emotional and behavioural adjustment and ODD. In school-aged children, ADHD symptom severity and related impairment, cognitive functioning, and family factors continue to be significant predictors of ADHD persistence and functional outcomes later in life. However, at this stage, comorbidity, particularly with ODD and CD, emerges as an additional important predictor of both ADHD persistence and impaired functioning in adolescence and adulthood. Thus, the outcome is the final result of the combined effects of characteristics of the child (e.g. severity of symptoms, IQ, comorbidity), characteristics of the family (e.g. parental psychopathology, parenting practices, SES), and possibly treatment.

## Clinical implications

The developmental view of ADHD and its predictors calls for a developmentally-informed approach to clinical practices.

Literature on early developmental risks suggests that optimal prenatal practices, family planning, and availability of support to the mother during pregnancy may help prevent some instances of ADHD or reduce symptom severity.

Childhood ADHD symptoms are an important intervention target, as they both confer impairment and predict outcome. Although ADHD symptoms can be treated effectively with stimulant medications, a remaining challenge is to ensure that these benefits persist long-term. As we have seen, the effects of time-limited pharmacological, as well as psychosocial interventions are short-lived (Molina, et al., 2009), which underscores a need for continued treatment or effective follow-up.

Many children with ADHD have additional problems, such as comorbidities and specific functional difficulties. For these lower functioning children, medication may not suffice as a treatment, and psychosocial treatments can be added to bring about additional benefits in the specific

functional domains they address, such as academic, social and emotional functioning (Hinshaw, Klein, & Abikoff, 2007; MTA-Cooperative-Group, 1999). In the MTA study, lower functioning children with comorbidity and access to fewer family resources benefitted most from the multimodal intervention (MTA-Cooperative-Group, 1999).

Given that early executive functioning predicts symptom persistence, it may be another fruitful intervention target. Though more research is necessary in this area, some initial evidence suggests that working memory training improves overall executive functioning, attentional focus, and ADHD symptoms (Beck, Hanson, Puffenberger, Benninger, & Benninger, 2010).

Having a child with ADHD places stress on parents and is associated with strained family relationships. Parenting practices have been found to predict emotional and behavioural adjustment, as well as ODD symptoms in children with ADHD. Parent training may hence be instrumental in improving outcomes. A number of (though not all) studies have found parent training programs effective for both preschoolers and school-aged children in terms of reducing symptoms, increasing parental competence, and reducing the level of family distress (Young & Myanthi Amarasinghe, 2010).

Pharmacotherapy provides a moderately effective treatment of ADHD symptoms in adults (Meszaros et al., 2009). However, adults with ADHD also struggle in many functional domains, including education, jobs, relationships, and home responsibilities. Thus, they may benefit from acquiring adaptive skills that are necessary to function effectively in these domains, such as organization, time management, problem solving and emotional control. Cognitive behavioural therapy focusing on acquisition of such skills is a promising intervention, which has demonstrated some success in initial trials (Rostain & Ramsay, 2006; Safren et al., 2010; Solanto, 2011; Weiss et al., 2012). In addition, comorbidity presents a particular challenge to treating ADHD in adults, since the rates of mood and anxiety disorders may increase with age (Biederman et al., 1993; Spencer, Biederman, & Wilens, 1999), and substance misuse is often present in adults with ADHD, which complicates pharmacotherapy. Generally, when treating comorbid conditions, the most disabling condition needs to be treated first with the most effective treatment available.

## Summary and conclusions

ADHD is often a lifelong condition, whose presentation evolves across development. Fortunately, about 1/3 of children no longer have disabling symptoms by adulthood and show relatively unimpaired functioning. Research has identified predictors of ADHD persistence and functional outcomes at different developmental stages. In addition to

genetics, there are early developmental factors that increase risk for ADHD. In preschool years, symptom severity, cognitive function, and family factors become significant predictors of school age outcomes. These continue to predict long-term outcomes in school aged children, while comorbidity emerges as another significant predictor of long-term outcomes at this stage. Clinical practices for ADHD need to be developmentally informed and may include: optimal prenatal practices; parent training for parents of preschool and school aged children; pharmacological or multimodal treatment during school years; and a combination of medication and CBT in adulthood. As a lifelong condition, ADHD may require ongoing treatment to promote optimal long-term outcome.

## Acknowledgments / Conflicts of Interest

M. Cherkasova and K. Dalena are supported by the Montreal Children's Hospital foundation via the Shire Endowment Fund. E. Sulla is supported by the National Institute on Drug Abuse. L. Hechtman has received support, served on advisory boards and has been a speaker for Ely Lilly, GlaxoSmithKline, Ortho Janssen, Purdue and Shire. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter discussed in the manuscript.

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